SCIENTIFIC OPINION

Scientific Opinion on Polybrominated Biphenyls (PBBs) in Food[1]

EFSA Panel on Contaminants in the Food Chain (CONTAM)[2, 3]

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ABSTRACT

EFSA was asked by the European Commission to deliver a scientific opinion on polybrominated biphenyls (PBBs) in food. PBBs are additive flame retardants which were applied in synthetic fibres and polymers. PBBs are present in the environment at low concentrations and likewise in biota and in food and feed. Data from the analysis of 16 PBB congeners in 794 food samples were provided to EFSA by 6 Member States, covering the period from 2003 to 2009. Toxicity studies were carried out with technical PBB mixtures of which the exact congener composition is not known. Main targets were the liver, thyroid hormone homeostasis and the reproductive, nervous and immune systems. PBBs are not directly genotoxic. The Panel on Contaminants in the Food Chain (CONTAM Panel) selected the hepatic carcinogenic effects as the critical effect, with a no-observed-effect level (NOEL) of 0.15 mg/kg body weight (b.w.). Since this NOEL was obtained in a study with a technical PBB mixture, the congener profile of which differs from that currently found in food, the CONTAM Panel concluded that it was inappropriate to use this NOEL to derive a health based guidance value. The intake of PBBs by high and frequent consumers of fatty fish, the subgroup with the highest dietary exposure, was approximately 6 orders of magnitude less than this NOEL. Exposure for high consuming breast-fed infants is 5 orders of magnitude less than this NOEL. Therefore the CONTAM Panel concluded that the risk to the European population from exposure to PBBs through the diet is of no concern. 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.

KEY WORDS

Polybrominated biphenyls, PBBs, risk assessment, food, toxicity, exposure, occurrence, brominated flame retardants

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SUMMARY

Following a request from the European Commission, the Panel on Contaminants in the Food Chain (CONTAM Panel) was asked to deliver a scientific opinion on polybrominated biphenyls (PBBs) in food.

PBBs are additive flame retardants which were specially applied in synthetic fibres 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 DecaBB which was produced up till around 2000.

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.

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.

In 1983 it was regulated in the European Union (EU) that PBBs may not be used in textile articles, such as garments, undergarments and linen, intended to come into contact with the skin, and in 2006 regulation was placed in force ensuring that electrical and electronic equipment put on the market does not contain PBBs. However, a maximum concentration value of 0.1 % of PBBs by weight in homogeneous materials shall be tolerated.

PBBs are present in the environment at low concentrations and likewise in biota and in food and feed.

Following a CONTAM Panel advice, a monitoring exercise was carried out from 2006 and results obtained from the analysis of 16 PBB congeners on 794 food samples were provided to EFSA by 6 Member States, covering the period from 2003 to 2009.

The CONTAM Panel reviewed the available data on composition of technical mixtures, occurrence in food and toxicology of the various PBB congeners. Based on the reported data on occurrence in food, the Panel put special emphasis on the PBB congeners BB-3, -15, -29, -49, -52, -77, -80, -101, -103, -126, -153, -169, -180, -194, -206 and -209.

The food category “Fish and other seafood (including amphibians, reptiles, snails and insects)” dominated the total samples, followed by “Meat and meat products (including edible offal)” and “Animal and vegetable fats and oils” and “Milk and dairy products”. The data were characterised by a high proportion of non detects for the various congeners (overall more than 80 %), with some food categories, i.e. “Animal and vegetable fats and oils”, “Milk and dairy products”, close to 100 % non detects. The lowest proportion of non detects was reported for the food category of “Fish and other seafood (including amphibians, reptiles, snails and insects)”. For 7 congeners with a proportion of non detects below 90 % (BB-49, -52, -77, -80, -101, -153 and -209) analysed in the specific food category of “Fish meat”, an increasing fat content corresponded with increasing PBB levels (except for BB-209).

Due to the high proportion of non detects for certain food categories and certain congeners, the estimation of upper and lower bound was driven by the reported limits of detection (LODs) or limits

of quantification (LOQs). Therefore, the CONTAM Panel decide to focus only on a restricted list of food categories including "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". Additionally, in order to allow for a more reliable application of the upper and lower bound approach and to prevent an unrealistic exposure estimate, the exposure estimation was performed only on those congeners in the respective food categories where the proportion of non detects was lower than 80 %.

Limited studies have been published on the toxicokinetics of PBBs, demonstrating that gastrointestinal absorption of PBBs may occur to a significant extent (90 % of the dose for BB-153 in rodents) and that highly brominated congeners may accumulate in lipid-rich tissues. There is evidence for debromination and hydroxylation of PBBs. Limited data indicate that the apparent half life of BB-153 in rats varies between 9 and 69 weeks, depending on the tissue concerned. Epidemiological data indicate that the median serum half life of PBBs in humans varies between about 10 and 30 years.

The toxicological studies on PBBs date back decades ago, reflecting the phase-out of the manufacture and use of PBBs. Oral toxicity studies were carried out with technical PBB mixtures of which the exact composition of congeners is not known. Main targets were the liver, the reproductive system, thyroid hormone homeostasis and the nervous and immune systems.

PBBs have low acute oral toxicity, with lethal dose (LD_{50}) values > 1,000 mg/kg body weight (b.w.) after single exposure. After repeated exposure (60 days), lethality was in the range of 65-150 mg/kg b.w.

PBBs (i.e. FireMaster preparations) caused liver enlargement, hepatocellular hypertrophy, fatty degeneration and enzyme induction in experimental animals. Evidence from animal studies indicate that exposure to PBBs influences the thyroid hormone homeostasis. 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. 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.

In vitro and *in vivo* genotoxicity studies indicate that PBBs are not directly genotoxic.

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, with a no-observed-effect level (NOEL) of 0.15 mg/kg b.w. 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.

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.

Epidemiological studies indicate that there are some associations between exposure to PBBs and changes in health, such as neurodevelopmental effects, site-specific cancer and effects on fertility and offspring. However, these findings were limited and inconsistent, and confounding by other compounds and/or lifestyle factors and limitations in the study design hamper interpretation of the epidemiological results.

In considering the available toxicological information, the CONTAM Panel selected the hepatic carcinogenic effects of PBBs 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 end-point is 0.15 mg/kg b.w. 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, the congener composition of which is not representative of the congener profiles currently found in food. Therefore, the CONTAM Panel concluded that it was inappropriate to use this NOEL to derive a health based guidance value for PBBs.

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 b.w. per day. Compared to the NOEL for hepatocarcinogenesis of 0.15 mg/kg b.w. per day in rats, the CONTAM Panel noted that exposure in this specific high consumer group was approximately 6 orders of magnitude less than this NOEL. Dietary exposure of all other groups of the population even at the upper bound for the high consumers, was appreciably lower than that of the frequent and high fish consumers group.

The mean exposure for infants with high human milk consumption was in the region of 0.9 to 1.4 ng/kg b.w. per day. This is 5 orders of magnitude less than the toxicological reference point.

Due to the potential toxicological concerns related to the non-*ortho* PBBs, additional exposure estimates were performed for the three congeners BB-77, -126 and -169. A calculation for high consumers (95^{th} percentile) based on median upper bound concentrations resulted in exposures of around 0.3 pg/kg b.w. per day for the sum of the three congeners. Assuming similar toxicity equivalency factors (TEF) as for non-*ortho* PCBs, the exposure to non-*ortho* PBBs was estimated to be in the region of 0.01 pg toxicity equivalents (TEQ)/kg b.w. per day. Compared to background exposure of the European population to dioxins and dioxin-like compounds the CONTAM Panel considered this highly overestimated exposure to non-*ortho* PBBs as negligible.

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.

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.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Brominated flame retardants (BFRs) are anthropogenic chemicals that are added to a wide variety of consumer/commercial products in order to improve their fire resistance. There are 5 major classes of BFRs: brominated bisphenols, diphenyl ethers, cyclododecanes, phenols and phthalic acid derivatives.

Concern has been raised because of the occurrence of several chemical compounds from the group of BFRs in the environment, including feed and food, and in human biota. This has led to bans on the production and use of certain formulations of polybrominated diphenyl ethers (PBDEs).

EFSA concluded in its advice on a request from the Commission related to relevant chemical compounds in the group of brominated flame retardants for monitoring in feed and food of 24 February 2004 that the available occurrence data on brominated flame retardants in feed and food did not allow a comprehensive assessment of contamination in all feeds and foods and identified the following compounds as the most important ones to be monitored based on the analytical feasibility to measure the chemical compounds routinely in accredited laboratories, the production volumes, the occurrence of the chemical compounds in food and feed, their persistence in the environment and their toxicity:

- polybrominated diphenyl ethers (PBDEs): BDE congeners #28, 47, 99, 100, 153, 154, 183 and 209;
- hexabromocyclododecane (HBCD): total amount (isomer specific analysis of a limited number of samples and/or pools in case of significantly elevated levels or increasing trends);
- polybrominated biphenyls (PBBs): BB congener #153.

Optionally, the following brominated flame retardants were recommended to be monitored:

- TBBP-A and other phenols;
- decabromodiphenyl ethane;
- hexabromobenzene;
- bis(2,4,6-tribromophenoxy)ethane.

Subsequently EU-wide monitoring of these compounds was organised as of October 2006. Monitoring results will be made available to EFSA.

In order to assess the need for regulatory measures as regards BFR in food, EFSA is requested to assess the risks related to the presence of BFR in food.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In accordance with Art 29 (1) of Regulation (EC) No 178/2002, the European Commission asks the European Food Safety Authority for a scientific opinion on the risks to human health related to the presence of polybrominated biphenyls (PBBs) in food.

In particular, the opinion should

- evaluate the toxicity of the PBBs for humans considering all relevant toxicological information available and identify the PBBs congeners of toxicological relevance with particular reference to the congeners occurring in food;

- carry out an exposure assessment on the basis of the occurrence data obtained in the monitoring exercise and other occurrence data that may be available;

- consider the exposure situation for specific groups of the population (e.g. infants and children, people following specific diets, etc.) and indicate the relative importance from other non-dietary sources;

- take into account, if available, biomonitoring data when assessing the exposure and compare the results with the calculated exposure;

- explore whether individual compounds can be used as markers for dietary exposure to BFRs;

- identify potential data gaps for these specific groups of BFRs.

ASSESSMENT

1. Introduction

1.1. General information

Flame retardants include a broad and diverse group of compounds used to prevent fires or at least to slow down the development of a fire. There are three main categories of chemical flame retardants: halogenated hydrocarbons, organophosphorus compounds and inorganic products often based on metallic hydroxides (Vos et al., 2003). Within the halogenated hydrocarbons, the group of the brominated flame retardants (BFRs) consist of different chemicals with a variety of physicochemical properties and uses. The main BFRs are the polybrominated (i) neutral aromatic, (ii) neutral cycloaliphatic, (iii) phenolic, including neutral derivatives, (iv) aromatic carboxylic acid esters and (v) trisalkyl phosphate compounds. The major individual groups of BFRs within these five classes are tetrabromobisphenol A (TBBP-A), polybrominated diphenyl ethers (PBDEs), hexabromocyclododecane (HBCDD), decabromodiphenyl ethane (DBDPE), bis(2,4,6-tribromophenoxy)ethane (BTBPE) and 2,4,6-tribromophenol (WHO, 1997; Örn and Bergman, 2004; Harju et al., 2009). A set of 10-20 other BFRs is making up a group of miscellaneous brominated compounds. The polybrominated biphenyls (PBBs) have, according to our information, been phased out, first low and medium brominated biphenyls, most recently the decabrominated biphenyl (DecaBB) which was withdrawn from commercial production in the early 2000s (ATSDR, 2004).

The present opinion will focus on PBBs. These were used in a range of synthetic fibers and polymers. PBBs are additive flame retardants and as such they are not chemically bound to the polymers, and they can therefore leach into the environment. Based on the reported data on occurrence in food, special emphasis is put on the PBB congeners BB-3, -15, -29, -49, -52, -77, -80, -101, -103, -126, -153, -169, -180, -194, -206 and -209.

PBBs became known by an incident that happened in 1973 in Michigan (USA). A technical PBB mixture, FireMaster BP-6, was accidentally mixed with livestock feed instead of a feed additive called Nutrimaster. The contaminated feed was distributed to farms in Michigan and numerous farm animals consumed the contaminated feed (see also chapter 4.3. PBBs in the environment). Following reports on health effects in these animals it took until 1974 before PBBs were identified as the contaminants in the feed responsible for these effects. Then it also became obvious that many people in Michigan, both farmers and the general population, had been exposed to PBBs through contaminated milk and dairy products, meat and eggs (Di Carlo et al., 1978). A series of epidemiological studies were started to study the potential health effects in the affected population, the so-called 'Michigan cohort' (see chapter 8.4. Observations in humans).

1.2. Previous risk assessments

In 1994, the International Program on Chemical Safety (IPCS) issued an environmental health criteria on PBBs (WHO, 1994). Acute toxicity was reported to be low and chronic toxic effects were reported to be observed in experimental animals at doses of around 1 mg/kg body weight (b.w.) per day following long-term exposure. A no-observed-adverse-effect level (NOAEL) of 0.15 mg/kg b.w. per day was identified from the 2-year carcinogenicity study with FireMaster FF-1 by the National Toxicology Program (NTP, 1993). The report concluded that the total daily intake from food, water, air, and soil should be less than 0.15 µg/kg b.w. per day, extrapolating from the above-mentioned NOAEL, since these compounds probably produce cancer by an epigenetic mechanism, and using an uncertainty (safety) factor of 1,000. Very little information was available on the extent of the exposure

of the general population to PBBs at the time of the report. Based on a very limited and regional data base, the estimated dietary intake of PBBs by the general population was 2 ng/kg b.w. per day (assuming a concentration of 20 µg PBB/kg lipid in fish, considering a 60 kg person eating 100 g fish per day), or 0.02 ng/kg b.w. per day (assuming a concentration of 0.05 µg/kg lipid in milk and considering a consumption of 500 mL milk per day). For infants (6 kg b.w.) consuming 800 mL human milk, the intake was estimated at 10 ng/kg b.w. per day (assuming a concentration of 2 µg PBB/kg lipid in the human milk).

In 2004, the Agency for Toxic Substances and Disease Registry (ATSDR) issued a toxicological profile for PBBs and PBDEs (ATSDR, 2004). For PBBs, data from commercial PBB mixtures were considered to develop minimal risk levels for assessing health risks from environmental exposures to these compounds. A minimal risk level of 0.01 mg/kg b.w. per day for acute-duration oral exposure was derived, based on a NOAEL of 1 mg/kg per day for thyroid effects in rats treated with an unspecified mixture of PBBs by gavage (Allen-Rowland et al., 1981). Although serious developmental effects, e.g. foetal deaths and surviving infants having decreased birth weight and decreased postnatal weight gain were observed in monkeys exposed to 0.012 mg/kg b.w. for one year (Allen et al., 1978, 1979; Lambrecht et al., 1978), intermediate- and chronic duration oral minimal risk levels were not derived since the duration of the exposure to PBBs spanned the intermediate and chronic categories at the lowest dose tested. ATSDR concluded that a number of the toxic effects observed for PBBs such as immunotoxicity and hepatic changes, appeared to be mediated by a common mechanism of action involving the aryl hydrocarbon receptor (AhR).

In 2006, the Committee on Toxicity (COT) issued a statement on organic chlorinated and brominated contaminants in shellfish, farmed fish and wild fish (COT, 2006). Seven *ortho*-PBBs and 3 non-*ortho* PBBs were analysed. Sprats showed the highest concentrations of *ortho*-PBBs (0.1 µg/kg fresh weight). The estimated dietary intake assuming a 60 kg person and a weekly portion of 140 g of sprats was 0.4 ng/kg b.w. per day. The report concluded that the estimated intake is considerably lower than the tolerable daily intake (TDI) established by the World Health Organisation (WHO, 1994) of 0.15 µg/kg b.w. per day. For non-*ortho* PBBs, the Committee noted the increasing evidence that brominated dioxins, furans and coplanar and mono-*ortho* PBBs are dioxin-like in respect to their effects. The Committee therefore agreed that it would be prudent to apply the toxicity equivalency factors (TEFs) assigned to the chlorinated congeners and to combine the toxicity equivalents (TEQs) from the brominated contaminants with the WHO-TEQs for the chlorinated dioxins to provide an indication of the total intake of chemicals with dioxin-like properties. The statement concluded that the inclusion of brominated congeners in the TEQ for intake from fish and the rest of the diet did not raise additional toxicological concerns.

1.3. Chemical characteristics

PBBs are a class of brominated hydrocarbons with a basic structure consisting of two phenyl rings to which the 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 (Figure 1). PBBs form the same number of congeners and the substitution patterns are identical to the congeners of polychlorinated biphenyls (PCBs). Hence, the PBBs share the same numbering system as proposed for PCBs (Ballschmiter et al., 1993). Like PCBs, the benzene rings 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 (i.e. positions 2, 2', 6 and 6'). When the hydrogen atoms in the *ortho* positions are substituted with the larger bromine atoms, the benzene rings adopt a non-planar configuration, while for the non-*ortho* substituted PBBs, the benzene rings may assume a nearly planar configuration, that can interact with receptors determining the toxicological properties (ATSDR, 2004).

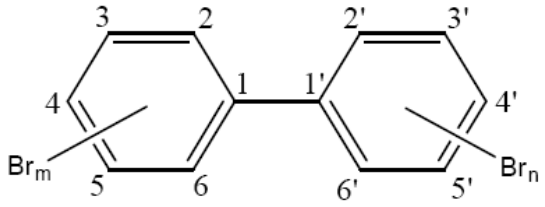

Figure 1: General structure of the PBB congeners.

The PBB congeners have molecular masses ranging from 233 g/mole for monoBBs to 943 g/mole for BB-209 (Table 1). PBBs are persistent lipophilic compounds, with low vapour pressures and low water solubilities, which decrease with increasing degree of bromination. The octanol-water partition coefficients (log K_{ow}) vary between congeners and are shown in Table 2, as well as their volatility. The chemical stability of PBBs depends on the degree of bromination and the bromine substitution pattern, but in general they are considered to be chemically stable and to show resistance to acids, bases, heat and oxidation.

Table 1: Homologues, chemical formulas, number of congeners for each homologue group and nomenclature for PBBs.

Homologues	Chemical formula (Molecular mass)	Number of isomeric congeners	Congeners
MonoBBs	$C_{12}H_9Br_1$ (MW: 233.1)	3	BB-1 to BB-3
DiBBs	$C_{12}H_8Br_2$ (MW: 312.0)	12	BB-4 to BB-15
TriBBs	$C_{12}H_7Br_3$ (MW: 390.9)	24	BB-16 to BB-39
TetraBBs	$C_{12}H_6Br_4$ (MW: 469.8)	42	BB-40 to BB-81
PentaBBs	$C_{12}H_5Br_5$ (MW: 548.7)	46	BB-82 to BB-127
HexaBBs	$C_{12}H_4Br_6$ (MW: 627.6)	42	BB-128 to BB-169
HeptaBBs	$C_{12}H_3Br_7$ (MW: 706.5)	24	BB-170 to BB-193
OctaBBs	$C_{12}H_2Br_8$ (MW: 785.4)	12	BB-194 to BB-205
NonaBBs	$C_{12}H_1Br_9$ (MW: 864.3)	3	BB-206 to BB-208
DecaBB	$C_{12}Br_{10}$ (MW: 943.2)	1	BB-209

Table 2: Physico-chemical properties of some selected PBBs congeners with a different number of bromine substituents.

PBB congeners	Log K_{ow} [(a)]	Volatility [(a)] (Torr)
BB-52 (2,2',5,5'-tetraBB)	6.5	3.73×10^{-6}
BB-101 (2,2',4,5,5'-pentaBB)	7.2	2.05×10^{-7}
BB-153 (2,2',4,4',5,5'-hexaBB)	8.0	1.04×10^{-8}
BB-180 (2,2',3,4,4',5,5'-heptaBB)	8.3	8.36×10^{-10}
BB-194 (2,2',3,3',4,4',5,5'-octaBB)	8.7	6.49×10^{-11}
BB-206 (2,2',3,3',4,4',5,5',6-nonaBB)	9.1	1.27×10^{-11}
BB-209 (2,2',3,3',4,4',5,5',6,6'-decaBB)	9.4	2.42×10^{-12}

PBB: polybrominated biphenyl; log K_{ow}: octanol-water partition coefficient.
(a): Calculated using Advanced Chemistry Development (ACD/Labs) Software v11.02 (©1994-2010 ACD/Labs).

The reactivity of PBB congeners is dependent on their structure and number of bromine substituents. Analyses of soil samples obtained from the former PBB manufacturing site in Michigan indicated significant degradation of the PBB residues in the soil. The degradation pattern observed supports a photochemical decomposition mechanism (Hill et al., 1982). The photochemical debromination of BB-209 leading to lower brominated compounds has also been reported (von der Recke and Vetter, 2007). Based on a limited number of studies, biodegradation does not appear to be significant for PBBs (Jacobs et al., 1976, 1978).

The present opinion is focussed on 16 PBB congeners. Congener, bromine substitution and CAS numbers are given in Table 3.

2. Legislation

In order to protect public health, Article 2 of Council Regulation (EEC) No 315/93[4] of 8 February 1993 laying down Community procedures for contaminants in food stipulates that, where necessary, maximum tolerances for specific contaminants shall be established. Thus a number of maximum tolerances are currently laid down in Commission Regulation (EC) No. 1881/2006[5] of 19 December 2006 setting maximum levels (MLs) for certain contaminants in foodstuffs. While MLs for organic contaminants such as dioxins, dioxin-like PCBs and benzo[*a*]pyrene were set for a number of food commodities, PBBs are not regulated so far under this Regulation.

Commission Directive 2002/32 regulates undesirable substances in animal feed. While maximum contents are set for a number of inorganic and organic contaminants in various feed materials, neither PBB nor other brominated flame retardants are regulated so far by the EU Commission under this Directive.

[4] OJ L 37, 13.2.1993, p. 1-3.
[5] OJ L 364, 20.12.2006, p. 5-24.

Table 3: Congener, bromine substitution, and CAS numbers of the 16 PBB congeners considered in this opinion.

Congener	Bromine substitution	CAS number
BB-3	4-monoBB	92-66-0
BB-15	4,4'-diBB	92-86-4
BB-29	2,4,5-triBB	115245-07-3
BB-49	2,2',4,5'-tetraBB	60044-24-8
BB-52	2,2',5,5'-tetraBB	59080-37-4
BB-77	3,3',4,4'-tetraBB	77102-82-0
BB-80	3,3',5,5'-tetraBB	16400-50-3
BB-101	2,2',4,5,5'-pentaBB	67888-96-4
BB-103	2,2',4,5',6-pentaBB	59080-39-6
BB-126	3,3',4,4',5-pentaBB	84303-46-8
BB-153	2,2',4,4',5,5'-hexaBB	59080-40-9
BB-169	3,3',4,4',5,5'-hexaBB	60044-26-0
BB-180	2,2',3,4,4',5,5'-heptaBB	67733-52-2
BB-194	2,2',3,3',4,4',5,5'-octaBB	67889-00-3
BB-206	2,2',3,3',4,4',5,5',6-nonaBB	69278-62-2
BB-209	2,2',3,3',4,4',5,5',6,6'-decaBB	1163-19-5

In 1983, Council Directive 83/264/EC[6] amending Council Directive 76/769/EEC[7] stipulated that PBBs may not be used in textile articles, such as garments, undergarments and linen, intended to come into contact with the skin. With effect from 1 June 2009, Regulation 1907/2006[8] repeals and replaces Directive 76/769/EEC. The conditions of PBB restrictions are now set in ANNEX XVII to this Regulation.

Directive 2002/95/EC[9] of the European Parliament and of the Council of 27 January 2003 on the restriction of the use of certain hazardous substances (RoHS) in electrical and electronic equipment stipulates that Member States shall ensure that, from 1 July 2006, new electrical and electronic equipment put on the market does not contain PBBs. According to Article 5(1)(a) of Directive 2002/95/EC a maximum concentration value of 0.1 % of PBBs by weight in homogeneous materials shall be tolerated.

Directive 2002/96/EC[10] of the European Parliament and of the Council of 27 January 2003 on waste electrical and electronic equipment (WEEE) stipulates that plastic containing BFRs has to be removed from any separately collected WEEE and treated separately.

[6] OJ L 147, 6.6.1983, p. 9-10.
[7] OJ L 262, 27.9.1976, p. 201-203.
[8] OJ L 396, 30.12.2006, p. 1-849.
[9] OJ L 37, 13.02.2003 p. 19-23.
[10] OJ L 37, 13.02.2003 p. 24-39.

Hexabromobiphenyl (CAS registry number: 36355-01-8) is, since 1998, included in Annex 1 of the Convention on Long-Range Transboundary Air Pollution on persistent organic pollutants (CLRTAP POP) protocol and at its fourth meeting in May 2009, the Conference of the Parties of the Stockholm Convention adopted amendments to the Annexes A implying the inclusion of hexabromobiphenyl (CAS registry number: 3655-01-08). The listing in these Annexes means that parties must take measures to eliminate the production and use of the chemicals.

3. Sampling and methods of analysis

3.1. Sampling

There are no specific guidelines for sampling of food to be analysed for their PBB content. Therefore, basic rules for sampling for organic contaminants or pesticides should be followed. Respective requirements are for example laid down in Commission Regulation (EC) No 1883/2006[11] of 19 December 2006 laying down methods of sampling and analysis for the official control of levels of dioxins and dioxin-like PCBs in certain foodstuffs. This Regulation contains inter alia a number of provisions concerning methods of sampling depending on the size of the lot, packaging, transport, storage, sealing and labelling. The primary objective is to obtain a representative and homogeneous laboratory sample with no secondary contamination.

3.2. Methods of analysis

Theoretically, 209 PBB congeners exist, but the number of analysed congeners is generally much lower. One reason for this is that commercial availability of pure standards of individual congeners is limited (less than 40 congeners). 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).

Extraction from biota takes place often with a mixture of a non-polar and/or a slightly polar solvent such as cyclohexane/acetone (v/v, 3:1), dichloromethane/n-hexane (25:75, v/v) or 100 % dichloromethane using cold-column or Soxhlet extraction (Vetter et al., 2008a; Gieron et al., 2010; Luross et al., 2002). Prior to extraction, the sample material may be dried by freeze drying (Gieron et al., 2010) or by mixing with sodium sulfate (Luross et al., 2002). PBBs in human samples can be extracted using *n*-hexane/ether and petroleum ether/diethyl ether or solid-phase-extraction (Burse et al., 1980; Domino et al., 1980; Fawkes et al., 1982, Sjödin et al., 2004a; Päpke et al., 2010). Separation from co-extracted lipids is done through gel permeation chromatography (GPC), aluminum oxide chromatography, acid silica, multilayer column chromatography and others (Krüger et al., 1988; Gieron et al., 2010). Further clean-up and fractionation can be achieved with e.g. silica column chromatography.

Gas chromatography (GC) is the method of choice for instrumental separation of PBBs. The injector types that can be used are similar to those for PCBs and PBDEs and include split/splitless, on-column injector and programmable temperature vaporizer (PTV) (de Boer, 1999; Fernandes et al., 2008; Gieron et al., 2010; Luross et al., 2002; von der Recke and Vetter, 2008). 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. Capillary columns provide good resolution and are nowadays applied. Comprehensive multidimensional GC (GC×GC) provided even better separation (Korytár et al., 2005) but single column separation generally provides sufficient resolution (de Boer, 1999). The majority of the columns used have slightly polar phases (5 % phenyl-

[11] OJ L 364, 20.12.2006, p. 32-43.

(arylene)-95 % methyl polysiloxane). On this phase, some congeners may co-elute such as BB-136 and -148 and BB-132 and -146 (Vetter et al., 2008b). Analysis of the higher brominated PBBs require high oven temperatures up to 300°C and these PBBs may become unstable at these high temperatures (de Boer, 1999). DecaBB is highly non-volatile and a very short capillary column and higher carrier gas velocity increases the analysis speed and reduces possible degradation at high temperatures in the GC oven. Enantiomeric pairs of PBB congeners can occur in the environment, and these pairs may be separated using enantioselective GC columns (Götsch et al., 2005).

Identification and detection is generally achieved by mass spectrometry (MS) (de Boer, 1999), although electron capture detection (ECD) has been used in the past (Sweetman and Boettner, 1982). Electron capture negative ionization (ECNI) provides excellent sensitivity, but selectivity is limited when the bromine ions [Br-] are used for detection, especially because other brominated compounds (such as PBDEs) may be present in the extract that co-elute. An example of such co-elution is BDE-154 and BB-153. Because BB-153 is a congener often found in the environment, it is important to separate it from BDE-154, either chromatographically or by MS. Electron impact (EI) is an alternative ionization mode, making use of the [M+], [M-Br+] or [M-Br2+] ions (Luross et al., 2002). Although EI provides less response for the higher brominated congeners, when combined with high resolution MS (HRMS), excellent sensitivity and selectivity is achieved. Good selectivity can also be achieved by using GC-ECNI-tandem mass spectrometry (MS/MS) (either triple quadrupole or ion trap instruments), with the molecular mass as the precursor ion and the bromide ion as the product ion (von der Recke et al., 2005; Vetter et al., 2008b; Gieron et al., 2010).

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. Mass labelled internal standards are commercially available and can be used when using GC-HRMS and GC-ECNI-MS/MS which is beneficial for accuracy and precision of the results. Burse et al. (1980) reported results from an interlaboratory study on PBBs in serum with 2 laboratories using exactly the same method. The difference between the laboratories in spiked serum samples was ≤3.5 %, which is precise given the fact that they were using packed GC columns and the technical mixture FireMaster for calibration. There are no known studies that show the current status of interlaboratory comparability.

4. Sources, use and environmental fate

Information on the production of PBBs is scarce. It is estimated that at least 11,000 tonnes of PBBs were produced worldwide, but production figures from some countries known to have produced PBBs are not available (IPCS, 1994). The commercial production of PBBs generally involved bromination of biphenyl, a process that produces a smaller number of product mixtures than the corresponding chlorination (Sundström et al., 1976).

4.1. Formation and production

PBBs were manufactured in the United States from approximately 1970 until 1976. As a result of the accident that occurred in Michigan in 1973, all PBB production in the USA was voluntarily discontinued (Di Carlo et al., 1978). In the United Kingdom (UK), PBBs were produced until 1977, in Germany until the mid-1980s and in France until 2000 (Hardy, 2002). The late production in France was for decabromobiphenyl only, manufactured by one company (Atochem) (Hardy, 2000).

It has not been possible to find information on production volumes in Europe. In the USA the total production of PBBs during 1970-1976 has been estimated to be 6,000 tons whereof more than 98 % were FireMaster FF-1 and FireMaster BP-6.

PBBs could still have been in production in Asia by 1999 (Lassen et al., 1999). No information could be identified on possible current production in Asia or elsewhere.

PBBs were commercially produced as three technical product groups containing brominated biphenyls with hexaBB, octaBBs and decaBB as main constituents. The first PBB compound group to be commercially produced was hexaBB, known as FireMaster, which was produced from 1970 to 1976 (Alaee et al., 2003). The commercial products had trade names and some of these are, together with their variation in composition, listed in Table 4.

Table 4: Trade names and variation in composition of commonly produced technical PBBs mixtures.

Commercial name	Main PBB congeners	Composition[(a)]
FireMaster FF-1 FireMaster BP-6 Hbb	hexaBBs	2-5 % tetraBBs 1-11 % pentaBBs 60-80 % hexaBBs 12-25 % heptaBBs
BB-8 Bromkal 80 Bromkal 80-9D Obb Octabromobiphenyl FR 250 13A Technical octabromobiphenyl	octaBBs	1 -30 % heptaBBs 25-70 % octaBBs 30-65 % nonaBBs 1-10 % decaBB
Adine 0102 Berkflam B10 Flammex B-10 HFO 101 Technical decabromobiphenyl	decaBB	0-7 % octaBBs 2-10 % nonaBBs 70-92 % decaBB

PBB: polybrominated biphenyl.
(a): According to IPCS (1994) and de Boer et al. (2000).

The technical PBB mixtures are complex and were reported to contain more than 22 compounds in the case of FireMaster BP-6 and 60 compounds in the case of Firemaster FF-1 (ATSDR, 2004; Orti et al., 1983). Both technical mixtures contained more than 50 % BB-153. The second most abundant congener was reported to be BB-180 (ATSDR, 2004). The analysis of a FireMaster BP-6 lot (No. 7062) gave concentrations for the coplanar congeners BB-77, -126 and -169 of 0.159, 0.079, and 0.294%, respectively (Orti et al., 1983; Robertson et al., 1983a, referenced in ATSDR, 2004). Tetra-, penta-, and hexabromonaphthalene were reported as impurities in FireMaster FF-1 and FireMaster BP-6 (Di Carlo et al., 1978). However, brominated dioxins and dibenzofurans were not detected in commercial FireMaster FF-1 or FireMaster BP-6 at a detection limit of 0.5 mg/kg (Hass et al., 1978). For commercial OctaBB and DecaBB mixtures information on the composition is only given for homologue groups rather than for individual congeners (ATSDR, 2004). Overall, data on the compositions of technical PBB mixtures with different degree of bromination are mainly available for the major congeners or homologue groups. Information on minor components such as non-*ortho* PBBs or impurities such as dioxin-like compounds in different commercial products is limited.

4.2. Use

The principal use of PBBs was as an additive fire retardant. These flame retardants are added to the polymer material, but are not chemically incorporated into the polymer matrix. Because PBBs are not chemically bound to the polymer matrix, they may migrate out of the matrix. PBBs were added to acrylonitrilebutadiene-styrene copolymers (ABS) (10 % PBBs), coatings, lacquers and polyurethane foam (IPCS, 1994).

4.3. PBBs in the environment

PBBs could be released into the environment during the production of the compounds but also when they were added to the polymers. There was also another incident that had a great impact on the occurrence of PBBs in the environment. In 1973, PBB-contaminated feed was unknowingly fed to dairy cattle, pigs, chicken and other farm animals over a period of approximately 9 months. The contaminated dairy products and eggs were widely consumed by farmers and their families, and later, by the general population of Michigan (Di Carlo et al., 1978). This incident resulted in the destruction of at least 29,800 cattle, 5,920 hogs, 1,470 sheep, and 1.5 million chickens. Also removed from the commercial market were at least 865 ton of animal feed, considerable amounts of cheese, butter and dry milk products as well as nearly 5 million eggs. This incident draw a lot of attention to PBBs (Anonymous, 1974) and it resulted in prompt actions in both United States of America (USA) and parts of Europe in order to reduce the risk for environmental and human exposure.

4.3.1. Air and dust

In the past, PBBs were released into the air during the manufacture. Another process that could release brominated biphenyls into the air is the incineration of PBB containing materials. Pyrolysis of hexaBB in the absence and presence of air has produced small amounts of lower brominated biphenyls (Thoma and Hutzinger, 1987). No data are available on the importance of this source for the release of PBBs in the air during the incineration of PBB containing materials. However, since the vast majority of products containing PBBs are today expected to be out of circulation, it is not likely that incineration is currently a significant source of PBBs to air.

4.3.2. Soil and uptake by plants

The important former sources of PBBs in soil are manufacturing operations and disposal of PBB-containing finished products. The concentrations of PBBs in soils from bagging and loading areas of the Michigan Chemical Corporation were 3,500 and 2,500 mg/kg, respectively (Di Carlo et al., 1978). It is likely that similar levels could have occurred at European production sites. The disposal into landfills of solid wastes generated during the production of PBBs was another important source of PBBs in soil (Neufeld et al., 1977). Photodecomposition of FireMaster BP-6 in soil could also be a source of lower PBBs in soil (Ruzo and Zabik, 1975; Trotter, 1977).

Soil could be contaminated with PBBs from municipal sludge applied on fields. There are very few European studies of PBBs in municipal sewage. In a study by Hellström (2000) on five different PBB congeners (BB-118, -138, 153, -167 and -180) in sludge samples from two treatment plants, all were below the limit of detection (LOD) (1.5 ng/g). The same study reported concentrations of the sum of PBDEs up to 500 ng/g.

Plant uptake from soil is related to the concentration in interstitial water and proportional to fat content of plants and K_{ow} of the chemical. Quantification of plant uptake can partly be misinterpreted through adhered soil particles in the analysis of a plant. Another possibility is that the substances evaporate from soil and attach to leaves.

Jacobs et al. (1976) investigated the uptake of PBBs from soil artificially contaminated with 10,000 and 100,000 ng/g of FireMaster BP-6. They identified at least 18 different brominated compounds in the technical product. No PBBs were detected in orchard grass cuttings or carrot tops. Detectable quantities of PBBs were found in carrot roots at about 20 to 40 ng/g.

Chou et al. (1978) have studied onion, carrot and radish, and found some uptake in the roots at high concentrations in soil (100,000 ng of a mixture of FireMaster BP-6 and 14C-PBB/g soil). At lower concentrations, uptake could only be detected when grown in sandy soil. The highest concentrations (50-500 ng/g) were observed for carrots. When the plants were washed, the concentrations decreased and they dropped even further when the plants were dipped in acetone. This indicates that a substantial

portion of the PBBs was attached to the root surface. No PBB could be detected in corn leaves exposed to dust from polluted soil (Chou et al., 1978). This indicates that direct intake of PBBs via plants is extremely low. The intake by grazing animals will be totally dominated by soil intake during grazing. Consequently, it is unlikely that plant uptake of PBBs currently could pose a problem for humans and animals.

4.3.3. Bioaccumulation in wildlife

The level of contamination of PBBs in biota is generally low in comparison to that of PBDEs. Götsch et al. (2004) determined PBBs in eggs of a white-tailed eagle in Norway. BB-153 is usually the most prominent congener, and in this egg sample its concentration was <10 ng/g wet weight (w.w.). Of the atropisomeric PBB congeners, only BB-132 and -149 were present at measurable concentrations, although still <1 ng/g w.w. The enantioselective analysis of these two congeners showed an enrichment of the second eluting enantiomer of BB-149, while for BB-132 no firm conclusions about the enantiomeric enrichment could be drawn.

Gao et al. (2009) found BB-153 in a study performed in the Yellow river delta on eggs from Oriental pratincole (*Glareola maldivarum*), Saunders's gull (*Saundersilarus saundersi*), Common tern (*Sterna hirundo*), Kentish plover (*Charadrius alexandrinus*) as well as Ring-necked pheasant (*Phasianus colchicus*). The concentrations of BB-153 were between 0.1 to 1.4 ng/g fat. For comparison, the recorded PBDE concentrations were between 1.1 to 233 ng/g fat. Not surprisingly, higher levels could be detected in specific contaminated areas. Luo et al. (2009) investigated various waterbird species in the vicinity of an extensive electronic waste recycling region in South China. Muscle samples of Chinese-pond heron were collected between 2005 and 2007 from Qingyuan County. BB-153 was detected in 93 % of the samples, at concentrations ranging from 1-2,800 ng/g fat.

Von der Recke and Vetter (2008) investigated PBBs in *i.a.* blubber of seals and harbour porpoises originating from the North Sea, the Baltic Sea and the coastal waters of Iceland and North America. In these samples, hexaBBs dominated, followed by pentaBBs and heptaBBs, whilst octaBBs were detected only occasionally and nonaBBs and BB-209 not at all. The hexaBB pattern in samples from Iceland was a mixture of those in samples from North America and continental Europe. BB-153 dominated, followed by BB-155 and -154. The patterns also indicated de-bromination of more highly brominated products in samples from Europe. The authors concluded that PBB residues in North America are mainly originating from technical hexabromobiphenyl, while the bulk of the PBB residues in the European marine samples originated from technical octa- and decabromobiphenyl. Concentrations of individual PBB congeners or of the sum of PBBs were however not reported.

There are very few European studies on PBBs in terrestrial animals. Jaspers et al. (2005) report on the occurrence of BB-153 in eggs from little owls (*Athene noctua*) from Belgium. Based on 39 samples the concentration of BB-153 ranged from 1 to 6 ng/g fat (mean 2 ng/g fat). For comparison, the corresponding levels of BDE-153 were 10 to 94 ng/g fat (mean 32 ng/g fat).

5. Occurrence and patterns of PBBs in food

5.1. Current occurrence of PBBs in food: call for data

Following a European Commission (EC) request in 2005 the CONTAM Panel (EFSA, 2006) identified eight PBDE congeners (BDE-28, -47, -99, -100, -153, -154, -183 and -209), HBCDD and BB-153 as the most important ones to be monitored; optionally TBBP-A and other phenols, DBDPE, hexabromobenzene, BTBPE were also recommended to be monitored.

From October 2006, and European Union (EU)-wide monitoring of these compounds was organised and the results were made available to the European Food Safety Authority (EFSA).

Additionally, a Data Collection and Exposure Unit (DATEX) call for data on BFRs[12] was issued by EFSA in December 2009, with different deadlines according to the chemicals to be collected. Particularly, the closing date for data submissions on PBDEs and PBBs was end of February 2010.

EFSA collected and evaluated the results obtained from the analysis of 794 food samples (5,643 analytical results covering 16 PBBs) which were provided by 6 Member States and covered the period from 2003 to 2009.

The data submission to EFSA followed the requirements of the Standard Sample Description model. On the EFSA webpage of the call for data detailed instructions on how to submit data[13] and the Guidance on Standard Sample Description for Food and Feed[14] specifying the data elements, the sample data structure of the analytical results for chemical contaminants and residues in food and feed were provided.

SAS Enterprise software was used to extract information from the occurrence data submitted. Data providers were asked to check and eventually confirm that the extracted information was correct and provide clarifications in case of unclear or missing detailed information.

5.1.1. Summary of data collected

The source of the 794 samples reported from the 6 Member States is illustrated in Figure 2. Belgium and the UK both provided 29 % of the data followed by France (16 %) and Ireland (12 %).

The EU-wide monitoring of BFR compounds, including PBBs, was organised from October 2006, but as specified in the call for data (DATEX call for data on BFRs[13]), any data available from 2000 to 2009 could have been provided to EFSA. The distribution of results over the years of sampling is illustrated in Figure 3. Almost 80 % of the samples were analysed in the latest years, specifically in the period from 2006 and 2008. The year 2009 was probably not a complete year of sampling, as the closing date of the call for data for PBDEs was set to February 2010.

Analytical results identified during the data cleaning steps with incomplete or incorrect description of any of the required variables (e.g. parameter type, food classification, results value or results LOD-limit of quantification (LOQ)) of the Standard Sample Description[15] template, were re-submitted to the respective data provider for further check, before excluding the records from the database.

Additionally, specific exclusions were performed concerning data from total diet studies (TDS) (19 samples) because of not correct matching between the reported food descriptions of the TDS composite food with the food categories of current FoodEx food classification system.

With final agreement of the respective data providers, a total of 5,643 analytical results covering 16 different PBB congeners were included in the PBB dataset for the calculation of the dietary intake of PBBs.

[12] http://www.efsa.europa.eu/en/data/call/datex091215.htm.
[13] http://www.efsa.europa.eu/en/datexcallsfordata/datexsubmitdata.htm.
[14] http://www.efsa.europa.eu/en/scdocs/scdoc/1457.htm.

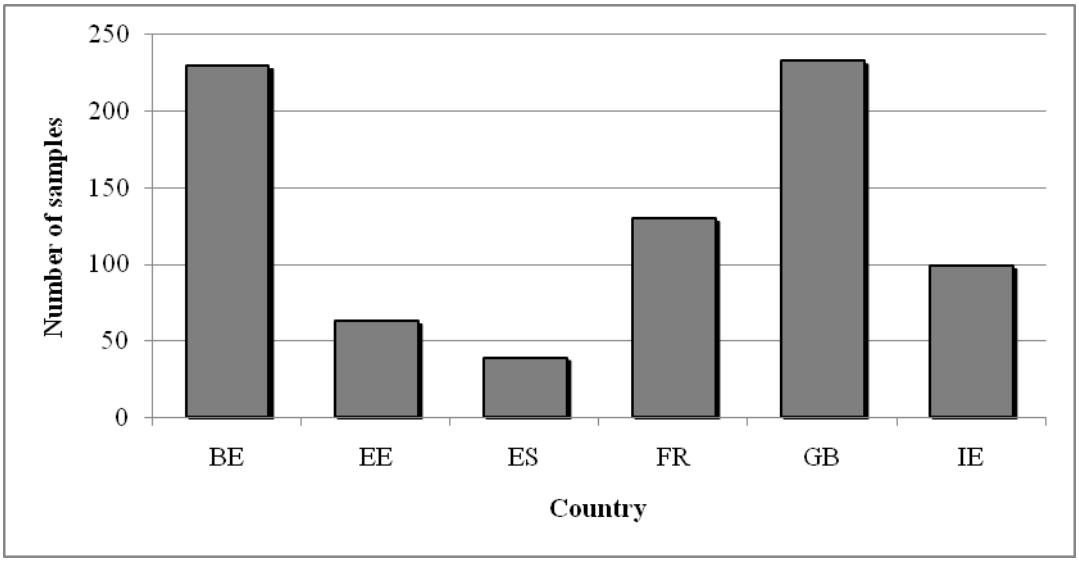

Figure 2: Distribution of samples across EU Member States (BE: Belgium, EE: Estonia, ES: Spain, FR: France, GB: Great Britain, IE: Ireland).

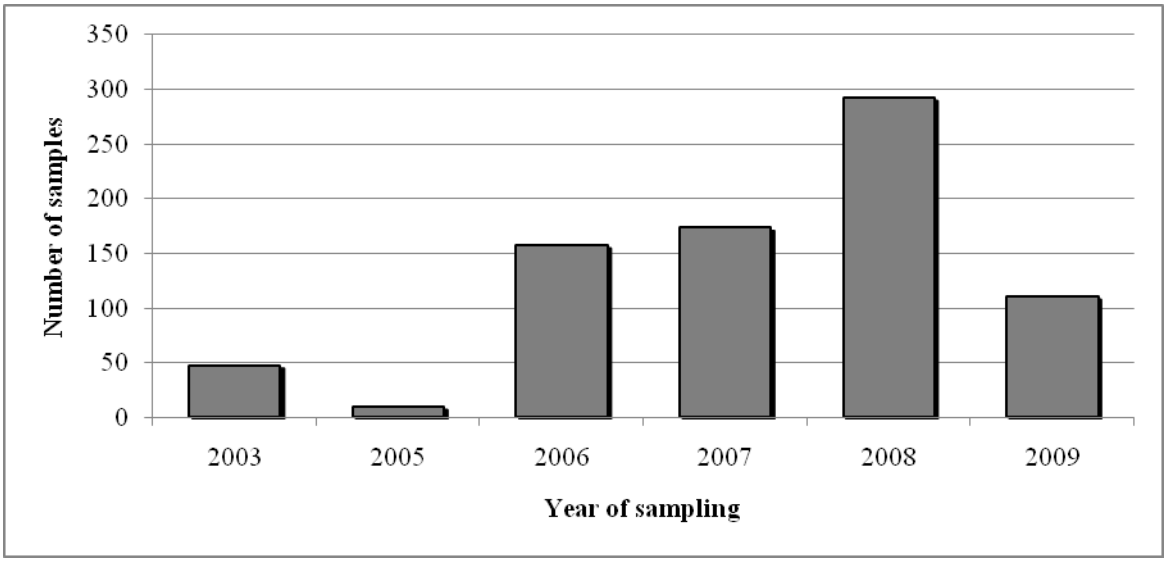

Figure 3: Distribution of samples over the years of sampling.

5.1.2. Distribution of analytical results reported for PBB congeners

A total of 794 samples were tested for different PBB congeners. The set of congeners tested in each food sample varies depending on the laboratory. The distribution of analytical results reported for each single congener is illustrated in Figure 4.

Following the CONTAM Panel advice (EFSA, 2006), the monitoring exercise that was carried out from 2006 was mainly focused on the analysis of the congener BB-153, as the reported number of analytical results from Figure 4 illustrates (over 600 analytical results). More than 400 records were collected for BB-15, -49, -101 and -52. For each of the remaining 11 congeners the frequency of reported analytical results was below 350.

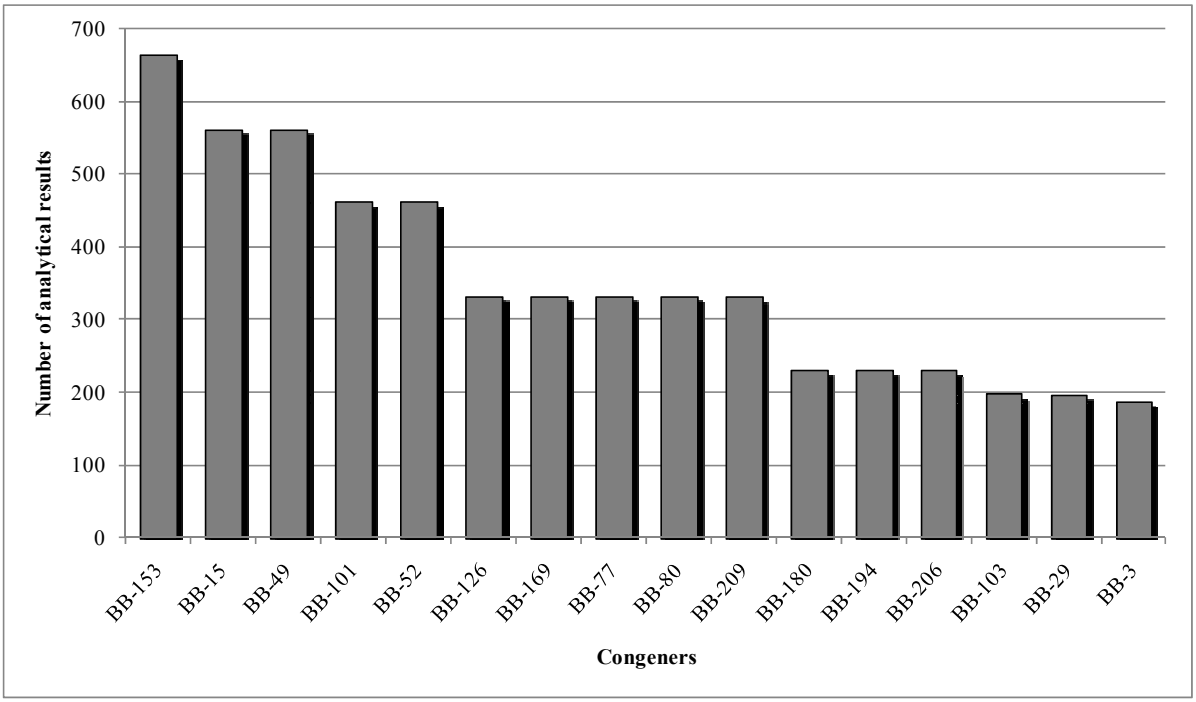

Figure 4: Distribution of analytical results across PBB congeners.

5.1.3. Distribution of samples reported for food categories

Data providers were asked to codify all food descriptors according to the food classification system of EFSA Concise European Food Consumption Database (EFSA concise food categories).[15]

In order to improve the estimation of the dietary exposure assessment, food classification was refined by applying an alternative food classification, named FoodEx.

FoodEx is a provisional food classification system developed by the DATEX Unit in 2009 with the objective of simplifying the linkage between occurrence and food consumption data when assessing the exposure to hazardous substances. It contains 20 main food categories (first level),[16] which are further divided into subgroups having 140 items at the second level, 1,261 items at the third level and reaching about 1,800 end-points (food names or generic food names) at the fourth level. It is based on a hierarchical coding for an easier cross-checking and it is structured as a child-parent relation.

[15] http://www.efsa.europa.eu/en/datex/datexfooddb.htm.

[16] Grains and grain-based products, Vegetables and vegetable products (including fungi), Starchy roots and tubers, Legumes, nuts and oilseeds, Fruit and fruit products, Meat and meat products (including edible offal), Fish and other seafood (including amphibians, reptiles, snails and insects), Milk and dairy products, Eggs and egg products, Sugar and confectionary, Animal and vegetable fats and oils, Fruit and vegetable juices, Non-alcoholic beverages (excepting milk based beverages), Alcoholic beverages, Drinking water (water without any additives except carbon dioxide; includes water ice for consumption), Herbs, spices and condiments, Food for infants and small children, Products for special nutritional use, Composite food (including frozen products), Snacks, desserts, classification not possible.

The distribution of samples across the aggregated food categories is shown in Figure 5.

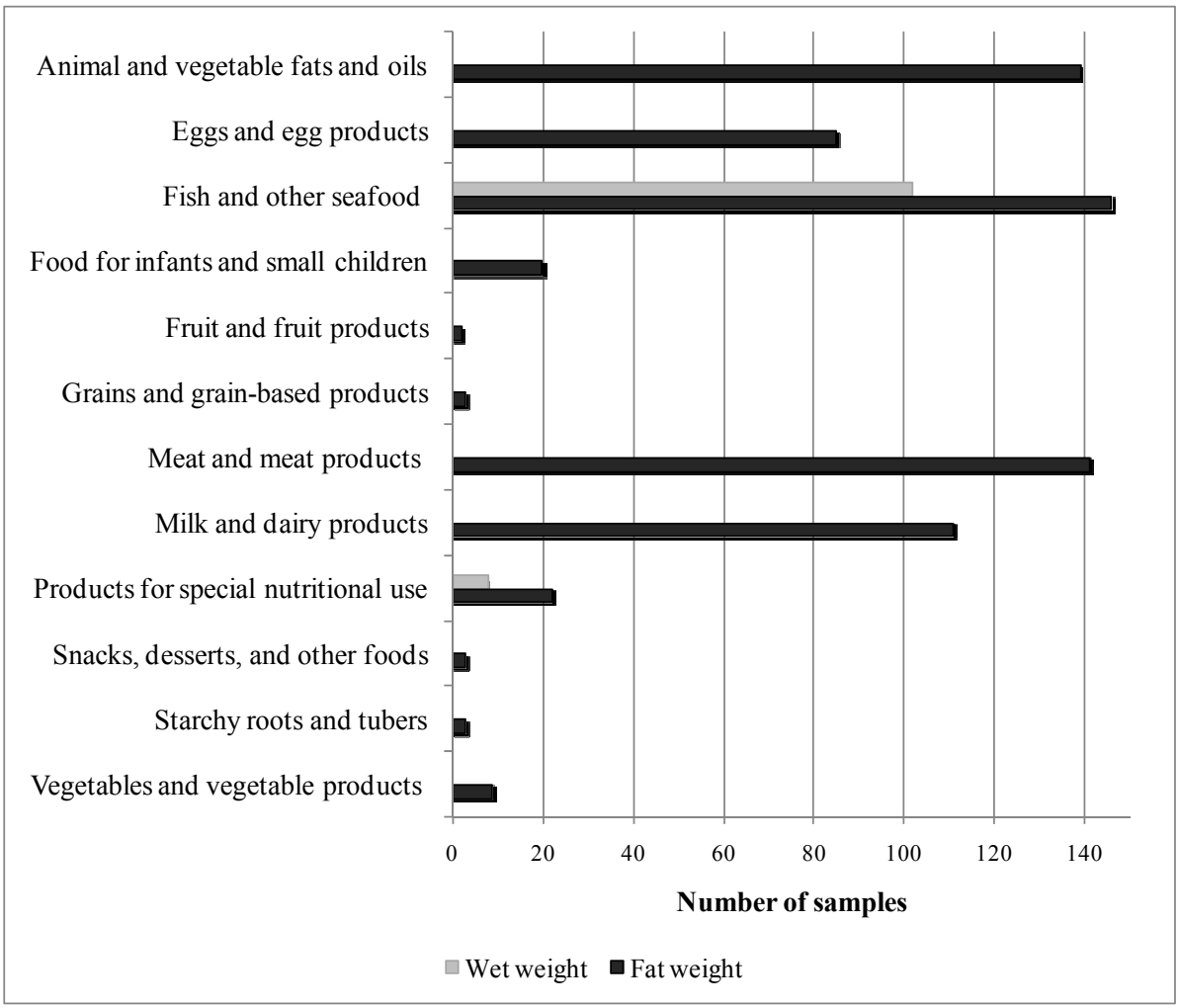

Figure 5: Distribution of samples in the FoodEx food categories (first level) and distribution of expression of results (wet weight, fat weight), across food categories.

The category "Fish and other seafood (including amphibians, reptiles, snails and insects)" dominated the product coverage with 31 % of the total samples, followed by "Meat and meat products (including edible offal)" and "Animal and vegetable fats and oils", at 18 %, "Milk and dairy products" and "Eggs and egg products", respectively, at 14 % and 11 %.

Less than 30 samples were reported for the remaining food categories.

Of the 20 food categories available in the first level of FoodEx, only 12 of them were covered in the current data collection. No analytical results for food products in the categories of "Grains and grain-based products", "Starchy roots and tubers", "Legumes, nuts and oilseeds", "Sugar and confectionary", "Fruit and vegetable juices", "Non-alcoholic beverages (excepting milk based beverages)", "Alcoholic beverages", "Drinking water (water without any additives except carbon dioxide; includes water ice for consumption)" were submitted to EFSA.

The analysis of the samples from products of animal origin, excluding fish, was mainly carried out on the fat fraction; therefore the analytical results were reported on a fat basis in almost 100 % of the cases. Only 8 samples out of 30 were reported on a wet weight basis from the food category of "Products for special nutritional use".

On the contrary, in the case of "Fish and other seafood (including amphibians, reptiles, snails and insects)" 41 % of the sample results were expressed on a wet weight basis.

For estimating the dietary exposure to PBBs, all analytical concentrations expressed on fat weight need to be converted to whole weight basis (wet weight). For this reason the data providers were requested to report the fat content in the Standard Sample Description template for each analysed sample. For 86 % of the samples, the results were provided on a fat basis and accompanied with the respective fat content; in only one case, a "Cow milk, 3-4 % fat (whole milk)" sample (FoodEx third level) was reported without the original fat content. In this case the missing information was replaced by the average fat content calculated on the samples for which the percentage of fat was given in the original data of the current EFSA database on BFRs[17] (3.61 %).

5.1.4. Analytical methods used and limits of quantification

The 5,643 original results were reported in pg/g (or ng/kg; 53 %), in ng/g (29 %) and in µg/kg (19 %). All the measurements were converted to pg/g.

The most common analytical method used to perform the analyses of PBBs is GC-HRMS with 93 % of coverage of the reported results; the remaining samples were analysed with GC-MS without stating the MS mode.

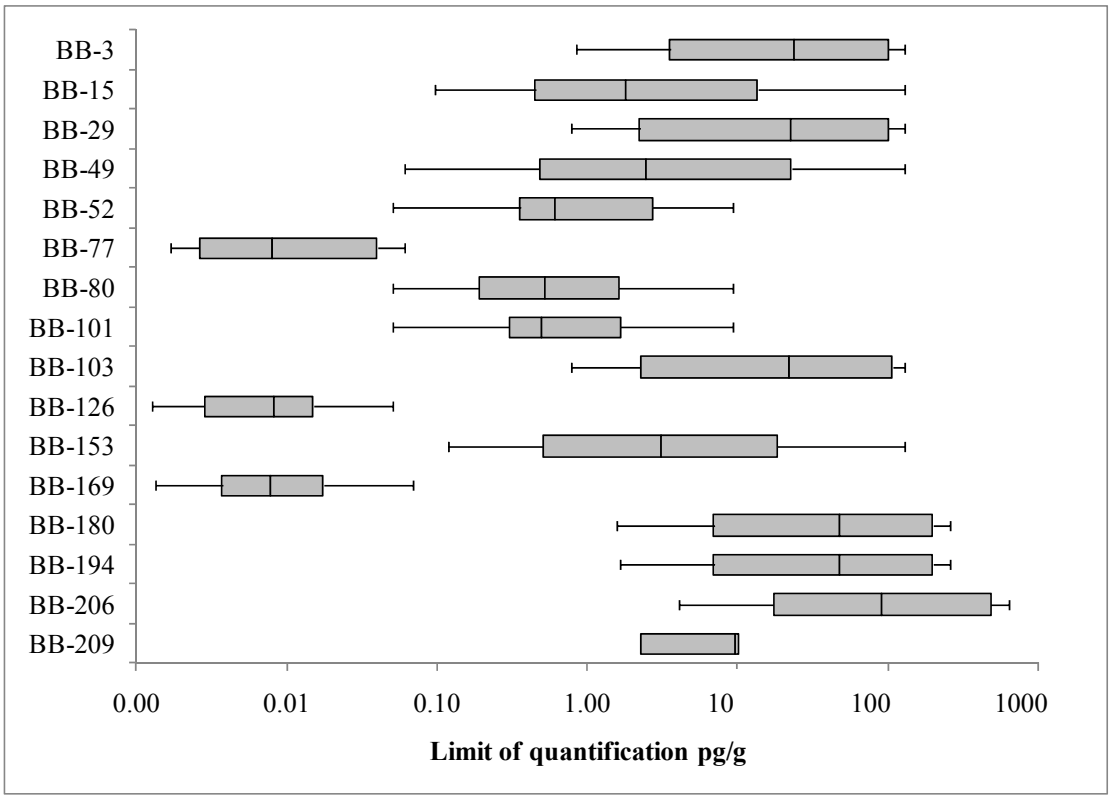

Figure 6: Distribution of the limit of quantification (LOQ) according to the 16 PBB congeners.

The LOD and LOQ for the analyses could vary with the congener under analysis (Figure 6), the analytical technique, the food matrix (Figure A1, in Appendix A) and the laboratory. In Figure 6 and Figure A1, the boxes indicate the 25th and the 75th percentiles with a line at the medians, and the ends

[17] As a consequence of the first deadline of the DATEX call for data asking for analytical results on PBDEs and PBBs, the current EFSA database on BFRs includes results reported from PBDEs and PBBs.

of the whiskers represent the 5th and 95th percentiles. Those percentiles refer to the LOQ values reported across congeners and food categories because in most of the reported analyses the LOQ was given in the original data. Only 63 results for BB-153 were reported as below LOD. In order to compare the values reported for LOQs across congeners and across different food matrices, all LOQs have been expressed on wet weight (w.w).

The lowest LOQs were reported for the congeners BB-77, -126 and -169 with medians of 0.01 pg/g w.w. The highest LOQs were reported for BB-206 with a median of 91.11 pg/g w.w.

BB-77, -126 and -169 are non-*ortho* substituted congeners, reported to have similar mode of action as dioxins and therefore are expected to be more toxic than the other congeners (e.g. *ortho* substituted PBBs).

A possible explanation for the considerably lower LOQs for BB-77, -126 and -169, could be that the adopted analytical strategy was to improve the LOQ similarly to those used for non-*ortho* and mono-*ortho* substituted PCBs.

The evaluation of the spread of the LOQs reported across food categories (Figure B in Appendix B) should also take into account the variability of the different congener specific LOQs within each food category. Specifically for BB-77, -126 and -169, the difference in analytical methods performances compared with the other congeners is relevant, as shown in Figure 6. Therefore, the LOQ variation analysis across food categories has been performed for all reported PBB congeners excluding BB-77, -126 and -169 (Figure A1, in Appendix A).

The lowest LOQs were found for "Vegetables and vegetable products (including fungi)" and "Starchy roots and tubers," with medians of 0.02 and 0.04 pg/g w.w. respectively; the highest LOQs were reported for "Animal and vegetable fats and oils", with median of LOQs of 82.69 pg/g w.w. (conversion on wet weight was applied, where needed, to the original reported LOQs).

No separate evaluation of LOQs across food category was carried out for BB-77, -126 and -169 due to the limited number of data.

5.1.5. Occurrence data by food category

The number of analytical records reported as quantified values was only 14 % out of 5,643 observations across the 16 PBB congeners. Only in the case of the food category of "Fish and other seafood (including amphibians, reptiles, snails and insects)" the proportion of quantified values reached 30 %, followed by "Meat and meat products (including edible offal)" and "Eggs and egg products" with 22 and 18 % of quantified values, respectively (Figure 7).

The CONTAM Panel focused the analysis of the occurrence data on the 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) (Table B1**,** in Appendix B). This decision was supported by the high proportion of non detects in other food categories.

Since the exposure assessment will be based on a restricted list of food categories, the data set of PBBs will include only 659 samples (out of 794) for which 4,663 analytical tests were performed for the presence of at least one of the 16 PBB congeners.

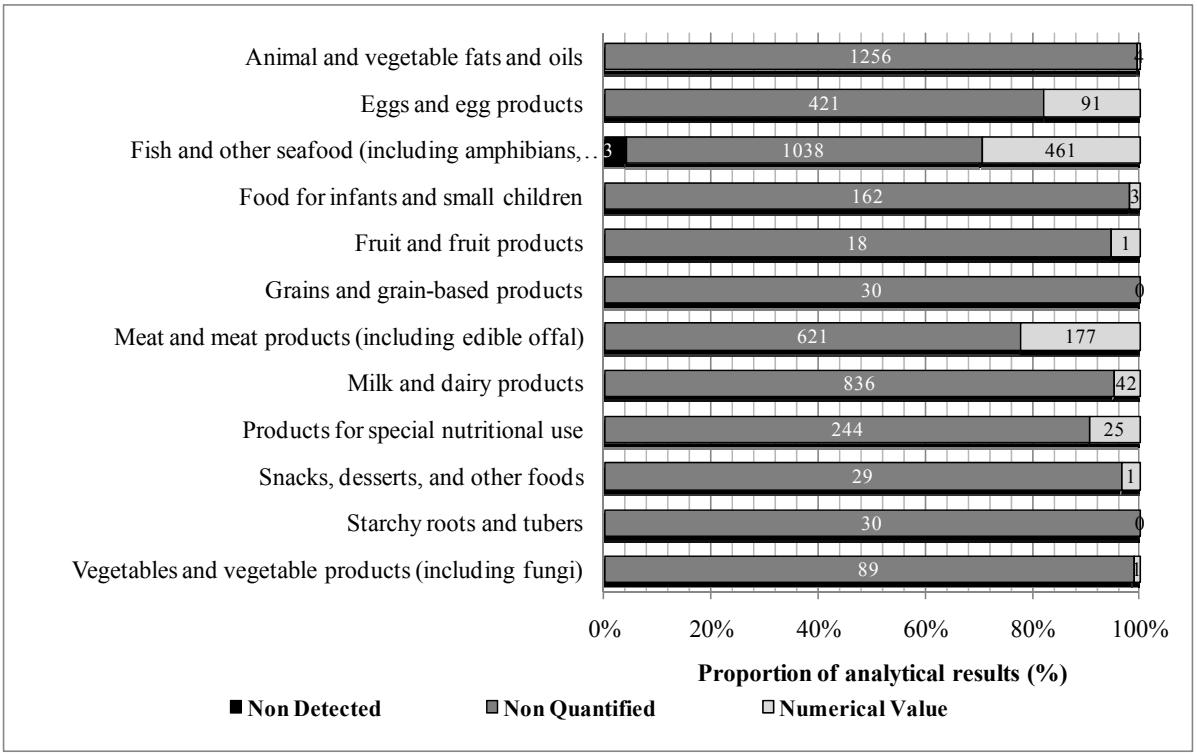

Figure 7: Proportion of non detected, non quantified and quantified analytical results across food categories in the first level (broad food categories) of the FoodEx classification system. Figures in the bars represent the frequency of analytical results.

The number of reported analytical results and the respective proportion of not detected (and not quantified) results was inspected for each of the 16 PBB congeners for the five main food categories of the FoodEx food classification system selected above. Table 5 describes in detail the distribution of analytical results and quantified values across congeners and food categories. N is the number of results reported. The column ND (%) indicates the percentage of results below the LOD or the LOQ.

Not all 16 congeners were analysed for samples of the food category of "Fish and other seafood" or "Food for infants and small children" (Table 5). Additionally, although those five selected food categories are known to be contaminated with different PBBs, most of the analyses performed gave results below LOD (or LOQ). Only in the case of "Fish and other seafood", in testing BB-52 the proportion of not detected went down to 28 % over 146 analytical results, followed by BB-77, -49 and -101 with a proportion of not detected (and not quantified) of 30 %, 40 % and 56 %, respectively.

Despite the high number of non detects, the evaluation of the left-censored data in the PBB database was performed in accordance with the guidelines of the WHO-Global Environment Monitoring System-Food Contamination Monitoring and Assessment Programme (GEMS/Food). As mentioned in the guidance the lower and upper bounds approach should be used when the quantified results are below 40 % (WHO, 2003). The lower bound (LB) is obtained by assigning a value of zero (minimum possible value) to all samples reported as lower than the LOD (<LOD) or LOQ (<LOQ). The upper bound (UB) is obtained by assigning the numerical value of LOD to values reported as <LOD, and LOQ to values reported as <LOQ (maximum possible value), depending on whether LOD or LOQ is reported by the laboratory.

Table 5: Frequency of results (N) and proportion of not detected (ND %) values across 16 PBBs congeners and five broad food categories of the FoodEx food classification system that are used for the exposure assessment. The column ND (%) indicates the percentage of results below the limit of detection (LOD) or the limit of quantification (LOQ). The results are estimated from 4,663 analytical results obtained by the analysis of 659 samples. If no data are given in the table ("-"), it means that no analytical results were available.

	Food categories (FoodEx_Level 1)									
PBB congeners	**Meat and meat products**		**Milk and dairy products**		**Animal and vegetable fats and oils**		**Fish and other seafood**		**Food for infants, small children**	
	N	**ND (%)**	**N**	**ND (%)**	**N**	**ND (%)**	**N**	**ND (%)**	**N**	**ND (%)**
BB-3	12	92	45	100	80	100	-	-	15	100
BB-15	69	99	92	98	139	99	146	93	20	90
BB-29	16	94	41	100	91	100	-	-	15	100
BB-49	69	99	92	100	139	100	146	40	20	100
BB-52	121	40	59	68	41	100	146	28	-	-
BB-80	49	100	40	100	41	100	146	89	-	-
BB-101	121	40	59	68	41	100	146	56	-	-
BB-103	16	94	42	100	91	100	-	-	15	100
BB-153	69	87	92	100	139	100	248	79	20	100
BB-180	20	95	52	100	98	100	-	-	20	95
BB-194	20	95	52	98	98	100	-	-	20	100
BB-206	20	85	52	98	98	98	-	-	20	100
BB-209	49	98	40	100	41	100	146	88	-	-
BB-77	49	92	40	100	41	100	146	30	-	-
BB-126	49	82	40	100	41	100	146	95	-	-
BB-169	49	100	40	100	41	100	146	100	-	-

PBB: polybrominated biphenyl; N: frequency of results; ND: not detected; LOD: limit of detection; LOQ: limit of quantification.

The food samples were classified according to the FoodEx classification system. The spread of the analytical results across the several FoodEx categories and the high percentage of not detected or not quantified analytical results prevented from calculating summary statistics, at a very detailed level of the food classification system.

In order to report a description of contamination values for the 16 PBB congeners, Table 6 provides information on the mean occurrence for the food categories in the first level of the FoodEx. The mean fat content (%) calculated on the reported original samples is also given.

While PBB levels (mean concentration) are reported on a fat basis (pg/g fat) for the food categories of "Meat and meat products", "Animal and vegetable fats and oils" and "Milk and dairy products", the concentrations for "Fish and other seafood" and "Food for infants and small children" are reported on a wet weight basis (pg/g w.w.). In order to harmonise all analytical results, conversion of the reported data was applied, where needed.

Meat and meat products (including edible offal)

In the food category "Meat and meat products (including edible offal, pg/g fat)" a total of 141 samples were analysed and 88 samples gave a result with a quantified value for at least one of the 16 PBB congeners. The proportion of not detected or not quantified results varies from 40 % for BB-52 and BB-101, to 100 % for BB-80 and -169. The LB and UB occurrence means in the "Meat and meat

products (including edible offal)" food category for BB-52 and -101 each are 1.99 and 6.04 pg/g fat, respectively (Table 6).

Table 6: Occurrence means for the 16 PBB congeners across five broad food categories of the FoodEx food classification system. The occurrence values reported are calculated on 4,663 analytical records (659 samples). Lower (LB) and upper bound (UB) mean values shown are expressed on a fat (pg/g fat) or wet weight basis (pg/g w.w.) according to the different food categories. If no data is given in the table ("-"), it means that no analytical results were available.

PBB congeners	Occurrence means by Food categories (FoodEx_Level 1)									
	Results expressed on fat basis (pg/g fat)						Results expressed on wet weight basis (pg/g w.w.)			
	Meat and meat products[(a)]		Milk and dairy products[(b)]		Animal and vegetable fats and oils[(c)]		Fish and other seafood[(d)]		Food for infants, small children[(e)]	
	LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
BB-3	10.8	223	0.00	105	0.00	108	-	-	0.00	7.67
BB-15	1.88	61.1	1.36	66.1	0.47	76.9	0.09	0.87	5.75	8.33
BB-29	8.1	108	0.00	97.8	0.00	88.9	-	-	0.00	6.46
BB-49	1.88	61.1	0.00	64.2	0.00	76.7	1.32	1.52	0.00	6.24
BB-52	1.99	6.04	0.48	7.26	0.00	10	4.19	4.31	-	-
BB-80	0.00	10	0.00	10	0.00	10	0.07	0.59	-	-
BB-101	1.99	6.04	0.56	7.34	0.00	10	1.55	1.86	-	-
BB-103	8.13	108	0.00	115	0.00	96.2	-	-	0.00	6.46
BB-153	9.28	99.6	0.00	87.1	0.00	99	0.81	18.9	0.00	7.64
BB-180	13	372	0.00	211	0.00	208	-	-	0.74	13.2
BB-194	13	372	3.46	212	0.00	208	-	-	0.00	12.7
BB-206	40.9	630	11.5	414	4.08	427	-	-	0.00	26.8
BB-209	18.6	227	0.00	58.3	0.00	40.7	1.14	5.86	-	-
BB-77	<0.01	0.07	0.00	0.06	0.00	0.06	0.02	0.02	-	-
BB-126	0.09	0.18	0.00	0.05	0.00	0.05	<0.01	0.01	-	-
BB-169	0.00	0.11	0.00	0.08	0.00	0.06	0.00	0.01	-	-

PBB: polybrominated biphenyl; LB: lower bound; UB: upper bound; w.w: wet weight.
(a): Mean (%) fat in original samples: 6.44 %.
(b): Mean (%) fat in original samples: 12.96 %.
(c): Mean (%) fat in original samples: 89.45 %.
(d): Mean (%) fat in original samples: 5.70 %.
(e): Mean (%) fat in original samples: 6.58 %.

It should be mentioned that the mean levels for BB-180, -194, -206 and -209 are heavily influenced by only single samples with extraordinary concentrations of 260, 260, 640 and 910 pg/g fat respectively. Moreover the mean concentration estimated for the UB of each congener is highly dependent on the LODs or LOQs reported (0.07 to 630 pg/g fat).

Milk and dairy products

Within the food category "Milk and dairy products" a total of 111 samples (878 analytical results), were analysed. Overall BB-52 and -101 were the predominant congeners. Within this category, 61 % and 34 % of the samples were "Liquid milk" and "Cheese" respectively (FoodEx level 2; data not reported). The reported fat content varied considerably from 3.5 to 28 % for liquid milk and cheese, respectively. In liquid milk numerical values were reported only for BB-52 and -101 (proportion of not detected: 63 % out of 51 samples analysed). The reported mean occurrence concentration in liquid milk for BB-52 and -101 varies from 0.55 to 6.83 pg/g fat (LB and UB) and 0.64 to 6.92 pg/g fat (LB and UB), respectively.

All other congeners analysed were below the LOD (or LOQ). The median of LOQs estimated across all 13 PBB congeners (excluding BB-77, -126 and -169) reaches 3.5 pg/g fat (Figure A1, in Appendix A).

One sample described as "Milk and dairy products" (FoodEx level 1) showed concentrations for BB-15, -194 and -206 of 38, 180 and 600 pg/g fat, respectively.

Animal and vegetable fats and oils

The food category "Animal and vegetable fats and oils" consists of 139 samples. The analysis of only four samples gave results above the LOQ; two analytical results for BB-15 and two for BB-206. The mean concentration estimated for the UB of each congener is highly dependent on the LODs or LOQs reported (from 0.05 to 427 pg/g fat).

Fish and other seafood (including amphibians, reptiles, snails and insects)

Most of the PBB data reported by the Member States belong to the food category "Fish and other seafood (including amphibians, reptiles, snails and insects)" with 248 samples analysed. The proportion of not detected or not quantified results varies from 28 % for BB-52, to 100 % for BB-169 (Table 6).

A more detailed analysis of the occurrence data reported by fish species (food category "Fish meat"), highlights the relationship between the fat content of fish and the contamination level of certain PBBs. Table 7 shows the average fat content (%) calculated on the reported fat percentage in the original fish samples. Depending on the fat content reported, three ranges of fat content were defined (more than 8 %, between 2 and 8 % and lower than 2 %). The mean occurrence (pg/g w.w.) of the analysed PBB congeners was estimated for each group of samples falling into the three different ranges of fat content (Table 8).

Table 7: Average fat content (%) calculated on the reported fat percentage in the original samples of the current PBBs data base. Data reported refer to the samples classified according to the fish species available at the third level of the FoodEx system (from "Fish meat").

Fish species	Fat content (%)
Eel	22.1
Anchovy	13.7
Mackerel	11.9
Sprat	11.5
Sardine and pilchard	10.7
Salmon and trout	10.2
Herring	8.6
Bass	7.7
Bream	6.5
Halibut	4.4
Grey mullet	4.3
Flounder	4.0
Fish meat	3.8
Tuna	3.5
Carp	2.6
Plaice	2.1
Perch	1.2
Sole	1.2
Hake	1
Cod and whiting	0.7

Table 8: Mean concentrations of the 10 PBB congeners analysed in the FoodEx food category "Fish Meat" across three groups of fish species defined according to the respective fat content. Lower (LB) and upper bound (UB) mean values shown are expressed on wet weight basis.

	Mean occurrence values (pg/g w.w.)					
PBB	**≥ 8 % fat**		**8 % >fat > 2 %**		**≤ 2 % fat**	
congeners	**LB**	**UB**	**LB**	**UB**	**LB**	**UB**
BB-15	0.00	1.56	0.00	0.43	0.00	0.11
BB-49	3.22	3.76	1.79	1.97	0.32	0.41
BB-52	11.5	11.7	4.82	4.96	0.57	0.68
BB-80	0.05	1.56	0.23	0.53	0.04	0.14
BB-101	4.1	4.72	2.35	2.51	0.22	0.41
BB-153	1.45	29.8	1.11	22	0.15	5.81
BB-209	0.21	8.49	1.22	7.91	3.07	8.37
BB-77	0.02	0.03	0.01	0.01	<0.01	<0.01
BB-126	<0.01	0.01	<0.01	0.01	<0.01	0.01
BB-169	0.00	0.01	0.00	0.01	0.00	0.01

PBB: polybrominated biphenyl; LB: lower bound; UB: upper bound; w.w: wet weight.

Only 10 congeners (BB-15, -49, -52, -77, -80, -101, -126, -153, -169 and -209) were analysed within the food category "Fish meat", and in almost all cases, except BB-209, an increasing fat content corresponds with increasing PBB contamination levels. In the case of fishes with a fat content higher than 8 %, the PBB levels are on average almost double of those for fishes with fat contents between 2 and 8 % and more than 10 times higher in the case of fish species with fat content below 2 %. In contrast the LB concentrations for BB-209 increase with decreasing fat content.

An additional evaluation was performed on the data reported in the food category "Fish and other seafood (including amphibians, reptiles, snails and insects)". Among the total of 248 samples analysed, 146 were simultaneously tested for the presence of all the 10 above mentioned PBB congeners. Within this sub-set of samples, 17 "salmon and trout" and 63 "molluscs" samples were selected. These two groups of fish species allowed for a specific evaluation on the contribution of each of these 10 congeners to their sum in salmon and trout and in molluscs. Figure 8 and 9 describe the contribution of each of the 10 PBBs to the sum of LB and UB occurrence. The main contributors to the PBB contamination of salmon and trouts (pg/g w.w.) are the congeners BB-52, -101 and -209 vapour pressures and low water solubilities, which decrease with increasing degree of bromination. The octanol-water partition coefficients (log K_{ow}) vary between congeners and are shown in Table 2, as well occurrence mean) and 21.4 and 14 % (LB and UB occurrence mean), respectively. BB-209 contributes to LB and UB occurrence mean with 4.9 and 34 %, respectively, which reflects a high proportion of non detects. Those main contributors are followed by BB-49 and -153 with respectively 16.5 and 11 % (LB and UB occurrence mean) and 18.4 and 11 % (LB and UB occurrence mean).

A different PBB profile was identified for molluscs as shown in Figure 9. The highest contributors to the overall contamination with PBBs is BB-209 with 44 % and 53 % for LB and UB occurrence, followed by BB-52 with 29 % and 14 % (LB and UB occurrence mean, respectively).

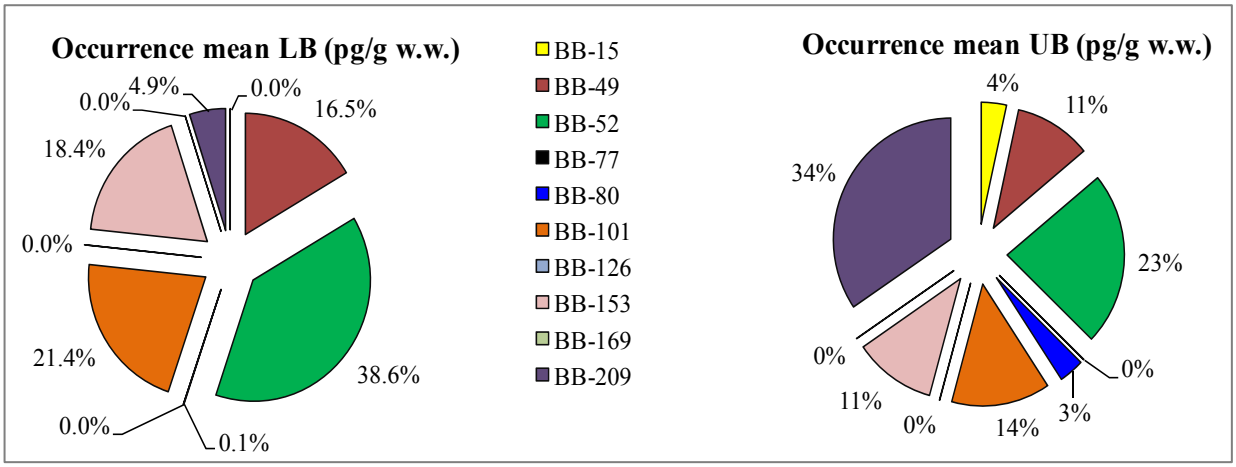

Figure 8: Mean LB and UB occurrence relative contribution of 10 PBB congeners in salmon and trout samples. The LB and UB means of occurrence were estimated from the results reported for 146 samples which were simultaneously analysed for the above listed 10 congeners.

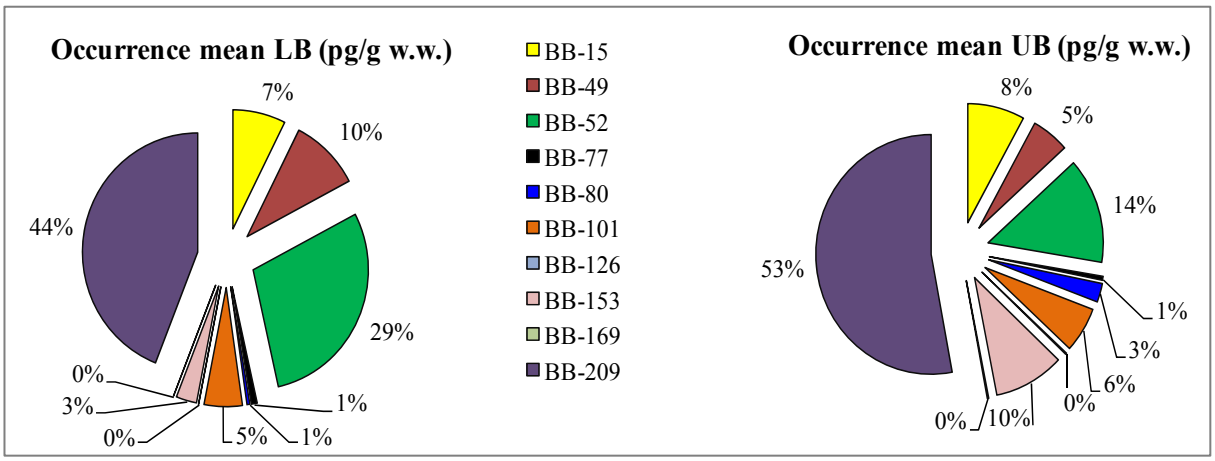

Figure 9: Mean LB and UB occurrence relative contribution of 10 PBB congeners in molluscs. The LB and UB means of occurrence were estimated from the results reported for 63 samples which were simultaneously analysed for the above listed 10 congeners.

Food for infants and small children

The food categories "Food for infants and small children" consists of 20 samples. Analytical data for only a limited set of congeners were submitted to EFSA (BB-3, -15, -29, -103, -153, -180, -194 and -206). The analysis of only three samples gave results above the LOQ; two analytical results for BB-15 and one for BB-180. Also in this case, the LB and UB occurrence means for all congeners are highly affected by the respective LOQ and LOD values.

5.1.6. Summary of occurrence

A detailed analysis of the occurrence levels of 16 PBB congeners was performed on the basis of the data submitted for 5 broad food categories ("Fish and other seafood", "Meat and meat products", "Animal and vegetable fats and oils", "Milk and dairy products", "Food for infants and small children"), as explained in chapter 5.1.5. Despite the high number of non detects (including not detected or not quantified results), the treatment of the left-censored data was performed following the LB and UB approach as suggested by GEMS/Food when the quantified results are below 40 % (WHO, 2003).

As shown in Table 5, the proportion of non detects often exceeded 60 % for most of the congeners, reaching up to 100 %. As a consequence, especially where the proportion of not detects was above 80 %, the estimation of UB and LB was mainly driven by the reported LODs or LOQs. The estimated occurrence values in those cases were more reflecting the variation of LOD and LOQ values and the performance of the analytical methods rather than the actual PBB levels.

On the basis of these observations, the CONTAM Panel decided to focus the exposure estimation only on those congeners, in the respective food categories where the proportion of non detects was lower than 80 %. This further data selection allows for a more reliable application of the UB and LB approach and prevents an unrealistic exposure estimate. Additionally, due to the specific toxicological concerns of the non-*ortho* PBBs, BB-77, -126 and -169 are considered relevant for the dietary exposure estimation, regardless of the proportion of non detects. Table 9 summarises the occurrence values for the selected 7 PBB congeners (BB-49, -52, -77, -101, -126, -153 and -169) that are used for the exposure assessment in the respective food categories ("Fish and other seafood", "Meat and meat products", "Milk and dairy products", "Food for infants and small children"). In the case of "Food for infants and small children", although all data reported were not detects, it was decided to include mean values for BB-153 as it will be used for a separate exposure calculation for infants.

All PBB levels (mean concentrations) are reported on a wet weight basis (pg/g w.w.). Where needed, conversion from fat weight to wet weight was applied as described in chapter 5.1.5.

An additional food classification system was applied to the current reported samples. In Table C1 (Appendix C) the occurrence values of the seven target PBB congeners are reported following the food categories defined by Commission Regulation (EC) No 1881/2006 on setting maximum levels for certain contaminants in foodstuffs. The food categories of "Other products" (pg/g w.w.) and "Infant and baby food" (pg/g w.w.) were added to include all those products addressed respectively to adults and to children that could not be classified according to the food categories defined in the Commission Regulation.

5.2. Previously reported literature data on PBB occurrence

5.2.1. Occurrence in Food

Due to the scarce number of European studies reporting PBB concentrations in food samples, this chapter describes also studies carried out in countries outside the EU.

Table 9: Occurrence means (pg/g w.w.) for the 7 PBB congeners across four broad food categories of the FoodEx food classification system that are used for the exposure assessment. Where "n.a." is reported, it means that a statistical evaluation for that specified congener in that food category is "not applicable".

PBB congeners	Occurrence means (pg/g w.w.) by Food categories (FoodEx_Level 1)							
	Meat and meat products[(a)]		Milk and dairy products[(b)]		Fish and other seafood[(d)]		Food for infants, small children[(e)]	
	LB	UB	LB	UB	LB	UB	LB	UB
BB-49	n.a.	n.a	n.a.	n.a	1.32	1.52	n.a.	n.a
BB-52	0.06	0.39	0.01	0.58	4.19	4.31	n.a.	n.a
BB-101	0.06	0.39	0.01	0.58	1.55	1.86	n.a.	n.a
BB-153	n.a.	n.a	n.a.	n.a	0.81	18.9	0.00	7.64
BB-77[(f)]	0.0002	0.0055	0.0000	0.0051	0.0168	0.0226	n.a.	n.a
BB-126[(f)]	0.0045	0.0107	0.000	0.004	0.0005	0.0087	n.a.	n.a
BB-169[(f)]	0.0000	0.0077	0.0000	0.0071	0.0000	0.0088	n.a.	n.a

PBB: polybrominated biphenyl; LB: lower bound; UB: upper bound; w.w: wet weight.
The number of figures after the decimal point does not reflect precision.
(a): Mean (%) fat in original samples: 6.44 %.
(b): Mean (%) fat in original samples: 12.96 %.
(c): Mean (%) fat in original samples: 89.45 %.
(d): Mean (%) fat in original samples: 5.70 %.
(e): Mean (%) fat in original samples: 6.58 %.
(f): Original data on non-*ortho* PBBs were reported with considerably LOQs, therefore the number of digits after the decimal point have been extended to 4 in this table, for descriptive reasons.

5.2.1.1. Fish

The number of studies reporting concentrations of PBBs in edible fish is very limited. The studies selected originate from the UK, Poland and USA. Only studies reporting congener specific data were selected, meaning that studies which reported levels quantified with a technical standard were excluded. Generally, these are studies from before the year 2000. A study from the UK (FSA, 2006a) reported PBB concentrations in a large number of fish, shellfish and crustacean samples obtained in the UK in 2006. They reported data on three non-*ortho* congeners (BB-77, -126 and -169) and the *ortho* congeners BB-15, -49, -52, -80, -101, -153 and -209. In a study by Gieron et al. (2010), edible fish from the Baltic and North Sea were investigated and they reported a smaller set of congeners (BB-29, -49, -52, -101 and -153). The data is presented in Table B1 (Appendix B).

The highest level was observed in lake trout (whole fish) from the Great Lakes in the USA. BB-153 was the predominant congener (189-2,083 pg/g w.w.) in this study, followed by BB-101, -52 and -49 (Luross et al., 2002). Levels in cod livers from Poland were also high (93-313 pg/g for BB-101 and 134-443 pg/g for BB-52) (Gieron et al., 2010). The congeners most frequently detected in the UK study were BB-77, -49, -52, -101 and -153 and the highest concentration was detected in sprat for BB-52 (50 pg/g w.w.) (FSA, 2006a). BB-209, -196, -126, -15 and -80 were only detected in a couple of samples. Päpke et al. (2010) investigated fish (n=4) from Europe for 5 PBBs (BB-30, -52, -101, -153 and -209) and found BB-52 and -101 to be the predominant congeners (mean values 6.1 and 3.0 pg/g w.w., respectively).

Von der Recke and Vetter (2008) analysed the distribution of several hexaBBs (BB-132, -133, -135, -136, -140, -146, -148, -149, -150, -153, -154 and -155) in one mackerel sample from the North Sea and two cod liver samples from the Baltic Sea. BB-155 was the prevalent congener (53-63 %) followed by BB-154. BB-153 contribution was rather low (1.9-8.4 %). The authors stated that it was not possible to determine the concentrations in the samples. Thus, the contribution of the individual

hexabrominated isomers was expressed as contribution to the total amount of hexaBBs. Moreover, some samples were already collected and prepared between 10 and 20 years ago and therefore it can not be ruled out that the patterns might have changed as a consequence of changes in the PBB release into the environment or by metabolism (von der Recke and Vetter, 2008). In contrast, Luross et al. (2002) showed BB-153 being predominant and BB-155 in small amounts in samples from the USA. Von der Recke and Vetter (2008) suggest that this difference may be related to the use of different technical products in the USA and Europe and degradation of more highly brominated technical mixtures used in Europe.

5.2.1.2. Food samples other than fish

Data on PBB occurrence in food samples other than fish are scarce. Gieron et al. (2010) reported mean concentrations of five PBB congeners (BB-29, -52, -49, -101 and -153) in beef, pork and butter samples. None of the examined samples contained PBBs above the limits of detection (LODs) (0.45-1.05 pg/g fat).

Päpke et al. (2010) reported on results for milk samples (n=15) from Northern Europe. No PBBs were found (BB-30, -52, -101, -153 and -209) at LODs between 3 and 60 pg/g w.w.

Tlustos et al. (2008) conducted a surveillance study on the levels of 10 PBB congeners (BB-15, -49, -52, -77, -80, -101, -126, -169, -153 and -209) in pooled samples of avian, bovine, porcine and ovine carcass fat and liver, avian eggs and bovine milk produced in Ireland. PBBs were not detected in milk samples. BB-209 was the predominant congener which occurred in all eggs samples (0.1-2.84 µg/kg fat), in half of avian fat samples (0.03-0.26 µg/kg fat) and in all avian, ovine and porcine liver samples (0.15-0.30 µg/kg fat). BB-126 occurred in bovine and ovine liver only (0.16-0.78 ng/kg fat) and BB-77 was detected in 5 samples with levels close to the LOD (0.05-0.08 ng/kg fat). BB-153 was detected in one ovine liver. The other PBB congeners were not detected.

Nineteen composite food group samples collected from the 2003 and 2004 total diet studies in the UK (FSA, 2006b) were analysed for the PBB congeners BB-15, -49, -52, -77, -80, -101, -126, -153, -169 and -209. Most of the food group samples presented PBB values below the LOD. Non-*ortho* PBBs (BB-77, -126 and -169) showed values above the LOD in "offal" and "sugar and preserves" composite samples. BB-77 concentration were 0.01 ng/kg w.w. in these food groups, while for BB-126 the concentrations were 0.02 and 0.007 ng/kg w.w. for offal and sugar and preserves, respectively. From the remaining congeners (*ortho*-PBBs), BB-153 was the only one detected in "offal" at 0.003 µg/kg w.w. BB-209 was found at values above the LOD in several food groups. The highest values were found in oils and fats (0.11 µg/kg w.w.).

Voorspoels et al. (2007) carried out a market-basket survey and analysed various meat and meat products, eggs, dairy products and fast food for the levels of PBDEs and BB-153 in Belgian food. BB-153 showed values < LOQ in all samples analysed.

5.2.1.3. Effects of processing

Zabik et al. (1978) studied the effects of processing and cooking on PBB residues in milk. Milk from four dairy herds containing less than 0.3 mg PBB/kg fat of physiologically incorporated PBBs was processed individually into cream, skim milk, butter, and stirred curd cheese. Pasteurized and freeze-dried whole milk, skim milk, and cream, spray-dried whole milk and skim milk, and condensed whole milk were also made. PBBs were concentrated in the high-fat products. Spray-drying reduced PBBs in whole milk and skim milk while pasteurization, freeze-drying, aging of cheese, and condensation were not effective. To study the effect of cooking on PBB levels, thigh meat, thigh skin, drumstick and breast (with skin) from half of chickens fed PBBs were analyzed raw, and pieces from the other halves were analyzed following separate pressure cooking. The level of PBBs expressed as parts per million on a solids basis was lower in the cooked sample than in the corresponding raw piece and part of the

PBBs lost were found in the drip. Recoveries of PBBs in cooked tissue and broth ranged from 68.1 % in the thigh skin to 84.6 % in the drumstick, with approximately two-thirds of the recovered PBBs found in the cooked meat itself. Therefore, pressure cooking resulted in a loss ranging from 36 % for the drumstick to 53 % for the thigh skin (Zabik et al., 1978).

Zabik et al. (1980) also studied the retention and distribution of PBB in raw and cooked beef by roasting beef sirloin tip samples to an internal temperature of 65°C, braising and broiling adductor and semimembranosus steaks to an internal temperature of 77°C, broiling ground round and hamburger patties to 77°C and comparing cooked values with those in the raw. Rounds were obtained from four Holstein cows with known PBB contamination. Significant reductions in PBBs occurred with cooking of all cuts. Roasting sirloin tips reduced the PBBs by 45.7 %. Broiling reduced PBBs as follows: adductor steaks (53.2 %), semimembranosus steaks (71.2 %), ground beef patties (32.3 %) and hamburger patties (31.5 %). Braising reduced PBBs in the adductor steaks by 37.2 % and in the semimembranosus steaks by 34.9 % (Zabik et al., 1980).

In a further paper, 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.

5.2.2. Occurrence in human milk

Eyster et al. (1983) and Jacobson et al. (1984) showed that PBBs can be transferred across the human placenta and into maternal milk. In a cohort of 313 women and their newborn infants residing in counties which were sites of the PBB incident 1973 in Michigan, Jacobson et al. (1984) reported a mean level in human milk of 105.1 ng/g fat. While these analyses were performed with packed column GC and using a technical PBB mixture for quantification without differentiating the various congeners, Krüger et al. (1988) analysed 25 human milk samples congener specific by capillary GC-ECNI-MS from mothers in Germany with no known specific contamination. All samples showed a similar PBB pattern. The highest concentrations were found for hexaBBs and heptaBBs. OctaBBs were only found at traces and nonaBBs (BB-206, -207 and -208) were not detected at an LOD of 0.01 ng/g fat. The predominant congener found was BB-153 with a mean concentration of 1.03 ng/g fat (range: 0.29-2.8, median: 0.75 ng/g fat), followed by BB-187/182 with a mean level of 0.33 (range: 0.07-1.07, median: 0.28 ng/g fat). BB-138 was determined with a mean concentration of 0.11 ng/g fat (range: 0.02-0.39, median: 0.07 ng/g fat).

Recent data on PBB levels in human milk are scarce. Shen et al. (2008) analysed 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.

6. Food consumption

6.1. EFSA's Comprehensive European Food Consumption Database

In most of the latest EFSA opinions concerning contaminants, the EFSA Concise European Food Consumption database was used in order to assess exposure. The Concise database was operational since 2008 and contained information from individual dietary surveys from the majority of EU Member States. However, it was intended to be used as a screening tool for exposure assessment as well as a first step towards generating a more comprehensive database.

As a next step, EFSA established in 2010 the "Comprehensive European Food Consumption Database" (Merten et al., in press). This is built on existing information for adults and children at a detailed level. Through a procurement project (DPPA/EFSA/DATEX/2008) 20 Member States provided food consumption data at the individual level to EFSA collected within the most recent national dietary surveys including the adult population (Table D1 and D2, in Appendix D). All food consumption data were codified according to the FoodEx classification system which has been developed by the DATEX Unit in 2009.

However, like the Concise European Food Consumption database, the "Comprehensive European Food Consumption Database" still includes methodological differences making these data not fully suitable for country-to-country comparisons.

Overall, the food consumption data gathered at EFSA in the Comprehensive European food consumption database are the most complete and detailed data currently available in the EU. Thanks to the detailed structure of the food classification (FoodEx) the "Comprehensive European Food Consumption Database" will allow intake estimation from more detailed food categories than using the Concise Database.

For calculating PBB exposure, food consumption and body weight data at the individual level were accessed in the "Comprehensive European Food Consumption Database".

6.2. Food consumption data for specific age and consumers group

Infants and young children are often more highly exposed to chemicals than adults when considering the food intake in relation to their body weight.

Estimating the potential PBB exposure for infants from human milk and infant formula requires information about the quantity of liquid consumed per day and the duration over which such consumption occurs. According to the Institute of Medicine of the U.S. National Academies of Sciences (IOM), average human milk consumption is about 750-800 g per day (range, 450-1,200 g per day) for the first 4-5 months of life. Infant birth weight and nursing frequency have been shown to influence consumption (IOM, 1991). The WHO related human milk consumption to body weight rather than age with an estimated 125 mL/kg or 763 mL for a 3 month old child weighing 6.1 kg (Onyango et al., 2002). According to the German DONALD study, mean consumption of infant formula for a three month old child weighing on average 6.1 kg, was 780 mL per day with a 95th percentile consumption of 1,060 mL per day (Kersting et al., 1998). A common mean of 800 mL per day is used in this opinion for consumption of human milk and infant formula when calculating exposure, with a high of 1,200 mL per day.

Within the Comprehensive European Food Consumption Database, detailed food consumption data for children are also included. In particular, results from consumption surveys from 13 different Member States for children gathered by means of the EFSA Article 36 project "Individual food consumption data and exposure assessment studies for children" (acronym EXPOCHI) (Huybrechts et al., in press) were incorporated in the database. All food consumption data were collected from infants to children of 18 years old and grouped according to the following ranges of age: 0 to 1 year old, 1 to 3 years old,

3 to 6 years old, 6 to 10 years old and from 10 to 18 years old.[18] Consumption records were codified according to the FoodEx classification system which has been developed by the DATEX Unit in 2009. The consumption data for children from the Comprehensive European Food Consumption Database (including the EXPOCHI data) are used in this opinion for the estimation of PBBs dietary intake of children according to the different age groups.

Due to the comparatively elevated PBB contamination levels of fish and seafood products, specific diet characterised by high fish consumption might lead to higher dietary intake for this population in the long term. Therefore, the 95th percentiles of fish and seafood consumers across countries are retrieved from the Comprehensive European Food Consumption Database and considered for exposure assessment estimation.

Additionally, among the high fish consumers, people who might consume fish every day (with particular focus on "Fish meat" only, regardless of the fish species; FoodEx level 2) like fishermen or fish sellers might be at even higher risk. In order to estimate the dietary intake of PBBs for this specific scenario, a daily consumption of 179 g of fish meat eaten by the European population was retrieved from the Comprehensive European Food Consumption Database. This value was identified as the 95th percentile of consumers only by selecting the dietary surveys with more than one day dietary record, where more than 50 individuals participated in the survey.

Another group of people that might have an elevated PBB intake are consumers of food supplements, especially if these consist of fish oil capsules or fish liver oil. Since the consumption recommended on the package varies according to the different brands (e.g. one tea spoon or one table spoon), the CONTAM Panel assumed a maximum daily consumption of 15 mL of fish oil for the exposure estimate to cover a worst case scenario.

7. Human exposure assessment

7.1. Current estimates of mean and high dietary exposure to PBBs for adults

For this opinion the mean and the 95th percentile of the dietary PBB exposure (pg/kg b.w. per day) by food category were calculated separately for each country for the whole population using consumption data recorded at the individual level from the Comprehensive European Food Consumption Database.

The CONTAM Panel focussed the exposure estimation only on those congeners, in the respective food categories where the proportion of non detects was lower than 80 % i.e."Milk and dairy products", "Meat and meat products (including edible offal)" and "Fish and other seafood (including amphibians, reptiles, snails and insects)") (see Table 9).

Tables 10, 11 and 12 summarise the estimated dietary exposure to PBBs for average and high consumers from fish and seafood, meat and meat products, and milk and dairy products, respectively. The dietary intake was estimated using the LB and UB PBB concentrations. Minimum (MIN), median (MEDIAN) and maximum (MAX) values are reported as estimated across European countries.

The highest exposure to PBBs is due to the consumption of fish and other seafood. Median dietary LB and UB exposure to BB-52 across countries are 1.23 and 1.26 pg/kg b.w. per day, respectively, followed by BB-101 and -49 with an intake from to 2 to 3 times and from 3 to 4 times lower than BB-52, respectively. The median LB and UB estimated exposure across countries for BB-153 is 0.24 and 5.53 pg/kg b.w. per day for average consumers, respectively. These values are considerably

[18] Age classes are defined as follows: 0 to 1 year old refers to infants up to and including 11 months; 1 to 3 years old refers to toddlers from 12 up to and including 35 months of age; 3 to 6 years old refers to children from 36 months up to and including 71 months of age; 6 to 10 years old refers to children from 6 years up to and including 9 years and 11 months; and the last group includes individuals from 10 years up to and including 18 years old.

influenced by the 79 % non detects of the occurrence values reported. This is also demonstrated in the case of high fish consumers, where the median LB and UB exposure estimates for BB-153 are 1.21 and 28.2 pg/kg b.w. per day.

The median exposure to individual non-*ortho* PBBs was always lower than 0.04 pg/kg b.w. per day.

In the case of consumption of meat and meat products, the UB and LB median exposures across countries for BB-52 and BB-101 are below 1 pg/kg b.w. per day for average consumers, and below 2 pg/kg b.w. per day for high consumers.

Consumption of milk and dairy products leads to a median intake across countries for BB-101 of 0.049 and 1.91 pg/kg b.w. per day (LB and UB, respectively), followed by BB-52 with 0.041 and 1.91 pg/kg b.w. per day for average population. For high consumers, the median UB and LB exposure remain below 5 pg/kg b.w. per day for both congeners. Also in these exposure estimates, the almost 50-fold difference between LB and UB highlights the impact of high proportion of non detects (68 %) in the reported occurrence data.

Table 10: Summary statistics of the exposure (pg/kg b.w. per day) to 7 PBB congeners for average and high consumers (95th percentile) from the food category of "Fish and other seafood (including amphibians, reptiles, snails and insects)" (FoodEx level 1).

Summary statistics of exposure (pg/kg b.w. per day) to PBBs from "Fish and other seafood (including amphibians, reptiles, snails and insects)"						
PBB congeners	**MIN**		**MEDIAN**		**MAX**	
	LB	**UB**	**LB**	**UB**	**LB**	**UB**
Average consumers						
BB-49	0.16	0.18	0.39	0.45	1.49	1.72
BB-52	0.51	0.52	1.23	1.26	4.74	4.88
BB-101	0.19	0.22	0.46	0.54	1.76	2.10
BB-153	0.10	2.28	0.24	5.53	0.91	21.3
BB-77[(a)]	0.002	0.003	0.005	0.007	0.019	0.026
BB-126[(a)]	<0.001	0.001	<0.001	0.003	0.001	0.010
BB-169[(a)]	0.000	0.001	0.000	0.003	0.000	0.010
95th percentile consumers						
BB-49	0.98	1.13	1.97	2.28	3.84	4.43
BB-52	3.11	3.2	6.27	6.45	12.2	12.6
BB-101	1.15	1.38	2.32	2.78	4.52	5.41
BB-153	0.6	14	1.21	28.2	2.35	55
BB-77[(a)]	0.012	0.017	0.025	0.034	0.049	0.066
BB-126[(a)]	<0.001	0.006	0.001	0.013	0.001	0.025
BB-169[(a)]	0.000	0.007	0.000	0.013	0.000	0.026

b.w.: body weight; PBB: polybrominated biphenyl; LB: lower bound; UB: upper bound; MIN: minimum values; MEDIAN: median values; MAX: maximum values.

(a): Original occurrence data on non-*ortho* PBBs were reported in ng/kg, therefore the number of digits after the decimal point have been extended to 3 in this table, for descriptive reasons.

Table 11: Summary statistics of the exposure (pg/kg b.w. per day) to 5 PBB congeners for average and high consumers (95th percentile) from the food category of "Meat and meat products (including edible offal)" (FoodEx level 1).

Summary statistics of exposure (pg/kg b.w. day) to PBBs from "Meat and meat products (including edible offal)"						
PBB congeners	**MIN**		**MEDIAN**		**MAX**	
	LB	**UB**	**LB**	**UB**	**LB**	**UB**
Average consumers						
BB-52	0.06	0.45	0.10	0.74	0.22	1.58
BB-101	0.06	0.45	0.10	0.74	0.22	1.58
BB-77[(a)]	<0.001	0.006	<0.001	0.010	0.001	0.022
BB-126[(a)]	0.005	0.012	0.008	0.020	0.018	0.043
BB-169[(a)]	0.000	0.009	0.000	0.015	0.000	0.031
95th percentile consumers						
BB-52	0.13	0.88	0.25	1.76	0.55	3.85
BB-101	0.13	0.88	0.25	1.76	0.55	3.85
BB-77[(a)]	<0.001	0.013	0.001	0.025	0.002	0.055
BB-126[(a)]	0.010	0.024	0.020	0.048	0.044	0.105
BB-169[(a)]	0.000	0.017	0.000	0.035	0.000	0.076

b.w.: body weight; PBB: polybrominated biphenyl; LB: lower bound; UB: upper bound; MIN: minimum values; MEDIAN: median values; MAX: maximum values.

(a): Original occurrence data on non-*ortho* PBBs were reported in ng/kg, therefore the number of digits after the decimal point have been extended to 3 in this table, for descriptive reasons.

Table 12: Summary statistics of the exposure (pg/kg b.w. per day) to 5 PBB congeners for average and high consumers (95th percentile) from the food category of "Milk and dairy products" (FoodEx level 1).

Summary statistics of exposure (pg/kg b.w. day) to PBBs from "Milk and dairy products"						
PBB congeners	**MIN**		**MEDIAN**		**MAX**	
	LB	**UB**	**LB**	**UB**	**LB**	**UB**
Average consumers						
BB-52	0.02	1.05	0.04	1.91	0.01	3.59
BB-101	0.03	1.06	0.05	1.91	0.09	3.61
BB-77[(a)]	0.000	0.009	0.000	0.017	0.000	0.032
BB-126[(a)]	0.000	0.008	0.000	0.014	0.000	0.027
BB-169[(a)]	0.000	0.013	0.000	0.024	0.000	0.044
95th percentile consumers						
BB-52	0.07	3.16	0.10	4.84	0.18	8.35
BB-101	0.08	3.17	0.12	4.86	0.21	8.38
BB-77[(a)]	0.000	0.028	0.000	0.043	0.000	0.074
BB-126[(a)]	0.000	0.023	0.000	0.036	0.000	0.062
BB-169[(a)]	0.000	0.039	0.000	0.060	0.000	0.103

b.w.: body weight; PBB: polybrominated biphenyl; LB: lower bound; UB: upper bound; MIN: minimum values; MEDIAN: median values; MAX: maximum values.

(a): Original occurrence data on non-*ortho* PBBs were reported in ng/kg, therefore the number of digits after the decimal point have been extended to 3 in this table, for descriptive reasons.

The median LB daily intake of the non-*ortho* congeners (BB-77, -126 and -169) for average and high consumers is below 0.01 pg/kg b.w. per day and 0.025 pg/kg b.w. per day, respectively, for all food categories. The corresponding UB dietary intakes are below 0.024 and 0.06 pg/kg b.w. per day.

In the case of fish and other seafood, BB-77 is the predominant non-*ortho* substituted PBB congener with LB and UB exposures for average and high consumers of 0.005 and 0.007 and, accordingly, 0.025 and 0.034 pg/kg b.w. per day.

While the LB dietary exposure for BB-126 for fish and other seafood as well as milk and dairy products is below 0.001 pg/g kg b.w per day, the respective intake for meat and meat products is estimated as 0.02 pg/kg b.w. per day.

For BB-169 all occurrence results were reported as non detects with very low LODs (see chapter 5.1.4.) and thus the potential exposure based on these data is negligible.

Tables E1, E2, E3, E4, E5 and E6 (Appendix E) describe in more detail the dietary intake of the 7 PBBs congeners for each respective broad food category of the FoodEx system across European countries for average and high consumers.

7.2. Dietary exposure to specific sub-groups of the population

7.2.1. Infants (less that 1 year old)

Breast-fed infants

For the exposure assessment of infants below six months of age, a value of three months was selected, equivalent to a weight of about 6.1 kg, with an estimated average daily consumption of about 800 g, and a high consumption of 1,200 g of human milk and/or infant formula (see chapter 6.2.). Moreover, an average fat content of 3.5 % for human milk was considered.

Based on the recent Danish and Finnish data on PBB contamination of human milk (see chapter 5.2.2.) the mean daily exposure to BB-153 for infants with an average milk consumption in Denmark and Finland ranges from 0.19-6.9 (mean: 0.92) and 0.12-5.5 (mean: 0.62) ng/kg b.w., respectively. For infants with a high human milk consumption the respective daily exposure ranges from 0.28-10.3 (mean: 1.4) and 0.18-8.3 (mean: 0.92) ng/kg b.w., respectively. These ranges are around 10-20 % higher when also the other PBB congeners are included that were determined in the human milk samples.

Infants fed ready-to-eat meals

No data were reported for the food category “Milk based infant formula”. Only 17 samples described as “Ready-to-eat meal for infants and young children” and 3 samples from the general category of “Food for infants and small children” were analysed for the presence of BB-3, -15, -29, -49, -103, -153, -180, -194 and -206. Only two analytical results for BB-15 and one result for BB-180 were quantified values. For all the other congeners, the reported values were below the LOD/LOQ with an overall median across the reported LOQs of 2.2 pg/g w.w.

Despite the high proportion of non detects, the CONTAM Panel decided to estimate the exposure to BB-153 for infants from 0 to 1 years old, by using the available consumption data from the Comprehensive European Food Consumption Database (including EXPOCHI data). Only two consumption surveys reported dietary habits for children younger than 1 year, therefore the exposure estimate should be considered as not representative of the European children population. Additionally, the available occurrence data were limited to “Ready-to-eat meal for infants and young children”.

Taking into account all the above mentioned limitations, and considering also that the LB exposure is zero for both exposure assessments, the UB exposure of BB-153 was estimated to be 0.17 and 0.64 ng/kg b.w. day across the two consumption surveys.

7.2.2. Children (1-18 years old)

Individual food consumption data from 13 different Member States for children were combined with the PBB means concentration data (LB and UB) for the estimation of the PBB intake across different age groups (0 to 1 year old, 1 to 3 years old, 3 to 6 years old, 6 to 10 years old and from 10 to 18 years old). Not all Member States provided consumption information for all age groups or in certain cases more than one consumption survey was provided by the same country. Details are given in Tables 13, 14 and 15 on the number of surveys and the number of individuals included in the exposure assessment depending on the age group.

Tables 13, 14, 15 summarise the estimations of exposure to PBB congeners from the consumption of certain food categories of the FoodEx system as defined previously for the adults exposure assessment ("Milk and dairy products", "Meat and meat products (including edible offal)", "Fish and other seafood (including amphibians, reptiles, snails and insects)").

Children from 1 to 3 years old have higher exposure to PBBs from the consumption of milk and dairy products where the median average intake, in particular of BB-52 and -101, calculated across different dietary surveys is 4 times higher than for adults (0.34 and 16.09 pg/kg b.w. per day for LB and UB for BB-52, and accordingly 0.41 and 16.16 pg/kg b.w. per day for LB and UB for BB-101).

On the contrary, probably due to change of the dietary habits, the age class from 3 to 6 years old is the most exposed to PBBs from the consumption of fish and seafood and of meat and meat products. The consumption of products from the these last two food categories leads to an average median intake of BB-52 and -101 across European dietary surveys which is almost double than the corresponding exposure estimates for adults.

The estimated dietary exposure to non-*ortho* PBBs was higher than 0.1 pg/kg b.w. per day only for consumption of milk and dairy products and especially for 1 to 6 years old children. The highest UB exposure was estimated for BB-169 (although all occurrence data were reported as non detects, i.e. LB exposure equals zero pg/kg b.w. per day), in the case of 95th percentile consumer of milk and dairy products within children of 1 to 3 years old.

Table 13: "Fish and other seafood (including amphibians, reptiles, snails and insects)" (FoodEx level 1). Summary statistics of the exposure (pg/kg b.w. per day) to 7 PBB congeners for average and high children consumers (95th percentile). The dietary intake was estimated using the lower (LB) and upper (UB) bound PBB concentrations. Minimum (MIN), median (MEDIAN) and maximum (MAX) values are reported as estimated across consumption surveys (N surveys) in European countries. The total number of individuals participating at the surveys in each age group is also reported (N individuals).

Average exposure to 7 PBB congeners (pg/kg b.w.per day) from Fish and other seafood (including amphibians, reptiles, snails and insects)																	
				BB-49		BB-52		BB-101		BB-153		BB-77		BB-126		BB-169	
Age class (years)	N surveys	N Subjects		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
1-3	10	1,679	MIN	0.03	0.04	0.11	0.11	0.04	0.05	0.02	0.49	0.00	0.00	0.00	0.00	0.00	0.00
			MEDIAN	0.54	0.62	1.71	1.76	0.63	0.76	0.33	7.7	0.01	0.01	0.00	0.00	0.00	0.00
			MAX	3.30	3.81	10.5	10.8	3.89	4.65	2.02	47.3	0.04	0.06	0.00	0.02	0.00	0.02
3-6	16	4,603	MIN	0.15	0.18	0.49	0.50	0.18	0.22	0.09	2.21	0.00	0.00	0.00	0.00	0.00	0.00
			MEDIAN	0.76	0.88	2.44	2.50	0.9	1.08	0.47	11	0.01	0.01	0.00	0.01	0.00	0.01
			MAX	2.49	2.88	7.94	8.17	2.94	3.52	1.53	35.7	0.03	0.04	0.00	0.02	0.00	0.02
6-10	17	4,230	MIN	0.26	0.31	0.84	0.87	0.31	0.37	0.16	3.79	0.00	0.00	0.00	0.00	0.00	0.00
			MEDIAN	0.57	0.65	1.80	1.86	0.67	0.80	0.35	8.12	0.01	0.01	0.00	0.00	0.00	0.00
			MAX	1.95	2.25	6.21	6.38	2.3	2.75	1.19	27.9	0.02	0.03	0.00	0.01	0.00	0.01
10-18	20	7,226	MIN	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
			MEDIAN	0.45	0.52	1.44	1.48	0.53	0.64	0.28	6.46	0.01	0.01	0.00	0.00	0.00	0.00
			MAX	1.26	1.46	4.01	4.13	1.49	1.78	0.77	18.1	0.02	0.02	0.00	0.01	0.00	0.01
95th percentile exposure to 7 PBB congeners (pg/kg b.w. per day) from fish and other seafood (including amphibians, reptiles, snails and insects)																	
Age class (years)	**N surveys**	**N Subjects**		**LB**	**UB**	**LB**	**UB**	**LB**	**UB**	**LB**	**UB**	**LB**	**UB**	**LB**	**UB**	**LB**	**UB**
1-3	10	1,679	MIN	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
			MEDIAN	2.91	3.36	9.26	9.53	3.43	4.1	1.78	41.7	0.04	0.05	0.00	0.02	0.00	0.02
			MAX	23.6	27.2	75.1	77.2	27.8	33.2	14.4	338	0.30	0.40	0.01	0.16	0.00	0.16
3-6	16	4,603	MIN	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
			MEDIAN	3.28	3.79	10.4	10.7	3.87	4.63	2.01	47	0.04	0.06	0.00	0.02	0.00	0.02
			MAX	8.58	9.91	27.3	28.1	10.1	12.1	5.25	123	0.11	0.15	0.00	0.06	0.00	0.06
6-10	17	4,230	MIN	1.70	1.97	5.42	5.58	2.01	2.4	1.04	24.4	0.02	0.03	0.00	0.01	0.00	0.01
			MEDIAN	2.53	2.93	8.07	8.3	2.99	3.57	1.55	36.3	0.03	0.04	0.00	0.02	0.00	0.02
			MAX	6.34	7.32	20.2	20.8	7.47	8.94	3.88	90.8	0.08	0.11	0.00	0.04	0.00	0.04
10-18	20	7,226	MIN	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
			MEDIAN	1.9	2.19	6.04	6.21	2.24	2.67	1.16	27.2	0.02	0.03	0.00	0.01	0.00	0.01
			MAX	4.11	4.76	13.1	13.5	4.85	5.8	2.52	59	0.05	0.07	0.00	0.03	0.00	0.03

Table 14: "Meat and meat products (including edible offal)" (FoodEx level 1). Summary statistics of the exposure (pg/kg b.w. per day) to 5 PBB congeners for average and high children consumers (95th percentile). The dietary intake was estimated using the lower (LB) and upper (UB) bound PBB concentrations. Minimum (MIN), median (MEDIAN) and maximum (MAX) values are reported as estimated across consumption surveys (N surveys) in European countries. The total number of individuals participating at the surveys in each age group is also reported (N individuals).

	Average exposure to 5 PBB congeners (pg/kg b.w.per day) from meat and meat products (including offal)												
				BB-52		BB-101		BB-77		BB-126		BB-169	
Age class (years)	N surveys	N Subjects		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
1 -3	10	1,679	MIN	0.10	0.69	0.10	0.69	0.00	0.01	0.01	0.02	0.00	0.01
			MEDIAN	0.20	1.39	0.20	1.39	0.00	0.02	0.02	0.04	0.00	0.03
			MAX	0.42	2.98	0.42	2.98	0.00	0.04	0.03	0.08	0.00	0.06
3 -6	16	4,603	MIN	0.10	0.69	0.10	0.69	0.00	0.01	0.01	0.02	0.00	0.01
			MEDIAN	0.23	1.66	0.23	1.66	0.00	0.02	0.02	0.05	0.00	0.03
			MAX	0.37	2.62	0.37	2.62	0.00	0.04	0.03	0.07	0.00	0.05
6 -10	17	4,230	MIN	0.09	0.67	0.09	0.67	0.00	0.01	0.01	0.02	0.00	0.01
			MEDIAN	0.14	1.01	0.14	1.01	0.00	0.01	0.01	0.03	0.00	0.02
			MAX	0.30	2.12	0.30	2.12	0.00	0.03	0.02	0.06	0.00	0.04
10-18	20	7,226	MIN	0.06	0.41	0.06	0.41	0.00	0.01	0.00	0.01	0.00	0.01
			MEDIAN	0.12	0.82	0.12	0.82	0.00	0.01	0.01	0.02	0.00	0.02
			MAX	0.24	1.69	0.24	1.69	0.00	0.02	0.02	0.05	0.00	0.03
	95th percentile exposure to 5 PBB congeners (pg/kg b.w. per day) from meat and meat products (including offal)												
Age class (years)	N surveys	N Subjects		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
1 -3	10	1,679	MIN	0.28	1.95	0.28	1.95	0.00	0.03	0.02	0.05	0.00	0.04
			MEDIAN	0.39	2.78	0.39	2.78	0.00	0.04	0.03	0.08	0.00	0.05
			MAX	1.12	7.91	1.12	7.91	0.00	0.11	0.09	0.22	0.00	0.16
3 -6	16	4,603	MIN	0.27	1.93	0.27	1.93	0.00	0.03	0.02	0.05	0.00	0.04
			MEDIAN	0.42	2.97	0.42	2.97	0.00	0.04	0.03	0.08	0.00	0.06
			MAX	0.90	6.35	0.90	6.35	0.00	0.09	0.07	0.17	0.00	0.13
6 -10	17	4,230	MIN	0.22	1.56	0.22	1.56	0.00	0.02	0.02	0.04	0.00	0.03
			MEDIAN	0.36	2.52	0.36	2.52	0.00	0.04	0.03	0.07	0.00	0.05
			MAX	0.69	4.90	0.69	4.90	0.00	0.07	0.06	0.13	0.00	0.10
10-18	20	7,226	MIN	0.10	0.69	0.10	0.69	0.00	0.01	0.01	0.02	0.00	0.01
			MEDIAN	0.25	1.78	0.25	1.78	0.00	0.03	0.02	0.05	0.00	0.04
			MAX	0.56	3.94	0.56	3.94	0.00	0.06	0.05	0.11	0.00	0.08

Table 15: "Milk and dairy products" (FoodEx level 1). Summary statistics of the exposure (pg/kg b.w. per day) to 5 PBB congeners for average and high children consumers (95th percentile). The dietary intake was estimated using the lower (LB) and upper (UB) bound PBB concentrations. Minimum (MIN), median (MEDIAN) and maximum (MAX) values are reported as estimated across European countries.

	Average exposure to 5 PBB congeners (pg/kg b.w. per day) from milk and dairy products											
				BB-52		BB-101		BB-77		BB-126		BB-169	
Age class (years)	N surveys	N Subjects		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
1 -3	10	1,679	MIN	0.25	11.5	0.29	11.6	0.00	0.10	0.00	0.09	0.00	0.14
			MEDIAN	0.34	16.1	0.41	16.2	0.00	0.14	0.00	0.12	0.00	0.20
			MAX	0.47	22	0.56	22.1	0.00	0.20	0.00	0.16	0.00	0.27
3 -6	16	4,603	MIN	0.18	8.35	0.21	8.38	0.00	0.07	0.00	0.06	0.00	0.10
			MEDIAN	0.25	11.6	0.3	11.7	0.00	0.10	0.00	0.09	0.00	0.14
			MAX	0.46	21.5	0.55	21.5	0.00	0.19	0.00	0.16	0.00	0.27
6 -10	17	4,230	MIN	0.07	3.15	0.08	3.16	0.00	0.03	0.00	0.02	0.00	0.04
			MEDIAN	0.18	8.42	0.21	8.45	0.00	0.07	0.00	0.06	0.00	0.10
			MAX	0.35	16.3	0.42	16.4	0.00	0.14	0.00	0.12	0.00	0.20
10-18	20	7,226	MIN	0.04	1.73	0.04	1.74	0.00	0.02	0.00	0.01	0.00	0.02
			MEDIAN	0.07	3.42	0.09	3.44	0.00	0.03	0.00	0.03	0.00	0.04
			MAX	0.13	6.27	0.16	6.29	0.00	0.06	0.00	0.05	0.00	0.08
	95th percentile_ exposure to 5 PBB congeners (pg/kg b.w.per day) from milk and dairy products												
Age class (years)	N surveys	N Subjects		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
1 -3	10	1,679	MIN	0.52	24.2	0.62	24.3	0.00	0.22	0.00	0.18	0.00	0.30
			MEDIAN	0.69	32.1	0.82	32.3	0.00	0.29	0.00	0.24	0.00	0.40
			MAX	1.19	55.8	1.42	56	0.00	0.50	0.00	0.41	0.00	0.69
3 -6	16	4,603	MIN	0.32	14.8	0.38	14.8	0.00	0.13	0.00	0.11	0.00	0.18
			MEDIAN	0.51	23.7	0.6	23.8	0.00	0.21	0.00	0.18	0.00	0.29
			MAX	0.83	38.7	0.99	38.9	0.00	0.34	0.00	0.29	0.00	0.48
6 -10	17	4,230	MIN	0.17	7.99	0.2	8.03	0.00	0.07	0.00	0.06	0.00	0.10
			MEDIAN	0.38	17.7	0.45	17.8	0.00	0.16	0.00	0.13	0.00	0.22
			MAX	0.57	26.8	0.68	26.9	0.00	0.24	0.00	0.20	0.00	0.33
10-18	20	7,226	MIN	0.04	1.85	0.05	1.86	0.00	0.02	0.00	0.01	0.00	0.02
			MEDIAN	0.17	7.72	0.2	7.75	0.00	0.07	0.00	0.06	0.00	0.10
			MAX	0.29	13.4	0.34	13.5	0.00	0.12	0.00	0.10	0.00	0.17

7.2.3. People following specific diets

7.2.3.1. High and frequent fish consumers

High consumption of fish is considered as a special diet with specific concern of PBB exposure. Details on the 95th percentile consumers of fish are reported in Table 10.

Furthermore, among the high fish consumers, people who might consume fish every day (with particular focus on "Fish meat" consumption), like e.g. fishermen or fish sellers, might be at even higher risk. In the case of these frequent and high consumers of fish meat, a daily fish consumption (179 g per day) was retrieved from the Comprehensive European Food Consumption Database, as described in chapter 6.2. and combined with the PBB occurrence values of fish meat, grouped according to the fat content (as described in Table 8). The exposure estimations reported in Table 16 are calculated assuming 60 kg as b.w.

Table 16: Exposure estimations (pg/kg b.w. per day) to 7 PBB congeners for high and frequent consumers of fish meat (FoodEx level 2) grouped according to the reported fat content in the original samples (>8 % fat, 8 % >fat > 2 %, < 2 % fat). The dietary intake was estimated using the lower (LB) and upper (UB) bound PBB concentrations.

Dietary exposure to PBBs for high and frequent fish consumers (pg/kg b.w. per day)						
	>8 % fat		8 % >fat > 2 %		< 2 % fat	
PBB congeners	LB	UB	LB	UB	LB	UB
BB-49	9.61	11.2	5.34	5.88	0.95	1.22
BB-52	34.4	35	14.4	14.8	1.70	2.03
BB-101	12.2	14.1	7.01	7.49	0.66	1.22
BB-153	4.33	89	3.31	65.7	0.45	17.3
BB-77	0.060	0.090	0.030	0.030	<0.001	<0.001
BB-126	<0.001	0.030	<0.001	0.030	<0.001	0.030
BB-169	0.000	0.030	0.000	0.030	0.000	0.030

b.w.: body weight; PBB: polybrominated biphenyl; LB: lower bound; UB: upper bound.

7.2.3.2. Consumption of food supplements

Additional intake of PBBs could also derive from high consumption of products for special nutritional use, and in particular "Supplements containing special fatty acids (e.g. omega-3, essential fatty acids)". These types of supplements are mainly based on fish oil derived from the tissues of oily fish. Fish liver is also an important primary source for the preparation of supplements, and in particular cod liver, sold as liquid oil or capsules.

A selection of 10 to 14 samples reported as "Supplements containing special fatty acids (e.g. omega-3, essential fatty acids)" (FoodEx level 4), were done among those congeners with less than 80 % non detects. In Table 17 the LB and UB mean concentrations of BB-49, -52, -77, -101 and -153 are reported. No specific information on the product form was provided (capsules or liquid). In order to cover the worst case scenario, a maximum daily consumption of 15 mL of fish oil for the exposure estimate to the listed congeners was assumed (see chapter 6.2.). Exposure estimates reported in Table 17 are made assuming 60 kg as b.w.

The highest intake of PBBs from "Supplements containing special fatty acids (e.g. omega-3, essential fatty acids)" is due to BB-153 with up to 18.9 pg/kg b.w. day (mean UB), followed by BB-49 (10.4 pg/kg bw.w day), BB-101 (4.8 pg/kg b.w. day), BB-52 (4.5 pg/kg b.w. day) and BB-77 (0.02 pg/kg b.w. day).

Table 17: Additional exposure to PBBs (BB-49, -52, -77, -101 and -153) (UB and LB) due to the consumption of "Supplements containing special fatty acids (e.g. omega-3, essential fatty acids)" to the base diet. Number of analytical results (N), percentage of non detects (ND (%) and lower and upper bound occurrence means (LB and UB) used for the intake estimation are also reported.

PBB congeners			Mean concentration (pg/g)		Additional intake in pg (assuming 15 mL oil consumption)		Additional intake assuming 60 kg b.w. (pg/kg b.w. day)	
	N	ND (%)	LB	UB	LB	UB	LB	UB
BB-49	14	79	7.86	41.4	118	621	2.0	10.4
BB-52	10	60	12	18	180	270	3.0	4.5
BB-77	10	50	0.04	0.074	0.66	1.11	0.01	0.02
BB-101	10	70	12	19	180	285	3.0	4.8
BB-153	14	57	15	75.7	225	1.14	3.8	18.9

b.w.: body weight; PBB: polybrominated biphenyl; LB: lower bound; UB: upper bound.

7.2.3.3. Vegetarians

PBBs are persistent and lipophilic compounds with low water solubility that bioaccumulate in the food chain. Thus, consumption of food of animal origin represents the main route of human exposure to PBBs. Since PBBs are no longer produced and taking into account the declining levels in the environment and the fact that plant uptake from soil is extremely low, the contamination of food of plant origin is of minor importance. This is substantiated by the occurrence data on PBBs in food samples of plant origin submitted by several member states to EFSA which were almost completely below LOD/LOQ. Consequently, it can be assumed that the dietary PBB exposure for vegetarians is even lower than that for people consuming a mixed diet.

7.3. Summary of dietary sources of human exposure to PBBs

A summary of the dietary sources of PBBs for different groups of the population is shown in Table 18. For children, those food categories with the highest contribution to the estimated exposure are shown. The congeners reported are those where the proportion of non detects was lower than 80 % in the respective food category.

For children of 1-3 years old an UB median for average milk consumers of about 32 pg/kg b.w. per day was estimated. For high consumers this intake was twice as high. For children of 3-6 years old the highest dietary intake stems from fish and other seafood, with an UB median estimate for average consumers of about 15 pg/kg b.w. per day and about 66 pg/kg b.w. per day for high consumers.

For adults, the consumption of fish and other seafood is the main contributor to the exposure to PBBs through the diet, with an UB median intake for the sum of BB-49, -52, -77, -101 and -153 of about 8 pg/kg b.w. per day for average consumers and about 40 pg/kg b.w. per day for high consumers. For high and frequent fish consumers the UB median exposure to the sum of BB-49, -52, -77, -101 and -153 is about 149 pg/kg b.w. per day.

The consumption of food supplements containing special fatty acids would add an additional exposure of about 39 pg/kg b.w. per day (UB median for the sum of BB-49, -52, -77, -101and -153).

With regard to infants, exposure estimates for BB-153 for average and high human milk consuming breast-fed infants is about 920 and 1,400 pg/kg b.w. per day. When fed with ready-to-eat meal, the mean UB intake estimated for BB-153 from two consumption surveys was 0.17 and 0.64 pg/kg b.w. per day, respectively.

Table 18: Overview of daily PBB exposure estimates by different population groups and different food categories.

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.

7.4. Previously reported literature data on dietary PBB intake

The dietary intake of PBBs by UK consumers was estimated based on nineteen composite food group samples collected from the 2003 and 2004 total diet studies in the UK (FSA, 2006b). The PBB congeners analysed were BB-15, -49, -52, -77, -80, -101, -126, -153, -169 and -209. The dietary intake was estimated for non-*ortho* PBBs (i.e. BB-77, -126 and -169) assuming the same TEFs as for the corresponding PCB congeners. For average adult consumers, the estimated total dietary intake was 0.002 and < 0.01 pg TEQ/kg b.w. per day for LB and UB, respectively. For high level adult consumers, the values were 0.01 and 0.02 pg TEQ/kg b.w. per day, for LB and UB, respectively. For average toddler consumers, the UB dietary exposure estimate ranged from 0.02 to 0.03 pg TEQ/kg b.w. per day, while for high level toddler consumers, the UB dietary exposure estimate ranged from 0.04 to 0.06 pg TEQ/kg b.w. per day. For average schoolchildren consumers, the UB dietary exposure estimate ranged from <0.01 to 0.02 pg TEQ/kg b.w. per day, while for high level schoolchildren consumers, the UB dietary exposure estimate ranged from 0.01 to 0.03 pg TEQ/kg b.w. per day. These estimates were considered negligible.

7.5. Non-dietary exposure

As the production and use of PBBs in most countries was terminated in the 1970s it is not likely that primary exposure (from production and/or products) today could contribute substantially to the exposure of the general European population. It has however not been possible to identify any current substantial data that can proof this presumption.

8. Hazard identification and characterization

8.1. Toxicokinetics

The knowledge on toxicokinetics of PBBs is mainly based on experimental studies carried out in experimental animals 30 to 40 years ago. These data have been reviewed by Hakk and Letcher (2003) and assessed by ATSDR (2004). A summary of these data is given below.

8.1.1. Absorption

Few quantitative data on gastrointestinal absorption of PBBs exist. The bioavailability of BB-153 was investigated in male rats by comparing its disposition after a single intravenous (*i.v.*) dose (1 mg/kg b.w.), a single oral dose (1 mg/kg b.w.) and multiple oral doses (4 × 1 mg/kg b.w., once daily) of ^{14}C-BB-153 (Tuey and Matthews, 1980). Intestinal absorption was estimated to be approximately 90 %. In similar experiments comparing a single intraperitoneal (*i.p.*) or gavage dose of BB-153 administered to female rats (112 mg/kg b.w. in both cases), Koss et al. (1994) calculated that about 95 % of the oral dose was absorbed. The comparison between these two studies suggests that absorption of this hexaBB congener was relatively independent of the dose. No studies were identified regarding quantitative gastrointestinal absorption of other PBB congeners.

8.1.2. Distribution

Several reports have been published regarding PBB levels in various tissues in rodents experimentally exposed to individual PBBs or PBB mixtures. The levels of radioactivity in adipose tissue, skin, muscle and liver were measured for 6 weeks after *i.v.* administration of ^{14}C-BB-153 (1 mg/kg b.w.) to male Sprague-Dawley rats (Matthews et al., 1977). After one day, muscle contained more than 40 % of the radioactivity, while fat, liver and skin contained 26, 12 and 18 % of the administered dose, respectively. Whereas skin concentrations did not change over time, the concentrations in liver and muscle decreased dramatically, and at 7 days, muscle retained only 5 % and the liver less than 2 % of the administered radioactivity. Most of this radioactivity was redistributed to the fat which contained

about 60 % of the dose on day 7. During the subsequent 5 weeks, muscle and liver slowly lost radioactivity while adipose tissue became enriched.

In female Wistar rats treated every other day for 6 weeks with oral doses of 112 mg BB-153/kg b.w., the distribution of the compound 1 day after the last application, indicated an accumulation in adipose tissue up to 5,600 µg/g (Koss et al., 1994). Concentrations in liver, kidney, brain and other tissues were 17-30 times less than adipose tissue. In blood, only 18 µg/mL was detected. In the same experiment, at the end of the treatment period, the animals were kept for a further period of 22.5 months but without supply of the PBB. Eleven months after cessation of treatment, the residues reached a maximum concentration in the adipose tissue followed by a gradual decline of its content to 25-30 % of its maximum value, by the end of the post-dosing period. In the liver, the concentration of BB-153 started to decrease 3 months after cessation of treatment, falling to 10 % of the maximum level by the end of the experiment.

The concentration of PBB in different tissues was determined in rats administered intraperitoneally a single dose of FireMaster BP-6 (10 mg/kg b.w.) (Miceli and Marks, 1981). Groups were killed at 6, 12, 24 and 36 weeks after treatment. Adipose tissue and adrenals contained the highest concentrations of PBBs at all time points, and residues in adipose tissue continued to increase with time, reflecting a redistribution of the residues away from other tissues. Liver, lung, and pituitary gland initially contained high concentrations, which declined quickly between 6 and 12 weeks. Brain, kidney, and spleen contained concentrations of PBBs that were several orders of magnitude lower than the adipose tissue and adrenals.

A single oral dose of ^{14}C-octaBB (congener or composition not specified) was administered by gavage to both male and female Sprague-Dawley rats at a dose of 1 mg/kg b.w. (Norris et al., 1975a). On day 16 post-dosing, radioactivity was found in the adrenals, adipose tissue, heart and skin at levels ranging from 0.14 to 0.25 % of the administered dose per gram of tissue. Lesser amounts were found in liver, pancreas and spleen. In the same study, rats were maintained for 180 days on a diet containing a commercially produced technical OctaBB (containing 45.2 % octaBBs, 47.4 % nonaBBs, 5.7 % decaBB and 1.8 % heptaBBs) providing a dose of 0.1 mg PBB/kg b.w. per day to the animals. At the end of the experiment, the bromine content in liver and adipose tissue was 6 and 40 fold higher compared with controls, respectively.

The placental transfer of PBBs was investigated in rodents and pigs. Pregnant rats were fed diets containing 50 mg FireMaster BP6 (in which BB-153 comprises about 70 %) per kg feed, from day 8 to day 21 of gestation (Rickert et al., 1978). GC-MS analysis of residues, present in pups sacrificed immediately after birth, indicated PBB levels of about 1.6 ± 0.4 µg/g demonstrating transfer via the placenta.

Guinea pigs of approximately 65 days gestation received a single oral dose of Firemaster FF-1 (50 mg/kg b.w.) (Ecobichon et al., 1983). The pregnant animals and their fetuses were killed 2 days later, at term. Tissues (liver, kidney, lung, perirenal fat) were removed for the analysis of BB-153 content by gas-liquid chromatography. Residue levels of about 45 µg/g were found in both maternal and foetal adipose tissue and in foetal liver. Residues in maternal kidney, lung and liver ranged from 4 to 7 µg/g, while in the foetuses levels in the kidney and lung were in the order of 1-2 µg/g. These data demonstrate transfer of PBBs in rodents via the placenta. A similar conclusion was reached in studies carried out in pigs exposed *in utero* (Werner and Sleight, 1981).

In humans, analysis of post-mortem tissue samples from 15 subjects in the Michigan area indicated that renal fat had the highest PBB concentration, followed by adrenal, atheromatous aorta, thymus, pancreas, liver, heart, kidney, lung, brain, skeletal muscle, thyroid, and nonatheromatous aorta (ATSDR, 2004).

8.1.3. Metabolism

Highly brominated PBB congeners can undergo some metabolic transformation in mammals. When BB-153 was administered to rodents, debromination and hydroxylation occurred to a limited extent since small amounts of different unidentified pentaBBs and hydroxylated hexaBB metabolites were isolated from the faeces and, to a lesser extent from the urine of treated animals (Koss et al., 1994). Hydroxylation of highly brominated congeners was also found in dogs (Gardner et al., 1979) and pigs (Kohli and Safe, 1976).

Treatment of rats with 2-, 3- and 4-monoBB resulted in the formation of a series of mono- and di-hydroxylated metabolites which were excreted in urine (Sparling et al., 1980). Similar results were reported for pigs and rabbits (Kohli and Safe, 1976; Kohli et al., 1978). Experiments with deuterated 4-monoBB, resulting in a 1,2-migration of deuterium from the site of hydroxylation to the adjacent carbon atom suggest that the metabolism of this congener involves the formation of an arene oxide (Safe et al., 1978). This metabolic pathway has been described for PCBs and it is known that these reactive intermediates can react with cellular macromolecules.

The major metabolites of diBB found in rabbit and pig excreta treated with BB-15 were mono- and di-hydroxylated diBB, but minor methoxylated metabolites were also observed (Safe et al., 1976; Kohli and Safe, 1976). The authors observed a 1,2-migration of bromine atom which was consistent with the formation of an arene oxide intermediate.

8.1.4. Elimination

In rats, the excretion of a single oral dose of ^{14}C-BB-153 (1 mg/kg b.w.) proceeded largely via the faeces. Elimination was very slow over the first 7 days and was almost negligible thereafter. Cumulative fecal excretion at 1, 7 and 42 days was 0.96 %, 3.3 %, and 6.6 % of dose, respectively, and < 0.1 % cumulative urinary excretion was detected at 7 days (Matthews et al., 1977). In the same set of experiments biliary excretion was studied from 0 to 4 h after *i.v.* administration of ^{14}C-BB-153 (1 mg/kg b.w.). Under these conditions, biliary excretion of radioactivity amounted to 0.68 ± 0.19 % of the dose after 4 hr and less than 4 % of the radioactivity was present as metabolites.

Rats treated by gavage with a single dose of ^{14}C-octaBB (congener or composition not specified) excreted less than 1 % of the administered dose in urine over a 16-day period (Norris et al., 1975a). Within the first 24 h after dosing, 61.9 % of the dose was present in the faeces and by day 16, the recovery amounted to 74 %.

Miceli and Marks (1981) estimated the elimination kinetics of PBBs from rats treated with a single *i.p.* dose of FireMaster BP-6 (10 mg/kg b.w.). Groups of animals were killed at 6, 12, 24, and 36 weeks after exposure. Based on BB-153 quantitation, serum, fat, liver and spleen had apparent first-order elimination kinetics with calculated half-times of 23.1, 69.3, 11.5 and 9.0 weeks, respectively. By extrapolating toxicokinetic results obtained in rats, Tuey and Matthews (1980) estimated the half life of BB-153 in humans to 6.2 years. This half-life is shorter than the 12 years (median, range 4-97 years) calculated by Lambert et al. (1990) for hexaBB and the 10.8 years (median, range 9.2-14.7 years) for total PBBs reported by Rosen et al. (1995) from cohorts of Michigan residents exposed to PBBs in 1973. More recently, Blanck et al. (2000a) estimated the PBB serum decay among women in the Michigan cohort. In women with an initial PBB level < 10 µg/L the median half-life was 12.9 years, whereas in those with > 10 µg/L, the median half-life was 28.7 years.

Whereas faeces is the most important excretory route in nonlactating animals, milk becomes the major route in lactating animals. When FireMaster BP-6 was administered as a single intraruminal dose to lactating cows (5 mg/kg), approximately 23 % of the dose was excreted in the milk at 95 days (Willett and Irving, 1976). Lactation constitutes the most important route of excretion of PBB in lactating women (ATSDR, 2004). PBB levels in human milk on a lipid basis ranged from undetected to

92,667 µg/kg, with a median of 250 µg/kg, in a group of parturient women from Michigan (Eyster et al., 1983).

8.1.5. Pharmacologically-based pharmacokinetic (PBPK) modelling

Tuey and Matthews (1980) developed a flow limited rat PBPK model for BB-153, with distribution between the blood and the tissues being determined by tissue: blood distribution ratios. Included compartments were blood, muscle, skin, liver, a gastrointestinal (GI) tract consisting of the stomach, intestine tissue and intestinal content and a growing adipose tissue compartment. The model (blood:tissue equilibration ratios, elimination from the body) was calibrated on *i.v.* administration of 1 mg/kg b.w. in male rats and a time-course up to 42 days after the administration. The adipose tissue was the main storage site for BB-153 (blood:tissue equilibration ratios: blood: 1, liver: 17, muscle: 5, skin: 57, adipose tissue: 340). The calibrated model was verified on two experiments performed separately. In the first one, rats received one or four 1 mg/kg b.w. doses by gavage, followed by a withdrawal period,and accumulation in adipose tissue, skin, liver, muscle, blood and BB-153 were measured at 1 or 7 days. The second experiment consisted of a repeated *p.o.* study (22 times 0.5 mg/kg b.w. for 30 days). Measurements in the adipose tissue, skin, muscle were carried out at the end of the 30 day exposure period. In the case of the single per oral *p.o.* study a quite acceptable fit of the model to the data was obtained, whereas the model slightly (i.e. less than 2-fold) overestimated tissue accumulation in the repeated *p.o.* study.

Adapting rat physiology to humans, keeping the blood:tissue equilibration ratios at their rat values and scaling elimination allometrically to the three-fourth power of body weight resulted in a human PBPK model with a half-life of 6.2 years.

The human PBPK model was used to simulate the accumulation of BB-153 in the adipose tissue and the blood of humans which had been exposed for 10 months to 0.1 mg BB-153 per day through contaminated cow's milk, followed by a 26 month withdrawal period. Depending on the amount of body fat (lean, average, overweight) simulated concentrations at the end of the withdrawal period amounted 1,103-2,769 µg/kg in adipose tissue and 3.2-8.1 µg/L in the blood. These predicted concentrations were very similar to the data obtained from 10 paired human tissue samples taken in 1977 from Michigan dairy farm residents, approximately 3 years after the suspected major exposure period (Gladen and Rogan, 1979). The BB-153 concentrations in these 10 individuals were 1,300±880 µg/kg and 5±4.6 µg/L, in adipose tissue and blood, respectively.

8.2. Biomarkers of exposure

Data on PBBs in human samples other than human milk at a European level are scarce. Therefore, this chapter describes also studies carried out in countries outside the EU. The majority of the studies were carried out in the USA, mainly focusing on the Michigan cohort, and in China.

Fernández et al. (2007) reported levels of nineteen PBB congeners (BB-18, -22, -29, -31, -38, -37, -49, -52, -53, -56, -75, -77, -80, -101, -103, -153, -154, -155 and -169) in adipose tissue of women living in the South of Spain. A total of twenty samples were analysed by GC-MS. Eight PBB congeners (BB-52, -56, -80, -101, -103, -153, -154 and -155) were found above the LOQ, which ranged from 0.0001 to 0.041 ng/g fat. Median values (ng/g fat) for such congeners were 0.004 (BB-52), 0.002 (BB-56), 0.004 (BB-80), 0.007 (BB-101), 0.002 (BB-103), 0.244 (BB-153), 0.031 (BB-154) and 0.025 (BB-155). BB-153 was the most abundant congener and contributed up to 79 % to the sum of all PBBs analysed. Total PBBs concentration was found to be 0.345 ng/g fat.

Shen et al. (2008) reported concentrations of 13 PBB congeners (BB-4, -31, -37, -49, -52, -77, -80, -101, -103, -126, -153, -155 and -169) and PentaBB and HexaBB, in Danish and Finnish placenta samples (n=168 and 112, respectively). BB-153 and -155 were the two most abundant congeners detected in 100 % and 76.6 % of the samples, respectively. Mean concentrations of BB-153 were

304 and 83 pg/g fat and for Danish and Finnish samples, respectively. Mean concentrations of BB-155 were 448 and 60 pg/g fat, respectively.

Concentrations of BB-153 were determined in paired samples of maternal and umbilical cord blood from 51 Danish mothers (Frederiksen et al., 2010). A total of 51 maternal and 43 umbilical cord plasma samples were analysed (from 8 umbilical cord samples it was not possible to obtain enough volume of blood for the analysis). The percentage of samples with values above the LOQ were 90 % and 50 % for maternal and umbilical cord plasma, respectively, and median (range) concentrations were 181 (<14.6-848) pg/g fat and 68.6 (<29.2-351) pg/g fat, respectively. Highly significant correlations (Sperman rank) were observed by the authors between the concentration of BB-153 in both types of samples.

Sjödin et al. (2004b) published a retrospective time-trend study of BB-153 in archived serum pools from the US (time period: 1985-2002). A significant decreasing trend was found with median values (range) (ng/g fat) of 8.0 (2.6-9.4), 5.3 (1.0-8.6), 4.7 (1.9-10) and 3.3 (1.4-5.5) for the periods 1985-1989 (n=9), 1990-1994 (n=14), 1995-1999 (n=10) and 2000-2002 (n=7), respectively. Serum concentrations (geometric mean) of BB-153 based on the National Health and Nutrition Examination Survey (NHANES) sampling conducted in the years 2003-2004 were 2.3 ng/g fat (95 % confidence interval (CI) 1.8-2.9) (Sjödin et al., 2008).

Serum PBB concentrations were determined in 145 mother-child pairs who were participants in the Michigan Long-Term PBB study (Joseph et al., 2009). The serum concentrations for the mothers (n=112) were determined at enrolment in the study during 1976-1979 and ranged from <LOD-933 µg/L (median, 2 µg/L). For the children (n=145), born from 1973-1982, the serum was analysed during infancy to 17 years old. 73 % of the children had levels <LOD (LOD=1 µg/L) whereas the remaining children had concentrations at or above the LOD (median, 2.9 µg/L).

Zhao et al. (2009) reported levels of 23 PBB congeners (BB-1, -2, -3, -4, -5, -7, -9, -10, -18, -26, -29, -30, -31, -38, -49, -52, -53, -80, -101, -103, -153, -155 and -209) in kidney (n=19), liver (n=55) and lung tissue (n=7) samples from surgical cancer patients living close to electronic waste disassembly sites. Median (range) concentrations for the sum of the PBBs analysed (ng/g fat) were 193.87 (38.86-1137.69), 193.17 (41.90-558.57) and 149.78 (102.40-676.57) for kidney, liver and lung samples, respectively. None of the samples showed BDE-209 levels above the LOD (< 0.80 ng/g fat). Lower brominated congeners such as BB-2, -10, -15 and -30 accounted for more than 59 % of the total PBB content, while BB-153 alone accounted for more than 12 %.

Wang et al. (2010) reported levels of BB-77, -103 and -209 in serum samples of occupationally and non-occupationally exposed people from electronic waste recycling and dismantling activity sites, and their relationship with thyroid hormone levels. Median (range) PBBs concentrations for the sum of the three PBBs analysed were 510.35 (<LOQ-4695.44) ng/g fat for the occupation exposure group (n=239), 613.81 (<LOQ-4048.69) ng/g fat for the non-occupational exposure group (people living around the electronic waste recycling site) (n=93), whereas the levels in the control group (mainly workers in green plantation) (n=116) were 246.03 (<LOQ-5833.52) ng/g fat. In all three groups, BB-77 was the most abundant congener with median levels of 338.89, 442.68 and 184.4 ng/g fat, respectively for the three groups.

8.3. Toxicity

The majority of the studies were conducted with commercial products such as FireMaster FF-1 and BP-6, whereas there are only few studies on the effects of individual congeners. The CONTAM Panel noted that due to batch-to-batch variation in the composition of technical mixtures of PBBs and the precise congener composition is not known, it is difficult to compare the results from different studies using even the same nominal product, e.g. “FireMaster BP-6”.

8.3.1. Lethality after acute exposure

Generally, the LD_{50} values of commercial mixtures were relatively low, with LD_{50} > 1,000 mg/kg b.w. in rats, rabbits and quails. Lethality was reported at lower repeated doses in rats than one single higher exposure (WHO, 1994).

FireMaster BP-6 given for 2 weeks to mice produced 63 % lethality at estimated doses of 130 mg/kg per day, but no lethality at ≤36 mg/kg b.w. per day (ATSDR, 2004).

The calculated LD_{50} of FireMaster FF-1 (Lot No. 1312FT) in rats observed for ≈ 60 days post-treatment (i.e., 90-day lethal dose (LD_{50})) was approximately 150 and 65 mg/kg b.w. per day for male and female rats, respectively. The cause of death was not specified, but metabolic wasting was observed (ATSDR, 2004).

No deaths occurred in rats administered up to 17,000 mg/kg of octaBB (one week observation time) or up to 2,000 mg/kg b.w. (two weeks observation time) or 1,000 mg/kg b.w. (four weeks observation time). In the only study of a decaBB mixture, a single dose at 5,000 mg/kg b.w. caused no deaths in rats observed for 14 days (ATSDR, 2004).

Studies of mortality in different species are most often not directly comparable, but data indicate that minks were more sensitive than other animals tested, and that Guinea pigs were far more susceptible than rats (WHO, 1994).

8.3.2. Sub-chronic and chronic toxicity

8.3.2.1. Endocrine system

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.

Reproductive organs

A summary of the effects of PBBs in the reproductive system is shown in Table 19.

Kimbrough et al. (1981) observed in rats increased incidence of uterine polyps 2 years after single gavage of FireMaster FF-1 (1,000 mg/kg b.w.). Increased cystic endometrial hyperplasia was observed in rats exposed to 1.5 mg/kg b.w. per day FireMaster FF-1 for up to 104 weeks, whereas in mice exposed to ≤ 3.9 mg/kg b.w. per day for up to 105 weeks no changes were observed (NTP, 1993). In rhesus monkeys exposed to 0.3 ppm FireMaster FF-1 (corresponding to 0.015 mg/kg b.w. per day) for 6-7 months prolonged menstrual cycle and lengthened and flattened serum progesterone levels were found, and after mating with control males prolonged implantation bleeding (in 2 of 7 females) and abortion/stillbirths (in 2 of 7 females) were observed (Lambrecht et al., 1978). These effects were not reported at higher dose levels (1.5 or 25 ppm, corresponding to 0.075 or 1.25 mg/kg b.w.). In the study of Allen et al. (1979) in addition to FireMaster FF-1 also 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) (500 ppt) and PCB mixture (Arochlor 1248) (2.5 and 5 ppm) have been studied and the above mentioned reproductive abnormalities occurred after the exposure to all three halogenated aromatic hydrocarbons. The authors suggested that these effects were related to changes in the sex hormones (i.e. progesterone). No histological abnormalities in reproductive organs were observed in male and female rats exposed to FireMaster FF-1 for two weeks at 30 mg/kg b.w. per day (Gupta et al., 1981). Reproductive performance was not affected in male and female mink exposed to up to 0.39 mg/kg b.w. per day of FireMaster FF-1 for 6-7 month before breeding (Aulerich and Ringer, 1979; Ringer et al., 1981).

Table 19: Summary of the effects of PBBs in the reproductive system. ns: not specified.

PBB mixture	Species	Exposure[(a)]	NOEL/LOEL[(b)]	Purity	Effects	Reference
FireMaster FF-1	Rat	Single dose 1000 *p.o.*	LOEL: 1000	ns	• Increased incidence of uterine endometrial polyps detected during the 2 year observations after the exposure	Kimbrough et al., 1981
FireMaster BP-6	Rat Multigeneration study: F0: GD-8 to PND 28; F1: PND 28 through mating and pregnancy up to PND 28 of F2 F2: up to PND 28 of F3	By feeding 10, 100 ppm	NOEL: 100 ppm	ns	• No effect on gestation period, number of offspring in a litter, body weight in the F1 and F2 generations • Increased mortality up to weaning of F1 at 100 ppm	McCormack et al., 1981
FireMaster BP-6	Rat Wistar GD 0-14	Gavage: 28.6; 57.1	LOEL: 28.6	ns	• Blocked impantation in 2 out of 5 females that survived the exposure	Beaudoin, 1979
FireMaster FF-1	Rat: 25 weeks Mouse: 4-5 weeks	Gavage: 10, 30, 100	NOEL: 30	ns	• No histological changes in reproductive organs • Necrosis, hyperplasia metaplasia in epithelial lining of ductus deferens in male rats that died following exposure to 100 mg/kg b.w per day	Gupta and Moore, 1979; Gupta et al., 1981
FireMaster FF-1	Female mink 6-7 months before breeding	Diet: 0.39	NOEL: 0.39	ns	• No effect on reproductive performance	Auerlich and Ringer, 1979; Ringer et al., 1981
FireMaster FF-1	Monkey 6-7 month	Diet: 0.3, 1.5, 25 ppm	-	ns	• Prolonged menstrual cycle (4/7 monkeys) • Lengthened and flattened serum progesterone peak levels • After mating with control males prolonged implantation bleeding (2/7 females) • Effects only reported in lowest dose group (0.3 ppm) and not mentioned at higher dosage groups	Lambrecht et al., 1978
HexaPBB OctaPBB	Rats Sprague Dawley 7 month	Diet: 50 ppm	LOEL: HexaBB: 50 ppm NOEL OctaBB: 50 ppm	ns (Monsanto Co., St Louis, MO)	• Relative increase in wet ovarian weights by HexaBB but not OctaBB	Sepkovic and Byrne, 1984

PBB: polybrominated biphenyl; NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; GD: gestational day; PND: postnatal day; ns: not specified; *p.o.*: per oral.
(a): mg/kg b.w. per day if not stated otherwise.
(b): mg/kg b.w. per day.

Administration of 28.6 or 57.1 mg/kg b.w. per day of FireMaster BP-6 on alternate days between gestational day (GD) 0 and GD14 completely blocked implantation in five of eight female rats that survived the treatment (Beaudoin, 1979). In a multiple generation study FireMaster BP-6 given to rats in the diet (0.5 and 5 mg/kg b.w. per day) from GD8 through PND28 did not affect the reproductive performance in terms of length of gestation and litter size in F1 and F2 (McCormack et al., 1981).

Sepkovic and Byrne (1984) reported increase in wet ovarian weights in rats exposed to 50 ppm of HexaBB, but not OctaPBB in the diet for 7 months.

Disruption of thyroid hormone homeostasis

Animal studies indicate that thyroid hormone homeostasis is a target of PBBs. The observed effects include decreases in serum levels of thyroxine (T4) and serum triiodothyronine (T3) hormones, thyroid enlargement, and effects in the follicular cells including reduced size, hyperplasia with columnar appearance and papillary projections, and accumulation of colloid droplets (Table 20).

Short-term exposure of rats to FireMaster FF-1 at doses up to 1,000 mg/kg b.w. per day for up to 2 weeks or mice to up to 30 mg/kg b.w. per day for 2 weeks did not show any thyroid histological alterations (Kimbrough et al., 1978; 1981; Gupta and Moore, 1979; Gupta et al., 1981). Also chronic exposure of rats to ≤ 1.5 mg/kg b.w. per day FireMaster FF-1 for up to 104 weeks caused no thyroid histological alterations, but thyroid ultrastructural changes and serum thyroid hormones were not assayed in this study (NTP, 1993). FireMaster FF-1 administered to male Sprague Dawley rats for 10 or 20 days by gavage at doses 1, 3 and 6 mg/kg b.w. per day caused a time- and dose-dependent decrease in plasma T4 levels (T3 was not measured), which was after 10 days significant at ≥3 mg/kg b.w per day. After 20 days of administration a decrease of T4 plasma levels were significant at ≥ 1 mg/kg b.w per day, and an increase in thyroid stimulating hormone (TSH) was noted. Furthermore, ^{131}I uptake and increase in iodide in the thyroid gland were noted at 6 mg/kg b.w. per day (Allen-Rowlands et al., 1981). Oral administration of Fire Master FF-1 at 0.3, 1.0, 3.0 and 10 mg/kg b.w. per day to male and female F344/N rats (7-8 weeks old) for 6 months, caused a dose-dependent decrease in serum T3 and T4 (Gupta et al., 1983a). Significant decrease of T4 serum value was observed in males at ≥0.3 mg/kg b.w. per day and in females at ≥1 mg/kg b.w. per day. The extent of decrease in T3 level was slightly smaller than in T4 level, and statistically significant difference was observed only in females at 3 and10 mg/kg b.w. per day group. The authors suggested that the changes could be attributed to enhanced T3 and T4 excretion (Gupta et al., 1983a). A decrease of serum T3 and T4 was observed in rats exposed to FireMaster FF-1 for 25 weeks (NTP, 1983). Thyroid ultrastructural changes were observed in rats exposed to ≥30 mg/kg b.w. per day FireMaster FF-1 for 4-5 weeks (Gupta and Moore, 1979), whereas chronic exposure of rats to ≤ 1.5 mg/kg b.w. per day FireMaster FF-1 for up to 104 weeks caused no thyroid histological alterations, but ultrastructure and serum thyroid hormones were not assayed (NTP, 1993).

Akoso et al. (1982b) reported thyroid ultrastructural changes, increased thyroid weight and decrease in serum T3 and T4 in rats exposed to FireMaster BP-6 by diet (estimated doses 0.05, 0.5 and 5 mg/kg b.w. per day) for 30 days. The ultrastructural changes were dose dependent and included increased number and decreased size of follicles, and extensive follicular changes (hyperplasia and hypertrophy of follicular cells) whereas significant increase in relative thyroid weight, and decrease in serum T3 and T4 were detected at 5 mg/kg b.w. per day. Two studies showed that gestational and postnatal exposure to FireMaster BP-6 causes reduction of serum T3 and T4 in offspring. Exposure of rats to 2.5 mg/kg b.w. per day FireMaster BP-6 in the diet from GD0 to PND15 resulted in reduced serum T4 levels in offspring (Meserve et al., 1992). Serum concentrations of T3 and T4 were significantly reduced also in 4-week-old nursing offspring of swine that were fed ≥1.25 mg/kg b.w. per day FireMaster BP-6 in the diet during the second half of gestation and throughout lactation (Werner and Sleight, 1981).

No histological alterations in the thyroid were observed in rats after dietary exposure to OctaBB up to 71 mg/kg b.w. per day for 4 weeks (Lee et al., 1975; Waritz et al., 1977), and to 1 mg/kg b.w. per day

for 8 months (Norris et al., 1975b), however serum T3 and T4 were not evaluated. Exposure of rats to OctaBB (Monsanto Co., St Louis, MO) at 5, 10 and 50 ppm in diet (equivalent to 0.25, 0.5 or 2.5 mg/kg b.w.) for 5 to 7 months induced neither thyroid histological alterations nor changes in serum T3 and T4 levels (Sepkovic and Byrne, 1984; Byrne et al., 1987). On the other hand, a technical HexaBB mixture (Monsanto Co., St Louis, MO) under the same exposure conditions caused a decrease in serum T3 and T4 (Sepkovic and Byrne, 1984; Byrne et al., 1987). In male juvenile Wistar rats that received a single *i.p.* administration of BB-169 (99 % pure) at 0, 20 and 40 mg/kg b.w. after 28 days a dose dependent decrease of serum T4 but not T3 was observed (Spear et al., 1990). In a later study the same authors reported decrease in total serum T4 measured at 1 to 8 days after injection of a single dose of 20 mg BB-169/kg b.w. to male Wistar rats, and they showed that the decrease was not related to the interference with T4 binding to transthyretin (TTR) transport protein (Spear et al., 1994).

Other endocrine effects

Several studies showed the effects of the exposure to PBBs on sex hormones and adrenal cortex hormones (Table 21).

FireMaster FF-1 administered to male Sprague-Dawley rats for 20 days at doses 1, 3 and 6 mg/kg per day did not cause changes in plasma corticosterone and testosterone levels, however at 6 mg/kg per day a decrease in plasma prolactin level was noted (Castracane et al., 1982). FireMaster BP-6 administered in diet to female Balb/c mice (6 weeks old) for 24 or 30 days at doses 1, 10 or 100 ppm (equivalent to 0.14, 1.4 or 14 mg/kg b.w.) caused a slight increase in plasma corticosterone level at the highest dosage (Fraker, 1980). In female Sprague-Dawley rats fed a diet containing 1, 5, 10 or 50 ppm of FireMaster BP-6 (equivalent to 0.05, 0.25, 0.5 or 2.5 mg/kg b.w.) for 5 to 7 months a dose-dependent decrease in serum corticosterone and dehydroepiandrosterone was noted except at the lowest dose (Byrne et al., 1988).

Adrenal histology was not evaluated in these studies, but other acute and sub-chronic studies with FireMaster BP-6 or FireMaster FF-1 showed no exposure related alterations in rats or mice (Gupta et al., 1981; Kimbrough et al., 1978, 1981; Akoso et al., 1982b; NTP, 1993, 1983). The exceptions are lethal doses (100-1,000 mg/kg b.w. per day FireMaster FF-1 for 4.5 weeks) at which in moribund or dead rats darkened adrenals were observed (Gupta and Moore, 1979).

Table 20: Summary effect of exposure to PBBs on thyroid hormone homeostasis. ns: not specified.

PBB mixture	Species	Exposure[(a)]	NOEL/LOEL[(b)]	Specifications/ Purity	Effects	Reference
FireMaster FF-1	Rat F344/N	Oral: 0.3; 1.0; 3.0; 10 for 6 months	NOEL: 0.1 LOEL: 1 (females) LOEL: 0.3 (males)	FireMaster BP-6 with 2 % calcium trisilicate (Lot No. 1312FT, Batch 03)	• A dose-dependent decrease in serum T3 and T4 • T4: males at ≥ 3.0 mg/kg b.w. per day; females ≥ 1.0 mg/kg b.w. per day. • T3: only females at ≥ 3.0 mg/kg b.w. per day	Gupta et al., 1983a
FireMaster FF-1	Rat F344/N	Oral: 0.1 0.3; 1.0; 3.0; 10 for 6 months	NOEL: 0.1 LOEL: 0.3	FireMaster BP-6 with 2 % calcium trisilicate (Lot No. 1312FT, Batch 03)	• Decrease of serum T4 in male and female • Decrease of serum T3 in female	NTP, 1983
FireMaster FF-1	Rat Sprague-Dawley, male	Gavage: 1, 3, 6 for 10-20 days	LOEL: 1	ns	• Time and dose dependent decrease in plasma T4 • ≥ 1 mg/kg b.w. per day: decreased plasma T4, increased TSH (day 20) • 6 mg/kg b.w. per day: increased ^{131}I thyroid uptake and iodide content.	Allen-Rowlands et al., 1981
FireMaster BP-6	Rat	In diet 0.05; 0.5; 5 for 30 days	NOEL: 0.05 (ultrastructural thyroid changes)	ns	• > 0.05 thyroid ultrastructural changes • At 5 mg/kg b.w. per day decreased serum T3 and T4; increased relative thyroid weight	Akoso et al., 1982b
FireMaster BP-6	Rat	Diet: 2.5 from GD 0 to PND 15	LOEL 2.5	ns	• Reduced T4 serum levels in offspring	Meserve et al., 1992
FireMaster BP-6	Pig female	In diet: 10, 100, 200 ppm (cca 0.125; 1.25; 2.5 mg/kg b.w. per day) during the second half of gestation and lactation	NOEL: 100 (dams) LOEL: 200 (dams) NOEL: 10 (piglets)	ns	• Dams: at 200 ppm decreased serum T3 and T4 • Piglets at birth: at 200 ppm decreased serum T3 and T4 • Piglets 4 weeks after birth: ≥ 100 ppm decreased serum T3 and T4	Werner and Sleight, 1981
HexaBB; OctaBB	Rat Sprague-Dawley female	In diet: 50 ppm for 7 months	NOEL: 50 ppm (OctaBB) LOEL: 50 ppm (HexaBB)	ns (Monsanto Co., St Louis, MO)	• OctaBB: no effect on T3 levels (T4 was not measured) • HexaBB: decrease of serum T3 levels • HexaBB: relative increase in wet thyroid gland weights	Sepkovic and Byrne, 1984

Table 20: Continued

PBB mixture	Species	Exposure[(a)]	NOEL/LOEL[(b)]	Specifications/ Purity	Effects	Reference
HexaBB; OctaBB	Rat Sprague-Dawley female	In diet: 5, 10 ppm for 5 months	NOEL: 5 ppm (OctaBB) LOEL: 5 ppm (HexaBB)	ns (Monsanto Co., St Louis, MO)	• OctaBB: no effect on T3 and T4 levels • HexaBB: decrease of serum T3 and T4 levels	Byrne et al, 1987
BB-169	Juvenile male Wistar Rats	Single *i.p.*: 20, 40	LOEL: 20	BB-169 (99 % pure)	• After 28 days dose dependent decrease in serum T4 but not T3	Spear et al., 1990
BB-169	Male Wistar Rats	Single *i.p.*: 20,	LOEL: 20	BB-169 (99 % pure)	• Decrease in total serum T4 measured at 1, 3, 6, 7 and 8 day after injection. (T3 was not determined)	Spear et al., 1994

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; ns: not specified; GD: gestational day; T3: thyroxine hormone; T4: triiodothyronine hormone; *i.p.*: intraperitoneal.
(a) mg/kg b.w. per day if not stated otherwise.
(b) mg/kg b.w. per day.

Table 21: Summary of effects of PBBs on endocrine system other than thyroid. ns: not specified.

PBB mixture	Species	Exposure [a)]	NOEL/LOEL[(b)]	Purity	Effects	Reference
FireMaster FF-1	Rat Sprague-Dawley	1, 3, 6 *p.o.* for 20 days	LOEL: 6	ns	No changes in plasma corticosterone and testosterone levels Decrease in plasma prolactin at 6 mg/kg b.w. per day.	Castrane et al., 1982
FireMaster BP-6	Female Balb/c mice (6 month old)	1, 10, 100 ppm in diet for 24 to 30 days	NOEL: 10 ppm	ns	Slight increase in plasma corticosterone at the highest dose.	Fraker, 1980
FireMaster BP-6	Sprague-Dawley rats	0.05, 0.25, 0.5, 2.5 (1, 5, 10, 50 ppm) in diet for 5 to 7 months	NOEL: 0.05	ns	Dose-dependent decrease in serum corticosterone and dehydroepiandrosterone levels except at the lowest dose.	Byrne et al., 1988

NOEL: no-observed-effect level. LOEL: lowest-bserved-effect level ns: not specified; *p.o.*: per oral.
(a) mg/kg b.w. per day if not stated otherwise.
(b) mg/kg b.w. per day.

8.3.2.2. Nervous system

Animal and human data provide evidence that PBB exposure causes diverse neurological symptoms and behavioural alterations in locomotor and general activity. Relatively few animal experiments have been performed to characterize the neurotoxic effects of PBBs. That PBBs accumulate in the brain is shown for both the adult (Geller et al., 1979) and developing brain, where exposure occurs *in utero* via placental transfer and postnatally via lactation (Rickert et al., 1978). A summary of the effects of PBBs on the nervous system is shown in Table 22.

Neurodevelopmental effects

The time window of exposure seems to be a critical aspect in PBB-induced developmental neurotoxicity: exposure of dams prior to breeding or during pregnancy did not cause alterations in offspring behaviour. In detail, prenatal exposure of Swiss-Webster mice via dams fed with PBB-contaminated diet (50 or 100 ppm FireMaster, equivalent to 7 or 14 mg/kg b.w.) (congener or composition not specified) from GD8 to GD16 did not affect swimming, righting reflex, locomotor activity or water-maze escape performance in the offspring tested at 7 weeks of age (Preache et al., 1976). Similarly, exposure of female Sprague-Dawley rats to FireMaster FF-1 (0.5 or 5 mg/kg b.w. PBB daily (5 days a week) for 4 weeks via gavage) prior to breeding did not alter behaviour in male offspring which were analysed at 75 days of age by 2-lever operant discrimination tasks (Geller et al., 1985). In contrast, postnatal dietary exposure of mice to FireMaster during lactation from postnatal day (PND) 1 to PND29 (50 or 100 ppm, equivalent to 7 or 14 mg/kg b.w.) resulted in decreased locomotor activity in the pups with a lowest-observed-adverse-effect level (LOAEL) of 100 ppm PBBs (Preache et al., 1976). Different exposure regimens by cross-fostering indicate that exposure via milk is more relevant for the appearance of PBBs in the brain (Rickert et al., 1978).

The offspring of dams exposed to 0.2 and 2 mg/kg b.w. FireMaster BP-6 from GD6-PND24 exhibited behavioural deficits at body fat concentrations similar to those found in highly exposed humans, i.e. highly exposed farmers from the Michigan cohort and workers engaged in the production of FireMaster. The acquisition of forward locomotion was delayed significantly after exposure to 2 mg/kg b.w. FireMaster BP-6, a dose that did not induce maternal toxicity. In addition, a marked difference in the willingness to enter a new environment, suppressed locomotor activity in the open-field, as well as a non-significant trend towards delayed cliff avoidance were reported (Henck et al., 1994).

Neurobehavioural effects in adults

A study performed in Fisher 344/N strain rats (5-6 weeks of age) indicates that oral administration via gavage of FireMaster FF-1 over a time period between 30 days or 6 months leads to behavioural suppression and muscular weakness, as indicated by open field forelimb grip strength and hindlimb response (Tilson and Cabe, 1979). The effects appear sex-specific (spontaneous motor activity was only altered in female rats after daily oral administration of 30 mg/kg b.w. FireMaster FF-1 for 30 days). In contrast, male rats seem to be more vulnerable regarding muscle strength. The LOAEL for males was 3 mg/kg b.w. and for females 10 mg/kg b.w. given over a time period of 6 months. Further, startle responsiveness to an air puff stimulus was decreased with a significant difference in susceptibility between the sexes with a LOAEL of 10 mg/kg b.w. in males and 3 mg/kg b.w. in females after exposure for over 6 months.

Studies in rats have shown that FireMaster FF-1 reduces the neuropharmacological effects of phenobarbital and amphetamine. These effects appear to be the consequence of induction of hepatic drug metabolizing enzymes (Tilson and Cabe, 1979; Geller et al., 1985).

Table 22: Neurobehavioural effects of PBBs.

PBB Mixture	Species	Exposure Time	Exposure Level	LOEL	NOEL	Outcome	Reference
Firemaster[(a)]	Swiss-Webster mice	GD8-GD16	7 or 14 mg/kg b.w. In the diet	-	14 mg/kg b.w.	No adverse effects on: -swimming ability - righting reflex - locomotor activity - water maze escape performance (tested at 7weeks of age)	Preache et al., 1976 (abstract)
FireMaster FF-1	Holtzman Sprague-Dawley rats	Prior breeding	0.5 mg/kg b.w. and 5 mg/kg b.w. for 4 weeks with 5 days a week	-	5 mg/kg b.w.	No effects on male offspring tested by 2-lever operant discrimination task (tested PND75)	Geller et al., 1985
FireMaster BP-6	Sprague-Dawley rats	GD6-PND24	0.2 mg/kg b.w., 2 mg/kg b.w.	-	0.2 mg/kg b.w.	- significant delay in the acquisition of forward locomotion (tested on PND1 and terminated on acquisition - trend towards delayed cliff avoidance (PND2 till day of acquisition), suppressed locomotor activity in open-field (PND12, 14-20, 22, 24) and difference in the willingness to enter a new environment (PND60)	Henck et al., 1994
Firemaster[(a)]	Swiss-Webster mice	PND1-29	7 or 14 mg/kg b.w. In the diet	-	7 mg/kg b.w.	Decreased locomotor activity	Preache et al., 1976 (abstract)
FireMaster FF-1	Fisher 344/N rats	26 weeks, 5 days per week	3 or 10 mg/kg b.w.	3 mg/kg b.w. (males)	3 mg/kg b.w. (females)	- decreased spontaneous locomotor activity - decreased muscle strength - no effect on learning ability (continuous avoidance response)	Tilson and Cabe, 1979
FireMaster FF-1	Sprague-Dawley Holtzman rats (male)	1, 4 or 6 months	1, 3 or 6 mg/kg b.w. daily gavage, 20 doses	-	-	Hyperativity in low doses and hypoactivity in higher doses determined in discrimination tasks.	Geller et al., 1979
FireMaster FF-1	Sprague-Dawley Holtzman rats (male)	1, 4 or 6 months	1, 3 or 6 mg/kg b.w. via gavage, 20 doses	-	-	Decreased calcium binding to synaptic membranes and uptake by synaptosomes at 1 mg/kg b.w., but not at 3 or 6 mg/kg b.w.	Gause et al., 1979

b.w.: body weight; NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; GD: gestational day; PND: postnatal day.
(a): Type of technical mixture not specified.

A second study showed that sub-chronic exposure to 1 mg/kg b.w. FireMaster FF-1 via daily gavage for 20 doses at the age of 3 months induced hyperactivity in Sprague-Dawley Holtzman male rats in a discrimination task. In contrast, hypoactivity was reported after exposure to a higher concentration (6 mg/kg b.w. for 20 doses) (Geller et al., 1979). Using a similar experimental design, Gause et al. (1979) found that calcium binding to synaptic membranes and uptake by synaptosomes was decreased after exposure to 1 mg/kg b.w., but not after 3 or 6 mg/kg b.w.

Fisher 344/N rats of both sexes were exposed 5 days a week for up to 22 doses to 16.8 mg BB-153/kg b.w. Neurobehavioural evaluation showed that BB-153 decreased spontaneous motor activity in an open field in male and female rats, whereas forelimb grip was decreased only in males (Tilson and Cabe, 1979). In rats exposed to 10 mg BB-153/kg b.w. 3 days per week over 8 weeks, after each exposure, continuous avoidance learning was tested by postponed electric footshock. The response was not altered after BB-153 exposure (Tilson and Cabe, 1979). Similarly to FireMaster FF-1, BB-153 reduced the responsiveness to phenobarbital and d-amphetamine. Altogether BB-153 appeared less potent than FireMaster FF-1 (Tilson and Cabe, 1979).

All together the available data show that PBB technical mixtures have potential developmental neurotoxic effects. No studies have investigated the effects of single congeners.

8.3.2.3. Immune system

The immunological effects of the commercial PBB mixtures FireMaster FF-1 and FireMaster BP-6 have been examined in rats, mice, Guinea pigs, dogs, pigs and cattle. The animals were exposed for an intermediate duration in most studies, and only two chronic exposure studies (rats and mice) were found. No data on toxicity to the immune system with individual PBB congeners was identified.

Rats

A single exposure to 1,000 mg FireMaster FF1/kg b.w. (Lot No. 7042) gave no histopathological changes in spleen and thymus in rats observed for 2 years (Kimbrough et al., 1978) or in rats treated for two weeks with 30 mg/kg b.w. per day (Gupta et al., 1981). Rats treated with FireMaster FF-1 for 25 weeks had increased spleen weight at ≥1 mg/kg b.w. per day and decreased thymus weight at ≥0.3 mg/kg b.w. per day (NTP, 1983). This was not accompanied by histopathological alterations in spleen, thymus or lymph nodes with doses of up to 10 mg/kg b.w. per day (NTP, 1983).

A dose of 100 mg FireMaster FF-1/kg b.w. per day for 4-5 weeks caused thymic atrophy and necrosis of lymphoblasts. This was not seen with a similarly administered dose of 30 mg/kg b.w. per day (Gupta and Moore, 1979). A much lower dose, 0.5 mg/kg b.w. per day FireMaster BP-6 in the diet for 150 days, caused moderate lymphoid depletion in thymus and spleen (Rezabek et al., 1989).

Reduced lymphocytic response to mitogen stimulation *in vitro* and reduced thymus and spleen weight was seen after treatment of rats for 30 days with 0.03, 3.0 or 30 mg/kg b.w. per day FireMaster FF-1 at the highest dose level (Luster et al., 1978). Relative thymus weight was reduced at 3 mg/kg b.w. per day, but the production of antibodies 4 days after immunisation with sheep red blood cells (SRBC) was not altered. Gavage treatment with 3 mg/kg b.w. per day FireMaster FF-1 for 6 months (5 days a week) led to decreased proliferative response of lymphocytes to mitogens or allogenic cells, whereas a dose of 1 mg/kg b.w. per day was without effect (Luster et al., 1980). Notably, in the studies by Luster et al. (1978, 1980) doses ≥3 mg/kg b.w. per day reduced body weight by ≥15 % indicating that FireMaster FF-1 can affect the rat immune system only at dose levels that produce other signs of toxicity.

FireMaster FF-1 in the diet for up to 104 weeks caused spleenic fibrosis following exposure to 1.5 mg/kg b.w. per day, but not to 0.5 mg/kg b.w. per day (NTP, 1993).

Mice

No histopathological changes were observed in lymph nodes, spleen and thymus in mice treated for two weeks with 30 mg FireMaster FF1/kg b.w. per day (Gupta et al., 1981). Mice treated with ≈130 mg FireMaster BP-6/kg b.w. in the diet for 14 days did not show an antibody-mediated response following immunization with SRBC. The thymus weight was reduced by 88 % and lethality was high (Fraker, 1980).

No histopathological effects were observed in the thymus, spleen or lymph nodes of mice treated with 30 mg/kg b.w. per day FireMaster BP-6 for 4-5 weeks (Gupta et al., 1981). Mice treated for 30 days with FireMaster BP-6 in the diet (0, 0.13, 1.3, 13 mg/kg b.w. per day) showed a reduced antibody-mediated response to SRBC at the two highest of the doses tested. Absolute thymus weight was reduced relative to controls with all dose levels tested. No alteration in delayed-type hypersensitivity was observed (Fraker, 1980).

Increased lethality was seen due to challenge with *Salmonella thyphosa* lipopolysaccharide after 3 or 6 weeks of dietary exposure to approximately 21.7 mg FireMaster FF-1/kg b.w. per day (Loose et al., 1981) and after bacterial inoculation in groups of mice treated with 10 mg FireMaster FF-1/kg b.w. per day for 6 months (Luster et al., 1980).

No histopathological changes were observed in the spleen, thymus, and lymph nodes of mice treated with up to 10 mg/kg b.w. per day FireMaster FF-1 for 25 weeks (NTP, 1983). Increased spleenic hematopoiesis was observed at 3.9 mg/kg b.w. per day for up to 105 weeks (NTP, 1993).

Dietary administration of FireMaster BP-6 at 0.4 mg/kg b.w. per day for 45 days to Guinea pigs resulted in a significant reduction in tetanus-antitoxin titers after injection of tetanus toxoid At 2.0 mg/kg b.w. per day, marked thymus atrophy, effects in spleen and lethality were observed (ATSDR, 2004).

Beagle dogs gavage fed for 61 days with 0.06-4 mg FireMaster BP-6/kg b.w. per day showed degenerating lymphocytes in blood smears at both doses, and depletion of lymphocytes in the lymph nodes, reduced erythropoiesis in the bone marrow, reduction in IgG-containing lymphocytes in the popliteal lymph nodes at the highest dose (Farber et al., 1978).

Dietary exposure of pregnant sows to approximately 2.5 mg/kg b.w. per day FireMaster BP-6 for a total of 12 weeks (last half of gestation and 4 weeks of lactation) gave a reduction in mitogen stimulated lymphocyte response relative to controls in sows and piglets. A dose of 1.25 mg/kg b.w. per day was without effect (Howard et al., 1980).

Immunotoxic effects (humoral and cell immunity, histopathologic alterations in thymus and spleen) have not been observed in cattle exposed to PBB at concentrations close to lethal doses (Kateley et al., 1982; Moorhead et al., 1977). Thymic involution and atrophy was seen in cows that received gavage doses of 67 mg/kg b.w. per day of FireMaster PB-6 for 60 days, but this dose was nearly lethal (Moorhead et al., 1977).

In summary, exposure to PBBs caused altered immune responses, such as spleen and thymus weights, antibody production and lymphoproliferative responses in a variety of animal species. These effects were most often only seen at PBB levels that produce other signs of toxicity.

8.3.2.4. Liver

Sleight and Sanger (1976) fed a diet containing 0, 1, 10, 100, or 500 mg/kg b.w. of a commercial PBB mixture (FireMaster BP-6) to young male Sprague-Dawley rats over 30 days. At 1 mg/kg b.w. and above relative liver weight was increased significantly. Hepatocellular swelling and vacuolization

were observed at 10 mg/kg b.w. and above, the activities of microsomal drug-metabolizing enzymes were induced at all dose levels. Hepatic mitochondrial size was increased at 1 mg/kg b.w. and above.

Babish and Stoewsand (1977) treated weanling male Sprague-Dawley rats with 0, 1, or 50 mg/kg b.w. Firemaster BP-6 in the diet over 5, 10, 15, and 20 days. At the highest level, a significant increase in relative liver weight and hepatic microsomal aryl hydrocarbon hydroxylase, aminopyrine N-demethylase and p-nitroanisole o-demethylase activities was found. Furthermore, total microsomal protein and total cytochrome P450 were also increased.

Waritz et al. (1977) refers to a study by the Dow Chemical Company showing that a technical octaBB mixture containing 60 % nonaBB(s), 33 % octaBB(s), 6 % decaBB and 1 % heptaBB(s), when fed to male rats at dietary levels of 10,000, 1,000 or 100 mg/kg (equivalent to 500, 50 or 5 mg/kg b.w.) for 30 days, produced increased liver weight, hepatic centrilobular cytoplasmic enlargement and vacuolization. The authors did not make any statements about impurities or minor contaminants.

Gupta and Moore (1979) applied oral doses of 30, 100, 300, and 1,000 mg/kg b.w. of FireMaster FF-1 per day, 5 days a week, over 4.5 weeks to young adult male and female Fischer 344/N rats and observed the animals over 90 days after the start of the treatment. Treated animals showed liver enlargement, focal proliferation of bile ducts, swelling of hepatocytes, moderate to marked fatty infiltration and focal necrosis.

Kasza et al. (1978) treated four-week-old male Holtzman rats with a diet containing 0, 5, 50, or 500 mg/kg FireMaster BP-6 (Lot No. 1050-74-55) (equivalent to 0.25, 2.5 or 25 mg/kg b.w.) for 5 weeks. At 50 and 500 mg/kg b.w., relative liver weights were increased. At all dose levels, fatty degeneration of the liver with lamellar cytoplasmic inclusions was observed. At 500 mg/kg, hypertrophic degenerative hepatocytes were found around the central veins. Electronic microscopy revealed a proliferation of the endoplasmic reticulum, an increase of lipid droplets, and a proliferation of Golgi vesicles containing lipoprotein particles. A decreased number of mitochondria and lysosomes was also seen.

In 1983, Gupta et al. (1983a) published a long-term study on the effects of FireMaster BP-6 (Lot #1312 FT, Batch 03), in rodents. In this study, adult Fischer 344 rats and B6C3F_1 mice were given 0, 0.1, 0.3, 1.0, 3.0, and 10 mg/kg b.w. per day, 5 days a week, over 6 months. After the end of treatment, the animals were observed for an additional 23 months for rats and 24 months for mice. At the six month observation (end of treatment) hepatic porphyrin was markedly increased.

Cagen et al. (1979) treated lactating Sprague-Dawley rat dams with 0 and 50 mg/kg b.w. Firemaster BP-6 in the diet. Thus, the litters were exposed to PBBs via milk between post-natal days (PND) one and 28. Between PND29 and 49, the litters were exposed to the same diet fed to their mothers. In 15 day old rats, liver weights and hepatic uptake and elimination of ouabain were increased. After 21, 35, and 49 days, liver weight was also elevated but hepatic ouabain uptake was no longer increased.

Arneric et al. (1980) exposed rat dams to FireMaster BP-6 (0 or 100 mg/kg b.w. in the diet) starting from GD8. The offspring were sacrificed after 4 weeks, or were kept on the same diets fed to their mothers until 12 (males) or 21 (females) weeks of age. In liver microsomes isolated from these animals, increased metabolism of progesterone was found, resembling the effects of treatment with phenobarbital.

McCormack et al. (1980) fed a diet containing 0 and 100 mg/kg b.w. FireMaster BP-6 from the eighth day of pregnancy through 28 days post partum. All pups were then weaned onto a diet free of PBBs and observed further. At days 28 and 150, relative liver weights were increased significantly. At days 28, 150 and 328 pups the offspring showed increased hepatic aryl hydrocarbon hydroxilase (AHH) activity which correlated with the persistence of the PBBs measured as BB-153 in the liver.

Allen-Rowlands et al. (1981) treated adult male Sprague-Dawley rats by gavage for 20 days at 1, 3, or 6 mg/kg b.w. per day with technical PBB mixture (Lot No. FF-1312-FT, batch 3). At all dose levels,

liver weights were significantly increased. The effect lasted two and five months after the end of treatment.

Robertson et al. (1981) could show that BB-156 has a number of 'dioxin-like' properties in immature male Wistar rats, i.e. in induced hepatic benzo[*a*]pyrene hydroxylase and a protein co-migrating with a 3-methylcholanthrene-inducible CYP. Furthermore, it partially displaced 2,3,7,8-TCDD from the AhR.

In a multi-generation study in rats exposed to 10 and 100 ppm FireMaster BP-6 (equivalent to circa 0.5 and 5 mg/kg b.w. per day) from GD8 until weaning at PND28, increased liver weights were observed in F1 generation rats whose only exposure was from the exposed mothers. In the 5 mg/kg b.w. per day treatment of the F0 rat dams, F2 offspring, but not F3 offspring, displayed increased liver weights, liver enzyme induction and hepatic histological alterations compared with controls (McCormack et al., 1981).

Newton et al. (1982) fed a diet containing 0 or 100 mg/kg b.w. FireMaster BP-6 to pregnant Sprague-Dawley rats starting from day 8 of pregnancy. At 4 weeks of age the offspring were weaned onto the same diet fed to their mothers. Experiments were conducted with male and female offspring at 1, 2, and 4 months of age. Hydroxylation of testosterone to 7α- and 6ß-hydroxytestosterone in microsomes isolated from both sexes at all ages was increased by PBB treatment. Microsomal conversion of testosterone to 16α-hydroxytestosterone and androstenedione was enhanced by PBBs in females at all ages and in 1-month-old males.

Robertson et al. (1983b) applied a single *i.p.* dose of 150 µmol/kg b.w. of BB-77 or BB-52 to immature male Wistar rats. After 2 weeks, BB-77 caused an increase in relative liver weight with fine to coarse vacuolization of hepatocytes and an accumulation of fat droplets in midzonal areas of the liver lobules. In contrast, BB-52 caused mild occasional hepatic vacuolization without cellular hypertrophy.

Robertson et al. (1984) provided evidence that FireMaster BP-6 caused induction of hepatic benzo[*a*]pyrene hydroxylase only in AhR-responsive C57BL/6J but not in 'AhR-insensitive' DBA/2J mice, suggesting that the induction is due to activation of the AhR by constituents of the mixture.

Bernert and Groce (1984) treated adult male Sherman rats with a diet containing either 25 or 200 mg/kg b.w. iron. Furthermore, some animals received a single oral dose (by gavage) of 500 mg/kg b.w. of FireMaster PB-6 (Lot No. 5143). The animals were then maintained on these diets for time periods ranging from 1 to 8 weeks. The different iron levels in the diet were applied in order to identify possible interactions between iron-induced lipid peroxidation and PBB effects. PBB treatment resulted in a profound change in fatty acid composition of liver lipids, and a decrease in the cholesterol to phospholipid ratio. The level of dietary iron did not markedly influence the effects of the PBB treatment.

Chen et al. (1992) fed adult male Sprague-Dawley rats a diet containing an adequate level of vitamin A for 30 days before a single *i.p.* injection of 150 µmol/kg b.w. of BB-77, -80, or -169. The PBBs had been synthesized and showed a purity of > 99 % as determined by gas chromatography. After one week, BB-77 and -169 had lowered the hepatic retinyl ester hydrolase activity, whereas the levels of hepatic retinol were not affected. Hepatic retinyl palmitate was decreased by BB-77 and -169.

Summarising, most toxicological studies aimed at investigating hepatic effects of PBBs in animals were carried out with technical mixtures. All studies demonstrate that these mixtures have the potency to cause liver enlargement, hepatocellular hypertrophy, and fatty degeneration of the liver. In some instances hepatic necrosis was also observed.

Only a few studies were carried out with individual congeners showing that some non-*ortho*-brominated congeners BB-156 can cause 'dioxin-like' effects, and seem to exert a more pronounced

hepatotoxicity than the di-*ortho*-brominated BB-52. The studies with individual congeners were not carried out with various dose levels, thus, not allowing a dose-response analysis.

8.3.2.5. Embryotoxicity and teratogenicity

Embryotoxic and teratogenic effects were first observed in PBB contaminated cattle (Damstra et al., 1982; Jackson and Halbert, 1974) and have subsequently been confirmed also in experimental studies. The results indicate that *in utero* exposure to PBBs can produce embryolethal effects, structural abnormalities and growth retardation in offspring.

In rats exposed to FireMaster FF-1 (200 mg/kg b.w.) by gavage on GD7 and GD14, decreased pup survival, decreased body weight gain in offspring, and increased mortality in offspring were observed over 24 month after the exposure (Groce and Kimbrough, 1984). In seven rhesus female monkeys that were fed 0.012 mg/kg b.w. per day FireMaster FF-1 in the diet for 7 months prior to conception and during pregnancy, one abortion and one stillbirth were observed whereas the surviving five infants had reduced birth weight and postnatal body weight gain, but no gross abnormalities (Allen et al., 1979; Lambrecht et al., 1978). Decreased body weight at birth and at 4 weeks after birth were observed also in mink offspring whose parents were fed diets containing 0.155 mg/kg b.w. per day FireMaster FF-1 from 7-8 months prior to mating through 4 weeks postpartum (Aulerich and Ringer, 1979; Ringer et al., 1981).

FireMaster BP-6 administered to rats in single doses of 200, 400 or 800 mg/kg b.w. on a specific day during pregnancy caused at 200 mg/kg b.w. increased fetal resorptions, while at 400 or 800 mg/kg b.w. caused maternal toxicity (expressed as a decrease in body weight gain) and fetal malformations including cleft palate and diaphragmatic hernia (Beaudoin, 1977). Increased fetal resorptions also were observed in rats receiving total doses of 14.3 mg/kg b.w. per day FireMaster BP-6 by gavage on alternate days from days 0 through 14 of pregnancy (Beaudoin, 1979). Dietary administration of FireMaster BP-6 to rats (42.9 mg/kg b.w. per day on GDs 7-15 or 50 mg/kg b.w. per day on GDs 7-20) resulted in decreased body weight of fetuses, but no other developmental effects in fetuses and pups that were monitored to up to 60 days postpartum (Corbett et al., 1975; Harris et al., 1978).

FireMaster BP-6 at 50, 100 and 1,000 ppm (equivalent to circa 8.8, 17.5 and 175 mg/kg b.w. per day) in the diet was administered to pregnant Swiss/ICR mice from GD7 to GD18, and then caesarean section was conducted on the day before delivery to examine foetuses. Decrease in body weight and malformation (ectoencephalopathy at 17.5 mg/kg b.w., cleft palate at 175 mg/kg b.w.) occurred in each dose group (Corbett et al., 1975). In rats administered a diet with the same concentrations of FireMaster BP-6 (equivalent to about 2.5, 5 and 50 mg/kg b.w. per day) from GD7 to GD20 no teratogenicity was observed although the foetal body weight was lower at ≥ 5 mg/kg b.w. per day (Corbett et al., 1975).

In a multi-generation study in rats exposed to 10 and 100 ppm FireMaster BP-6 (equivalent to circa 0.5 and 5 mg/kg b.w. per day) from GD8 until weaning at PND28, decreased pup survival to weaning, decreased body weight gain, delayed fur development, delayed eye and vaginal opening were observed in F1 generation rats whose only exposure was from the exposed mothers (McCormack et al., 1981). The survival of F2 and F3 generations was not affected by the 5 mg/kg b.w. per day treatment of the F0 rat dams (McCormack et al., 1981).

Increased incidences of foetuses with extra ribs were observed in rats fed diet containing ≥86 mg/kg b.w. per day of OctaBB mixture from GD6 to 15 (Waritz et al., 1977). No embryotoxic, fetotoxic, or teratogenic effects occurred in rats following gavage administration of ≤1,000 mg DecaBB mixture/kg b.w. per day on GDs 6-15 (Millischer et al., 1979).

Taken together, the studies indicate that intake of PBBs in very early pregnancy can lead to resorbtion of fetuses, while administration of PBBs later in pregnancy can give rise to offspring with lower birth weight and malformations at high doses.

8.3.2.6. Genotoxicity

In vitro and *in vivo* genotoxicity studies indicate that PBBs are not directly genotoxic. The results are summarized in Table F1 (Appendix F). PBBs were negative in bacterial mutagenicity tests with *Salmonella typhimurium* (Haworth et al., 1983; Millischer et al., 1979; NTP, 1983; Tennant et al., 1986) and *Escherichia coli* (Rossman et al., 1991) with or without activation systems. An exception is 4-bromobiphenyl which tested positive in *S. typhimurium* in the presence of metabolic activation (Kohli et al., 1978). Also *in vitro* testing in eukaryotic cells PBBs resulted in negative genotoxic response; they did not induce gene mutations (Kavanagh et al., 1985; Myhr and Caspary, 1991; Williams et al., 1984), chromosomal aberrations and sister chromatid exchange (Galloway et al., 1987) or unscheduled DNA repair (Williams et al., 1984).

In *in vivo* genotoxicity studies in mice and rats PBBs did not induce micronuclei (Shelby et al., 1993; Millisher et al., 1980), chromosomal aberrations (Wertz and Fiscor, 1978; Fiscor and Wertz, 1976; Garthoff et al., 1977) or unscheduled DNA synthesis (UDS) (Mirsalis et al., 1985, 1989).

8.3.2.7. Carcinogenicity

The carcinogenic potential of PBBs has been investigated with both commercial mixtures and a limited number of individual congeners of PBBs. Cancer bioassays have been undertaken in rats and/or mice and the tumour promoting activity of some PBBs has been investigated. These studies all date from 1992 or earlier, reflecting the phase out of manufacture and use of PBBs. There are more recent epidemiological studies on possible associations between exposure to PBBs and cancer risk. Information on the carcinogenicity of PBBs has been reviewed by a number of groups, including ATSDR (2004), IARC (1986) and WHO (1994). All studies were in rats or mice and most were performed by the National Toxicology Program/National Institute of Environmental Health Sciences (NTP/NIEHS). The principal site of tumours in both rats and mice was the liver, the incidence of hepatocellular carcinomas being significantly increased in males and females of both species administered commercial PBB mixtures orally at relatively high doses.

In a key study undertaken by the NTP (Gupta et al., 1983b; NTP, 1983), male and female Fischer-344/N rats and B6C3F1 mice were administered FireMaster FF-1 by oral gavage at doses 0, 0.1, 0.3, 1, 3 and 10 mg/kg b.w. per day on five consecutive days per week for 25 weeks. Animals were then observed for approx 24 months in total, i.e. for a further 18 months post-treatment. The incidence of hepatocellular carcinoma was statistically significantly increased ($p<0.01$), in both male and female rats at 10 mg/kg b.w. per day (7/31 cf. 0/33, high dose cf. controls in males; 7/20 cf. 0/20 in females) and at 3 mg/kg b.w. per day in males (7/33). There was also a statistically significant increase ($p<0.01$) in the incidence of cholangiocarcinoma in female rats at 10 mg/kg b.w. per day (7/20 cf. 0/20). There was a marginal, non-significant increase ($p=0.06$) in high dose males (2/31 cf. 0/33). There was a statistically significant, dose-related increase ($p<0.01$) in the incidence of hepatic neoplastic nodules in females at ≥3 mg/kg b.w. per day. There was no clear effect of treatment on the incidence of hepatic neoplastic nodules in males. Statistically significant increases ($P < 0.01$) in the number of atypical foci were observed in male and female rats. In mice, there was a statistically significant increase ($p<0.01$) in the incidences of hepatocellular carcinoma in both males and females at 10 mg/kg b.w. per day (21/22 cf. 12/25 in males; 7/8 cf. 0/13 in females), with increased pulmonary metastasis ($p<0.05$) in females at the high dose. Treatment had no effect on the incidence of hepatocellular adenomas or hepatoblastomas. There was a trend towards an increase in thyroid follicular cell adenoma in female mice treated with PBBs, but the incidences were low and the numbers of animals small.

Single or short term administration of PBBs has also produced hepatocellular carcinoma in rats (mice have not been studied). Female Sherman rats were administered a single oral gavage dose of 1,000 mg/kg b.w. FireMaster FF-1. After 2 years, the incidences of hepatocellular carcinomas (24/58 cf. 0/53), liver neoplastic nodules (42/58 cf. 0/53) and atypical foci (57/58 cf. 1/53) were increased (Kimbrough et al., 1981). It had previously been shown in groups of five Sherman rats per sex treated in the same way with FireMaster FF-1 and observed after 2, 6, 10 and 14 months, that

neoplastic nodules were not observed until after 10 months of treatment in females (4/5) and 14 months in males (2/5, 3/5 in females) (Kimbrough et al., 1978). No liver tumours were observed over the 14 months of observation in this study, although the number of animals per group was small. Sherman rats treated with a single dose of 200 mg/kg b.w. developed hepatic neoplastic nodules over the subsequent 18-22 months (5/16 cf. 0) (Kimbrough et al., 1981). In a study in pregnant rats, treated with an oral dose of 200 mg/kg b.w. FireMaster FF-1 on gestation days 7 and 14, the incidences of both neoplastic nodules (9/51 cf. 2/48 in females; males NS at 2/41) and hepatocellular carcinomas (4/41 and 3/51cf 0/42 and 0/48 in males and females, respectively) were slightly increased in offspring over the 24 months post-treatment (Groce and Kimbrough, 1984).

Treatment of female Sherman rats by oral gavage with FireMaster FF-1 at a dose of 100 mg/kg b.w. twice a week for two 3-week periods separated by approximately10 weeks (total of 12 doses) resulted in increased incidences of atypical foci (23/28 cf. 1/25), neoplastic nodules (24/28 cf. 1/25) and hepatocellular carcinoma (17/28 cf. 0/25) after 24 months of observation (Kimbrough et al., 1981).

The NTP conducted a study of perinatal and/or adult exposure of Fischer-344/N rats and B6C3F1 mice to FireMaster FF-1, in the diet (Chhabra et al., 1993; NTP, 1993). In adult-only exposed rats, the incidences of hepatocellular adenomas and carcinomas in both sexes were increased after 104 weeks (the duration of the study). At the doses of 0.5 and 1.5 mg/kg b.w. per day used, the incidences of adenoma in males were 10/49 and 38/50, respectively cf. 1/50 and of carcinoma they were 2/49 and 19/50, respectively cf. 0/50. In females, the figures were: adenomas 10/50 and 38/50 cf. 0/50; carcinomas 2/50 and 4/50 cf. 0/50. Most of these increases were statistically significant. In the perinatal-only exposure protocol, dams were exposed via the diet to FireMaster FF-1 at a dose of 0.5 mg/kg b.w. per day for 60 days prior to mating and throughout gestation and lactation until the pups were 8 weeks old. The animals were observed until 24 months of age. Perinatal-only exposure had no significant effect on the incidences of hepatic or other tumours in rats.

In combined perinatal and adult exposure, following exposure as for the perinatal only group, rats were switched to one of the dietary regimes described for the adult only groups and observed for 104 weeks. The incidence of hepatic tumours in females exposed both perinatally and as adults was statistically significantly greater than in those animals exposed only as adults. In the group exposed to 0.5 mg/kg b.w. per day in both periods, the incidence of adenomas was 35/50 cf. 22/50 in the adult-only group. The figures for carcinomas were 8/50 cf. 1/50, respectively. A similarly increased response in the combined perinatal and adult exposure group compared to the adult-only group was observed in the other dose groups, 0.5:0.5 (perinatal:adult dose) cf. 0.15:0.5 and 0.5:1.5 cf. 0:1.5 mg/kg b.w. per day. No such differences were observed in male rats. The lowest combined doses in this study, 0.05:0.15 mg/kg b.w. per day, had no adverse effects on the animals. Based on these results a dose of 0.15 mg/kg b.w. can be identified as a NOEL for hepatocarcinogenesis in rats.

The treatment regimen for perinatal and/or adult exposure in mice was similar to that in rats. In adult-only exposed mice, the incidences of hepatocellular tumours in both males and females were statistically significantly increased following administration of either 1.3 or 3.9 mg/kg b.w. per day FireMaster FF-1 in the diet (males - adenomas: 48/49 and 42/50 cf. 9/50; carcinomas: 30/49 and 36/50 cf. 8/50; females - adenomas 39/50 and 46/48 cf. 4/50; carcinomas: 28/50 and 41/48 cf. 1/50). There was also a statistically significant increase in the incidences of liver tumours in male and female mice exposed perinatally-only to 3 mg/kg b.w. per day (only dose tested) (males - adenomas: 31/50; carcinomas 17/50; females - adenomas: 19/50; carcinomas 7/50 (adenoma response in females not statistically significantly different from that in the controls).

Due to the high incidences of liver tumours in the adult-only exposed groups, it was not possible to determine whether the tumour incidence was any greater than this in the combined perinatal and adult exposure group, although there was some evidence for this for carcinomas in males (40/50, $P<0.001$for perinatal:adult doses of 3.9:1.3 – cf. 0:1.3) and females (44/50, $P<0.001$) and adenomas in females (47/50, $P=0.005$). At the higher doses, there were changes in adenomas in males (48/50, $P< 0.01$ for 3.9:3.9 cf. 0:3.9) and females, where the incidence decreased (41/47; $p=0.02$).

There was some indication for an effect of treatment on the incidence of thyroid follicular cell adenoma in male mice. In animals with combined perinatal:adult exposure to 3.9:1.3 mg/kg b.w. per day, the incidence (5/48) was statistically significantly increased (p=0.03) in males cf. that in adult-only exposure to 0:1.3 mg/kg b.w. per day (0/49). Although above the historical control range of 0-4 % for control males in NTP studies, no effect was observed in the 0:3.9 or 3.9:3.9 mg/kg b.w. per day groups. There was no effect of perinatal-only exposure on the incidence of thyroid tumours in either male or female mice.

There are some limited studies on the carcinogenicity of individual PBB congeners. Groups of 3 or 6 female Sprague-Dawley rats were fed diets containing 10 or 100 mg FireMaster BP-6 or 2,2',4,4',5,5'-hexaBB (BB-153)/kgb.w. diet or 0.1 mg 3,3',4,4',5,5'-hexaBB (BB-169)/kg b.w. diet for 140 or 180 days and were observed for 15 months. There was no increase in the incidence of hepatocellular carcinoma in any of the treatment groups, but in the groups administered 100 mg FireMaster or BB-153/kg b.w. of feed, there was an increased incidence of hepatic nodules (Jensen et al., 1982; Jensen and Sleight, 1986). The limited numbers of animals and less than lifetime observation period in this study limited the conclusions that could be reached on carcinogenic potential.

Male and female B6C3F1 mice, 50/sex/group, were fed diets containing technical NonaBB (Bromkal 80-9D) at concentrations of 100 or 300 mg/kg b.w. diet, for 18 months (Momma, 1986). There was a statistically significant increase in the incidences of neoplastic nodules in the liver and in hepatocellular carcinomas in both PBB treated groups. There was also a slight increase in the incidence of hepatoblastomas in males.

The carcinogenicity of technical OctaBB and DecaBB does not appear to have been investigated.

Based on the available, albeit somewhat limited, evidence, PBBs appear to have little if any activity as initiators of hepatic carcinogenicity (Buchmann et al., 1991; Dixon et al., 1988; Jensen et al., 1984).

The tumour promoting activity of PBBs has been investigated in a number of studies. In liver tumour promotion assays, female Sprague-Dawley rats were 70 % hepatectomised, then initiated with an *i.p.* dose of 10 mg/kg b.w. diethylnitrosamine 24 h later. Promotion with FireMaster BP-6 administered orally commenced 30 days later. Various promotion regimens have been investigated. Following gavage doses of 65 mg/kg b.w. , but not 6.5 mg/kg b.w. , for 2 days (Rezabek et al., 1987), dietary exposure to 0.5 or 5 mg/kg b.w. per day for 180 days (Jensen et al., 1982) and dietary exposure to 0.5 mg/kg b.w. per day for 140 days or 5 mg/kg b.w. for 15 days (Jensen et al., 1984) there was a statistically significant increase in the numbers of gamma-glutamyl transpeptidase (GGT) positive enzyme-altered hepatic foci. Promotion was also observed in a study of females Sprague-Dawley rats in which the liver remained surgically intact. Initiation was with dimethylnitrosamine or N-nitrosopyrrolidine and a single gavage dose of FireMaster BP-6 was administered 7-10 days later. Animals were killed 30, 60 and 180 days later. There was a statistically significant increase in the number of glutathione S-transferase P (GSTP)-positive altered hepatocellular foci (Rangga-Tabbu and Sleight, 1992).

The hepatic tumour promoting effects of some individual PBB congeners have also been investigated in partially hepatectomized rats, initiated with diethylnitrosamine. There were statistically significant increases in the numbers of GGT positive enzyme-altered foci and/or neoplastic nodules following promotion with BB-77 administered in the diet at a dose of 0.25 mg/kg b.w. per day 180 days, BB-153 (at a dietary dose of 0.5 mg/kg b.w. per day for 180 days), BB-169 (at a dietary dose of 0.05 mg/kg b.w. per day for 140 days) (Buchmann et al., 1991; Dixon et al., 1988; Jensen et al., 1982, 1983).

These and other studies on the promoting activity of PBBs, summarised by WHO (1994), have shown that FireMaster (and BP-6), its major congener BB-153 and the coplanar BB-169 can act as hepatic tumour promoters, the last only at hepatotoxic doses. FM was more potent that BB-153. Duration of

exposure was not critical, with feeding for short periods being as effective as long-term feeding, and even a single gavage dose promoted enzyme-altered foci.

IARC (1986) has classified PBBs (FireMaster BP-6, 059536-65-1) as 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.

It can be concluded that 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 NOEL for hepatocarcinogenesis of 0.15 mg/kg b.w. has been identified in a long-term NTP study (1993) with Firemaster FF-1. There is evidence that some PBB congeners may cause cancer through interaction with nuclear receptors, whereas others appear to cause tumours as a consequence of cytotoxicity, presumably via stimulation of regenerative proliferation (see ATSDR, 2004; WHO, 1994).

8.3.3. Biochemical effects and molecular mechanisms

PBB congeners have been reported to elicit hepatotoxicity, liver hyperplasia and interference with thyroid hormone regulation (see Chapter 8.3.2.1.), immunotoxicity (see Chapter 8.3.2.3.), teratogenicity (see Chapter 8.3.2.7.) and developmental neurobehavioral effects (see Chapter 8.3.2.2.). 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.

Non-*ortho* and mono-*ortho*-substituted PBBs elicited AhR-mediated gene expression and benzo[*a*]pyrene hydroxylase activity (Robertson et al., 1982) and depletion of thymus (Robertson et al., 1983b) in immature male Wistar rats. Non-*ortho* PBBs were further tested for AhR-inducing potency in the bioassay using a rat hepatoma H4IIE.Luc cell line stably transfected with luciferase reporter system (DR-CALUX). BB-77, -126 and -169 were potent inducers of AhR-dependent luciferase and 7-ethoxyresorufin-O-deethylase activities; relative potencies, calculated against 2,3,7,8-TCDD as a reference toxicant, were 0.080, 0.16 and 0.0047, respectively (Behnisch et al., 2003). Relative toxic potencies of PBBs were comparable with toxic equivalency factors of coplanar PCBs.

A series of PBB congeners have been reported for their ability to reduce serum retinol levels in male Sprague-Dawley rats. Interestingly, BB-169 had no effects on retinoid levels suggesting that a mechanism other than AhR activation was involved in this adverse effect (Chen et al., 1992). PBBs modulated also the content of retinol-binding protein and retinol palmitate. BB-77, -126 and -169 reduced significantly the retinyl ester hydrolase activity in liver. Additionally, high dietary levels of retinyl acetate had some inhibitory effect on the promotion of hepatic altered foci induced by BB-169 in initiated rats (Rezabek et al., 1989). The data show that these PBBs induce impairment of vitamin A and probably also retinoid signaling, and suggest that these effects result from different modes of action.

BB-52 has been reported to be a weak "phenobarbital-like" inducer of CYP enzymes (Robertson et al., 1983b), i.e. that BB-52 is an agonist of constitutive androstane receptor (CAR)/pregnane X receptor (PXR) transcription factors, responsible for gene expression of CYP2B, CYP3A and other drug metabolising enzymes and other adverse effects associated with inappropriate activation of CAR and PXR. The metabolism of progesterone was accelerated in liver microsomes (containing CYP enzymes) from rats exposed to different concentrations of PBBs; stimulation of hydroxylation of progesterone in positions 16α- and 6β- resembled the effects of phenobarbital, a prototype inducer of CAR and PXR-dependent gene expression (Arneric et al., 1980). This study confirmed induction effects of non-dioxin-like PBBs; certain effects of PBBs on the endocrine system may be a consequence of enhanced steroid sex hormone catabolism, which could lead to a decrease in progesterone, 17β-estradiol and testosterone levels as well as thyroid hormones.

No genotoxicity of PBBs has been reported in various bacterial and mammalian systems; on the other hand, PBBs inhibited gap junctional intercellular communication (GJIC), which is the one of modes of action of chemical tumor promoters (Williams et al., 1984). GJIC was blocked by PBBs in Chinese hamster V79 cells and human teratocarcinoma cells as well; *ortho*-substitution appeared to be a structural characteristic of this effect (Tsushimoto et al., 1982; Kavanagh et al., 1987). Kang et al. (1996) showed that BB-153 but not coplanar BB-169 inhibited GJIC in normal human breast epithelial cells. These data suggest no significant genotoxicity of PBBs and an AhR-independent mode of tumor-promoting action of *ortho*-substituted PBBs. The second set of hepatic tumor promoting effects might be associated with induction of CYP enzymes and hepatotoxic damage (ATSDR, 2004; WHO, 1994).

A part of immunotoxic responses such a decrease in thymus weight, may be related to binding to the AhR and induction of AhR-dependent gene expression and subsequent dioxin-like toxicity (Safe, 1984). However, *ortho*-substituted PBB congeners activated respiratory burst and elevated intracellular calcium in human granulocytes (Kristoffersen et al., 2002). PBBs activated inositol 1,4,5-triphosphate-specific phospholipase C and subsequently mobilized intracellular calcium. Di-, tri- and tetraBB congeners (including BB-18 and -49) were the most efficient inducers; activity was detected at 5 μM and maximum response was obtained by 15-20 μM. The most abundant hexaBB (BB-153) elicited significant but only a partial induction of oxidative burst and intracellular calcium; the effects were at the same, low micromolar concentrations. Also neurodevelopmental toxicity might be related to a calcium homeostasis disruption.

Taken together, the majority of experimental *in vivo* as well as *in vitro* studies was performed in the period around 1980-1990. Major adverse effects are:

- Hepatic toxicity, hyperplasia and tumor promotion,
- Endocrine mediated reproductive effects,
- Immunotoxicity,
- Neurodevelopmental toxicity.

The mechanisms of toxicity underlying these adverse effects include the induction of AhR, CAR/PXR-dependent biotransformation involved in catabolism of steroids; disruption of calcium homeostasis, disruption of gap junctional intercellular communication and probably some other effects on plasma membranes.

8.4. Observations in humans

To determine the effects of exposure to PBBs on human health, after the 1973 widespread contamination of livestock in Michigan, a cohort of persons with varying levels of PBBs exposure was established in 1976 and clinical studies conducted (Anderson et al., 1978a, b, c, 1979; Landrigan et al., 1979; Barr, 1978; Lilis et al., 1978). Many papers have been published from this cohort. The most relevant ones are listed in Table G1, G2, G3, G4 and G5 (Appendix G). In addition to the Michigan dairy farmers, other cohorts (CARDIA (Coronary Artery Risk Development in Young Adults), NHANES) and industrial groups were also studied.

8.4.1. Studies on immunological disfunction and thyroid and hormone disruption

Table G1 (Appendix G) reports the most relevant information on immunological disfunction and thyroid and hormone disruption.

A recent paper by Wang et al. (2010) suggested that people having worked on an electronic waste recycling and dismantling site had significantly lower TSH compared to the control group ($p<0.01$). BB-77, -103 and -209 were analysed. A weak negative relation was found between the levels of BB-103 and T3.

Bekesi et al. (1987) studied 336 adult Michigan farm residents, 117 general consumers for comparison, 75 dairy farm residents in Wisconsin, who had not eaten food contaminated with PBBs, and 79 healthy subjects in New York. Abnormalities in the Michigan groups included hypergammaglobulinemia, exaggerated hypersensitive response to streptococci, significant decrease in absolute numbers and percentage of T and B-lymphocytes, and increased number of lymphocytes with no detectable surface markers ("null cells"). Significant reduction of *in vitro* immune function was noted in 20-25 % of the Michigan farm residents who had eaten food contaminated with PBBs. The decreased immune function detected among the PBB-exposed farm residents tended to affect families as a unit and was independent of exposed individuals' age or sex.

Lipson et al. (1987) studied 18 Michigan dairy farmers. The comparison group was 18 adult Wisconsin dairy farmers who were not exposed to PBB-contaminated meat and/or dairy products. Enhanced secretory levels of immunoglobuline (Ig) G by cultured lymphocytes obtained from blood specimens of Michigan dairy farmers suggested a detrimental effect on the immune system by the PBBs. Furthermore, *in vitro* studies showed that the PBB increased the quantity of Ig synthesizing cells but decreased lymphocyte function in response to pokeweed mitogen. The results of these studies are similar to *in vivo* observations on Michigan dairy farmers and their families exposed to PBBs who displayed reduced cell function but showed defused polyclonal hypergammaglobulinemia. The data from this study suggest that PBBs exerted an adverse effect on cell function, but produced a nonspecific activation of B lymphocytes.

In August 1978, Bahn et al. (1980) conducted a comprehensive medical evaluation on workers (n=36) from a plant that had manufactured only brominated products (decaBB and decaBB-oxide) and on control groups of subjects from other industries/communities (n=89). Studies of thyroid function revealed four cases of primary hypothyroidism in the PBB workers but none in the control subjects. In the PBB workers, markedly elevated titers of thyroid anti-microsomal antibody (1:6400 or above) were found in these four men only. The PBB group had significantly more subjects with elevated serum concentrations of thyrotropin (P = 0.006). The free thyroxine indexes (P = 0.06) and serum T4 concentrations (P=0.11) did not differ significantly. Although more PBB workers than controls had anti-thyroglobin titers greater than l:100, the difference between groups was not significant (P=0.06). An unexpectedly high prevalence (11.4 %) of primary hypothyroidism was found among the PBB workers.

Bekesi et al. (1979a) studied 55 Michigan farm residents who consumed food contaminated with PBBs, 11 Michigan Chemical Company workers directly exposed to PBBs and 46 non-exposed Wisconsin farmers. Abnormalities included decreased number of T-lymphocytes with concomitant increase of lymphocytes with no detectable surface markers, "null cells", and altered lymphocyte function. PBB (hexaBB) in separated white blood cells and red cells was positively identified and quantified. Immunological abnormalities were not detected in non-exposed Wisconsin dairy farm residents.

Bekesi et al. (1979b) studied 45 adult Michigan farm residents and members of their families who consumed food contaminated with PBBs with respect to their immunologic status. Comparison groups were 46 dairy farm residents in Wisconsin and members of their families, who had not eaten PBB-contaminated food and 79 healthy subjects in New York City. Abnormalities in the Michigan group included a significant decrease in absolute numbers and percentages of T and B-lymphocytes and increased number of lymphocytes with no detectable surface markers (“null cells”). A significant reduction of *in vitro* immune function was noted in 35-40 % of the Michigan farm residents. Despite the absence of any apparent numerical reduction, both T and B lymphocyte subpopulations of peripheral blood lymphocytes showed evidence of functional defect. Ten of the 45 Michigan farmers studied showed impaired phytohemaglutin (PHA)-induced blastogeneic response, due to the decreased number and percent of T-cells in the peripheral blood lymphocytes (PBLs). There appeared to be no consistent correlation between the concentration of PBBs in the plasma and the altered lymphocytes. The decreased immune function detected among the PBB-exposed farm residents tended to affect families as a unit and was independent of exposed individuals’ age or sex.

Silva et al. (1979) assessed T and B lymphocyte numbers and transformations to 3 mitogens in two study groups, one with high and the other with low exposure to PBBs selected from the Michigan cohort. No correlation between serum PBB levels and lymphocyte numbers or function was found.

In summary, one study detected a high prevalence of primary hypothyroidism among the PBB workers. There are no consistent correlations between serum PBB and thyroid hormones levels. Furthermore, thyroid hormones regulate a number of metabolic pathways including lipid metabolism and the activity of some CYP-P450 enzymes which may alter PBB serum concentrations. As a result, it cannot be excluded that levels of thyroid hormones influence PBB serum concentrations and not *vice versa*. Lymphocyte changes and other cell abnormalities (decrease in numbers and percentage of peripheral blood lymphocytes that form rosettes, increases in lymphocytes with no detectable surface markers –"null" cells – and altered responses to tests designed to evaluate functional integrity of the cells) were often found in PBB-contaminated humans and not in healthy normal control subjects. Nevertheless, their short- or long-term influence on the health on PBB-exposed humans has not been established.

8.4.2. Neurodevelopmental effects

Table G2 (Appendix G) reports the most relevant information on neurodevelopmental effects.

Walker Seagull (1983) investigated whether ingestion of PBBs has an adverse effect on the neuropsychological development of young children exposed *in utero* and in infancy. Five tests of the McCarthy Scales of Children's Abilities were administered to nineteen PBB-exposed Michigan children. Multivariate analysis showed the existence of a significant main effect for fat PBB level, controlling for parental education. Children with higher body burdens of PBBs (> 0.100 ppm) scored significantly lower than exposed children with lower body burdens on the same four tests, and on a composite score representing overall performance. These results suggest the existence of an inverse relationship between body levels of PBBs and some developmental abilities in young children.

Valciukas et al. (1979) studied the prevalence of neurological symptoms in males and in females in the Michigan population exposed to PBBs (with comparison to similar data in the Wisconsin, non-PBB-exposed group). The study population was 626 adults from Michigan and 153 from Wisconsin. The sub-sample examined by means of performance tests consisted of 95 males and 67 females from Michigan and 50 males and 43 females from Wisconsin. Neurological symptoms were the earliest and most prominent symptoms recorded in Michigan farm residents exposed to PBBs as compared to non-PBB exposed control farm populations in Wisconsin. In Michigan (particularly among males) those who exhibited the most marked symptoms tended to show diminished performance as assessed by special tests, although population differences in performance were not as marked. Low indices of performance were also significantly correlated with intake of home-produced foodstuffs, particularly during the years 1972-1974 and store-bought products during the years 1975-1976. Serum PBB levels were not found to be significantly higher in Michigan males and females exhibiting the most prominent neurological symptoms. Serum PBB levels were negatively correlated with performance test scores, particularly in males in older age groups.

Stross et al. (1979) evaluated the neurobehavioural complaints in the Michigan cohort. The study population was 46 persons (37 men and 9 women) identified from previous studies with known exposure to PBBs and incapacitating health complaints. Physical examinations and psychological-psychiatric tests were performed. In this group of patients positive findings were hepatomegaly (72 %), skin abnormalities (28 %), objective joint abnormalities (13 %), neurological abnormalities (15 %) and depression (67 %). Nerve conduction studies were abnormal in 19 patients (41 %). There was no evidence of changes suggestive of organic brain syndromes. There was no relationship between the presence of abnormalities and serum or fat PBB levels.

Brown and Nixon (1979) compared 21 persons exposed to PBBs during the Michigan incident with hospital volunteers. Patients exposed to PBB were selected for this study only if they had persistent

medical complaints. A battery of tests measuring memory, motor strength and coordination, cortical-sensory perception, personality, and higher cognitive functioning was performed. The PBB adipose levels did not correlate with performance on any test in the battery. The two groups did differ on the Minnesota Multiphasic Personality Inventory, suggesting an adjustment reaction with depressive symptoms and somatizing defenses. Persons exposed to PBBs were also impaired relative to control subjects on tests of prose recall, short-term memory, concentration, and cognitive flexibility. However these differences vanished when results were controlled for group differences on education and personality.

The symptoms of 644 adults from Michigan and 153 from Wisconsin were analysed by Valciukas et al. (1978) for prevalence of neuropsychological symptomatology. The performance of the populations was studied with neurobehavioural tests in a sub-sample (102 males and 68 females from Michigan and 50 males and 43 females from Wisconsin) chosen at random during comprehensive cross-sectional clinical surveys in the two states. A significant constellation of neurological symptoms and of performance test scores occurred among dairy farmers during the period 1972-1976, when compared to a non-PBB-exposed dairy farm population.

Summarising, impaired behaviour was associated with exposure to PBBs in two studies. Analyses involved a large number of statistical tests and therefore some of the statistically significany findings may have occurred by chance due to multiple comparisons. Exposure to other halogenated contaminants could have interfered with the outcome. Inability to control for these concomitant exposures, limits the interpretation of the observed neurobehavioural effects.

8.4.3. Cancer

Table G3 (Appendix G) reports the most relevant information on cancer.

Zhao et al. (2009) found high burdens of PBBs (PBB-1, -2, -3, -4,-5, -7, -9, -10, -18, -26, -29, -30, -31, -38, -49, -52, -53, -80, -101, -103, -153, -155 and -209), PBDEs and PCBs in samples of 19 kidney, 55 liver and 7 lung tissue samples from surgical cancer patients living close to electronic waste disassembly sites. The results showed that, among PBBs, lower brominated PBBs and BB-153 were the predominant congeners.

Hoque et al. (1998) evaluated in a nested case-control study the association between site-specific cancer risk and serum PBBs levels among the Michigan cohort accidentally exposed to PBBs in 1973. The Michigan Department of Public Health has followed 3,899 people through 1993, among whom 195 primary cancers were identified in 187 persons. Controls were 696 randomly selected cancer-free individuals who were frequency matched to cases by sex and age (in 5-year strata). Baseline serum PBB levels were measured using standard methods. This study found an increasing dose-response relation for digestive system cancer risk with higher serum PBB category [4-20 ppb, 21-50 ppb, and >50 ppb] after adjustment for age, family cancer history, cigarette smoking, alcohol drinking, and baseline serum PCB level. Adjusted odds ratios (ORs) for each category were 8.23 [95 % confidence interval (CI) = 1.27-53.3], 12.3 (95 % CI = 0.80-191), and 22.9 (95 % CI = 1.34-392), respectively. Univariate analysis for PBB level and lymphoma risk also showed a dose-response relationship, with corresponding ORs of 3.24 (95 % CI = 0.24-95.9), 20.5 (95 % CI = 1.51-608), and 32.6 (95 % CI = 3.33-861).

Henderson et al. (1995) examined the association between breast cancer and serum PBBs in a case-control study with 1,925 women enrolled in the Michigan cohort. 20 women who developed breast cancer were matched to 290 control subjects on sex, race, and age. Women with serum PBB levels of 2.0-3.0 ppb [OR = 3.5; 95 % CI = 0.9-13] or 4.0 ppb or greater (OR = 3.1; 95 % CI = 0.8-12) had a higher estimated risk for breast cancer than women with less than 2.0 ppb. The odds ratios were unchanged when available breast cancer risk factors were included in the analysis.

Wong et al. (1984) conducted a historical cohort mortality study on 3,579 white male workers employed between 1935 and 1976 with potential exposures to brominated compounds including PBBs and DDT. Due to the lack of quantitative data, potential exposure of workers to PBBs were categorized as more highly exposed (routiney exposure) and less exposed (non-routine exposure). Of the 91 workers potentially exposed on a "routine" basis, none died during the study period; among the 237 "non-routinely" exposed male workers, two deaths were observed versus 6.4 expected, one of which was due to cancer of the large intestine (1 observed versus 0.1 expected).

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

Overall, the human data on the carcinogenicity of single PBB congeners and technical PBB mixtures are limited. Problems of confounding by other compounds and small sample size hamper interpretation of the risk for cancer. In some of the studies, subjects exposed to PBBs were also exposed to other contaminants. In the study by Wong et al. (1984) many of the workers were potentially exposed to a multitude of chemicals, and it was impossible to examine mortality as caused by exposure to PBBs. The limitations of the study by Henderson et al. (1995) include the small number of breast cancer cases and the lack of information on other exposures such as use of organochlorides and important breast cancer risk factors such as estrogen receptors status or oral contraceptives use.

8.4.4. Diabetes and metabolic syndrome

Table G4 (Appendix G) reports the most relevant information on diabetes and metabolic syndrome.

Lee et al. (2010) published the results of a case-control study nested in the CARDIA cohort of 5,115 African American and white participants recruited at baseline in 1985-1986 (year 0). The aim of the study was to evaluate several POPs as predictors of type 2 diabetes. Cases were 90 new cases of diabetes. Ninety controls were randomly selected among diabetes free subjects. Persistent Organic Pollutants (POPs) measured in 1987-88 sera included 8 organochlorine pesticides, 22 PCBs and BB-153. The highest risk was observed in the 2nd quartiles of trans-nonachlor, oxychlordane, mirex, highly chlorinated PCBs and BB-153. The adjusted odds ratios among subjects in the 2nd sextile was 5.3 compared to the lowest sextile; and 20.1 among those with body mass index (BMI) $\geq$30 kg/m^2. Odds ratios (sex, age, ethnic group, BMI, triglyceride, total cholesterol adjusted) for BB-153 only quartiles were 2.5 (95 % CI 0.9-6.9), 2.5 (0.8-7.6) and 1.8 (0.6-5.8) with no dose response.

In Lim et al. (2008) a sample of 1,367 adults from the NHANES cohort was examined with respect to diabetes status. For metabolic syndrome, analyses were restricted to 637 participants with a morning fasting sample. The authors selected 5 PBDE congeners and one PBB congener (BB-153) for which at least 60 % of the study participants has serum concentrations above the LOD. Compared with subjects with serum concentrations below the LOD, prevalent diabetes had differing dose-response associations with serum concentrations of BB-153. Adjusted odds ratios across not detectable/quartiles of serum concentrations for BB-153 were 1.0, 0.7, 1.4, 1.6 and 1.9 (P for trend <0.01). BB-153 was also positively associated with the prevalence of metabolic syndrome with adjusted odds ratios of 1.0, 1.5, 3.1, 3.1, and 3.1 (P for trend <0.01). Analyses involved a large number of statistical tests and therefore some of the statistically significant findings may have occurred by chance due to multiple comparisons. This is an intrinsic flaw in the analyses of the results of cross-sectional studies, and therefore inference should be made with caution.

Studies have reported an increased risk of diabetes related to PCB exposure. To determine the incidence of adult-onset diabetes, Vasiliu et al. (2006) analysed PBB and PCB serum levels measured from blood collected at enrolment in members of the Michigan cohort without diabetes at enrolment, ages 20 years and older, who participated in at least 1 follow-up survey (n = 1,384). Using Poisson regression, the incidence of diabetes for different serum levels of PBBs and PCBs was determined,

controlling for age, body mass index, smoking, and alcohol consumption at enrolment. ORs ranged from 0.5 to 1.5 with no dose response and wide confidence intervals. Analysing 25 years of follow-up data, the study did not find that higher PBB serum levels were a risk factor for the incidence of diabetes mellitus.

Some studies link diabetes and metabolic syndrome prevalences to serum concentrations of POPs. One diabetes incidence study failed to confirm this suggested association for PBBs, while one cross-sectional study (diabetes and metabolic syndrome) and one diabetes case-control study nested in a prospective cohort, suggested the possibility of this association for BB-153. The CONTAM Panel concluded that cross-sectional studies may not be the most appropriate study design to investigate the relationship between diabetes and exposure to PBBs, as they cannot rule out reverse causation in which diabetes may enhance POPs accumulation or inhibit their clearance.

8.4.5. Effects on fertility or offspring

Table G5 (Appendix G) reports the most relevant information on effects on fertility or offspring.

Small et al. (2009) examined self-reported data on genitourinary (GU) conditions among 464 male offspring in relation to maternal serum PBB levels in the Michigan cohort. After adjustment for gestational age at birth, sons of highly exposed women (> 5 ppb) were twice as likely to report any GU condition compared with sons of the least exposed women (≤ 1 ppb; OR = 2.0; 95 % CI): 8–5.1). This risk was increased when the authors excluded sons born after the exposure but before the mother's serum PBB measurement (OR = 3.1; 95 % CI, 1.0–9.1). The authors found evidence of a 3-fold increase in reported hernia or hydrocele among sons with higher PBB exposure (test of trend p-value = 0.04). Neither hypospadias nor cryptorchidism was individually associated with PBB exposure. Although cryptorchidism and hypospadias were not associated with *in utero* PBB exposure, this study suggests that other GU conditions may be associated with exposure to endocrine-disrupting chemicals during development.

Terrell et al. (2009) found a 0.542 proportion of male offspring among 865 live births in 479 mothers enrolled in the Michigan cohort. This was higher than the national male proportion of 0.514 (binomial test: p=0.10). In offsprings (n=300) whose parents were both enrolled in the Michigan cohort, the ratio of males to females was even higher (OR = 1.43, 95 % CI: 0.89-2.29). Even if many potential confounders were considered in the analysis, in this study it was not possible to separate exposure to PBBs and PCBs, limiting the interpretation of this potential association.

Sweeney and Symanski (2007) examined the association between early age at the time of elevated exposure to PBBs and subsequent birth weight and gestational length in 1,111 births that occurred from 1975 to 1994 among 560 women enrolled in the Michigan cohort. Maternal age at exposure was categorized into three groups: <10 years (n = 64), 11-16 years (n=149), and 17-42 years (n=347). Overall serum PBB levels ranged from 0 to 1,490 ppb, with a median of 2, 3, and 2 ppb in the three age groups, respectively. The effect of age at exposure (years) and initial PBB level (ppb) on birth weight, BMI (kg/m^2) and serum PCB level at enrolment were evaluated, controlling for potential confounders. Age <10 years at exposure was the most important predictor of increased birth weight (estimated regression coefficient 225 g, p = 0.012). Infant birth weight increased approximately 16 g for every 10 ppb increase in serum PBBs (p = 0.004). No association between initial PBB levels and gestational age was found.

Givens et al. (2007) examined the influence of maternal exposures on gestational age and birth weight in 444 mothers and their 899 infants born between 1975 and 1997 (Michigan cohort). No significant association was found between estimated maternal serum PBB at conception and gestational age or infant birth weight. A negative association with high levels of enrolment maternal serum PBB at enrolment and birth weight was suggested. Birth weight and gestational age among offspring of women with the highest decile of PBB serum concentration, showed no significant association.

Hoffman et al. (2007) examined the association between endometriosis and exposure to PBBs (and PCBs) in 943 women of the Michigan cohort. Seventy-nine women (9 %) reported endometriosis. Compared to women with low PBB exposure (≤ 1 ppb), women with moderate PBB levels (1-4 ppb) had a hazard ratio (HR) of 0.72 (95 % CI=0.39-1.35). HR for women with high PBB levels (≥ 4 ppb) was 0.90 (95 % CI=0.51-1.59). This study does not support an association between PBB exposure and endometriosis.

Small et al. (2007) evaluated the risk of spontaneous abortion among 529 women (1,344 potentially exposed pregnancies) of the Michigan cohort. Compared to pregnancies with PBB exposure below the LOD, those with levels above 2.9 ppb had a non-significant reduced odds of spontaneous abortion (adjusted OR=0.73; 95 % CI= 0.47-1.13). PBB (and PCB) exposure were not associated with risk of spontaneous abortion after adjusting for maternal age at conception, age at menarche, and prior infertility.

Davis et al. (2005) evaluated the menstrual cycle length among 337 women (age range: 24-56 years) of the Michigan cohort with self-reported menstrual cycles of 20-35 days. Average cycle length did not differ among women when stratified by PBB exposure at enrolment or by PBB exposure estimated at the time of the interview. An association between PBB exposure and menstrual cycle length or bleed length was only found for a subgroup of women with weight loss in the past year.

This study suggests that PBB exposure may impact ovarian function as indicated by menstrual cycle length and bleed length. However, these associations were found only among the small number of women with recent weight loss suggesting either a chance finding or that mobilization of PBBs from lipid stores may be important.

Blanck et al. (2004) evaluated time to menopause in 874 women, aged 24 years and older from the Michigan cohort. Serum PBB and PCB levels taken at enrolment (1976-1978) into the Michigan PBB registry was used as the measure of exposure. Women whose menopause occurred before their exposure to PBBs were excluded. Proportional hazard modelling was used to analyze the "risk" for menopause in relation to exposure. The authors did not find an association between either PBB or PCB exposure and time to menopause. Women who were current smokers had a shorter time to menopause than never smokers (menopause ratio 2.02, 95 % C.I. 1.21–3.37).

Blanck et al. (2002) examined the association of estimated PBB (and PCB) exposure during pregnancy in the Michigan cohort with current height and weight in 308 daughters, 5-24 years of age (mean age=15.2 years). Prenatal PBB exposure using maternal enrolment serum PBB and a model of PBB elimination was assessed. Self-reported height and weight were obtained from a 1997-1998 health survey. No association between prenatal PBB exposure and either daughter's current height or daughter's weight adjusted for height was found.

Blanck et al. (2000b) assessed pubertal development in 327 females (5-24 years of age) who were exposed to PBBs *in utero* and, in many cases, through breastfeeding (Michigan cohort). They estimated *in utero* PBB exposure using maternal serum PBB measurements taken after exposure (1976-1979) and extrapolated to time of pregnancy using a model of PBB decay. Breastfed girls exposed to high levels of PBBs *in utero* (≥7 ppb) had an earlier age at menarche (mean age = 11.6 years) than breastfed girls exposed to lower levels of PBBs *in utero* (mean age = 12.2-12.6 years) or girls who were not breastfed (mean age = 12.7 years). This association persisted after adjustment for potential confounders (menarche ratio = 3.4, 95 % confidence interval = 1.3-9.0). Perinatal PBB exposure was associated with earlier pubic hair stage in breastfed girls, but little association was found with breast development. The associations observed here lend support to the hypothesis that pubertal events may be affected by pre- and postnatal exposure to organohalogens.

Humble and Speizer (1984) carried out a study to evaluate fetal mortality (spontaneous abortions occurring after 20 weeks of gestation) in the Michigan cohort. The high exposure group consisted of

seven lower peninsula counties with between 6.8 per cent and 20.4 per cent of total farms quarantined per county. Thirteen upper peninsula counties with no quarantined farms were used as the comparison (low exposure) population. The annual RRs fluctuate widely and range from 0.53 in 1968 to 1.69 in 1981. However, over all the pre-exposure years the relative risk (RR) was significantly lower in the lower peninsula counties (RR = 0.83, CI 0.71-0.97). Comparison of fetal death rates among residents of Lower Peninsula counties with a high percentage of quarantined farms and among residents of Upper Peninsula counties with no quarantined farms reveals no important differences in rates or trends after the contamination. Since counts of early (up to week 20) spontaneous abortions are lacking, a complete assessment of the possible impact on reproductive outcome could not be made.

Rosenman et al. (1979) analysed semen from men exposed to PBBs (n=52, farmers and individuals who had consumed food directly from contaminated farms in Michigan and men employed at the chemical company where PBBs had been manufactured) compared with semen from a control group not exposed to PBBs (n=52, male graduate students at a Michigan university who were considered to have consumed little or no food contaminated with PBBs). No differences in the distribution of sperm counts, motility or morphology were revealed.

Overall results of the studies on members of the Michigan cohort and their offsprings, do not indicate any consistent effect on spermatogenesis, gestational age, time to menopause, increased odds of specific gender birth, foetal mortality, infant birth weight, spontaneous abortion, endometriosis, age at breast development. Suggestions of a trend to early menarch emerge from one study. Negative and inconsistent results might be due to inappropriate sample size. Many studies were heavily underpowered and a many-fold increase in sample size would have been needed to properly address the research question.

8.5. Consideration of critical effects and possibilities for derivation of a health based guidance value

The toxicological studies on PBBs date from 1976-1994, reflecting the phase-out of the manufacture and use of PBBs. All oral toxicity studies were carried out with technical PBB mixtures of which the exact composition of congeners is not known. Main targets were the liver, the reproductive system, the thyroid gland and the nervous and immune systems. Due to the bioaccumulative properties of PBBs, it is difficult to compare the effects of similar external doses given for different durations of time in different toxicological studies.

Limited information exists on the toxicokinetics of PBBs. This hampers the comparison between the studies, as well as the extrapolation of animal data to humans. The major part of metabolic studies have been carried out with BB-153, providing evidence that this congener is well absorbed (about 90 %), distributed in lipid-rich tissues, metabolized in the liver and eliminated, mainly in the faeces. The disposition of PBBs is most likely dependent on the molecular weight and the bromine substitution pattern of the congeners. The data collected from the Michigan cohort (see section 8.1.) provide indirect evidence that PBBs are absorbed to a significant extent in humans and that the serum half life varies between about 10 and 30 years.

PBBs have low acute oral toxicity, with LD_{50} values > 1,000 mg/kg b.w. after single exposure. After repeated exposure (60 days), lethality was in the range of 65-150 mg/kg b.w.

Technical mixtures of PBBs (i.e. FireMaster preparations) caused liver enlargement, hepatocellular hypertrophy, fatty degeneration and enzyme induction in experimental animals. In some instances hepatic necrosis was also observed. A LOEL in the range of 0.1-1 mg/kg b.w. for liver enlargement and enzyme induction has been reported in a six-month exposure study in rats. Studies conducted with individual congeners, i.e. BB-52, -77 and -156, at a single dose level via *i.p.* administration, indicated variable effects on liver enlargement and enzyme induction.

Evidence from animal studies indicate that exposure to PBBs influences the thyroid hormone homeostasis. The observed effects include decreases in serum levels of thyroid hormones (T4 and T3), elevated TSH levels, thyroid enlargement and morphological changes in follicular cells. The most sensitive marker was decreased serum T4. In 6 month exposure studies the NOEL was 0.1 mg/kg b.w. per day.

Based on the available data there is evidence that PBBs affect neurobehavioural development and the immune system. These effects occur at slightly higher levels than those on liver and thyroid.

Embryotoxicity and teratogenicity studies have shown that exposure to PBBs during early pregnancy can lead to resorption of foetuses at dose levels of 14 mg/kg b.w. or higher. Exposure to PBBs can also result in foetal malformations with some species difference in sentitivity. The LOEL in the mouse is 17.5 mg/kg b.w. whereas the LOEL in the rat is 400 mg/kg b.w.

In vitro and *in vivo* genotoxicity studies indicate that PBBs are not directly genotoxic.

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, with a NOEL of 0.15 mg/kg b.w. (NTP, 1993). *T*here is evidence that *ortho* substituted congeners may cause cancer through interaction with nuclear receptors, such as CAR, whereas the non-*ortho* congeners appear to cause tumours as a consequence of AhR activation and cytotoxicity, presumably via stimulation of regenerative proliferation.

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 PXR. Activation of these receptors can lead to increased catabolism of thyroid hormones. The effects on the liver, including hepatocarcinogenesis, and on the thyroid gland may be a consequence of such receptor activation. Changes in thyroid hormones are known to influence neurobehavioural development, although there is no specific information available as to whether, or to what extent, this underlies the neurodevelopmental effects observed for PBBs.

Epidemiological studies indicate that there are some associations between exposure to PBBS and changes in health such as neurodevelopmental effects, site-specific cancer and effects on fertility and offspring. However, these findings were inconsistent and confounding by other compounds and/or lifestyle factors and limitations in the study design hamper interpretation of the epidemiological results.

In considering all the different toxicological endpoints affected by PBBs, the CONTAM Panel 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 b.w. 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 b.w. 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.

9. Risk characterization

The CONTAM Panel selected a specific group of the population consisting of high and frequent fish consumers of fatty fish meat (>8 % fat) as those with the highest exposure to PBBs in their diet of all of the subgroups considered, other than breast-fed infants. An initial risk characterization was undertaken using the sum of the UB high consumer values for the 5 PBB congeners with non detects

less than 80 %. Exposure to PBBs for this group is 0.15 ng/kg b.w. per day. This was compared to the worst case toxicological reference point identified above, i.e. the NOEL for hepatocarcinogenesis of 0.15 mg/kg b.w. per day in rats.

The CONTAM Panel noted that exposure in this specific consumer group was approximately 6 orders of magnitude less than this NOEL. The mean intake for high consuming breast-fed infants was 1.4 ng/kg b.w. per day, i.e. 5 orders of magnitude less than this NOEL. Exposure of all other groups of the population even at the UB for the high consumers was appreciably lower than in the frequent and high fish consumers group.

Due to the potential toxicological concerns related to the non-*ortho* PBBs, additional exposure estimates were performed for the three cogeners BB-77, -126 and -169. A calculation for high consumers (95th percentile) based on median UB concentrations resulted in exposures of around 0.3 pg/kg b.w. per day for the sum of the three congeners (see Tables 10, 11 and 12). Assuming similar toxicity equivalence factors (TEFs) as for non-*ortho* PCBs (van den Berg et al., 2006), the exposure to non-*ortho* PBBs was estimated to be in the region of 0.01 pg TEQ/kg b.w. Compared to background exposure of the European population to dioxins and dioxin-like compounds, the CONTAM Panel considered this highly overestimated exposure to non-*ortho* PBBs as negligible.

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

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.

10. Uncertainty

The evaluation of the inherent uncertainties in the assessment of exposure to PBBs has been performed following the guidance of the Opinion of the Scientific Committee related to Uncertainties in Dietary Exposure Assessment (EFSA, 2007). In addition, the draft report on "Characterizing and Communicating Uncertainty in Exposure Assessment" which is in preparation to be published as WHO/IPCS monograph has been considered (WHO/IPCS, 2008). According to the guidance provided by the EFSA opinion (EFSA, 2007) the following sources of uncertainties have been considered: assessment objectives, exposure scenario, exposure model, and model input parameters.

10.1. Assessment objectives

The objectives of the assessment were clearly specified in the terms of reference. The CONTAM Panel assessed the new occurrence data that were collected by EFSA, and carried out an exposure assessment for the general population as well as for specific subgroups. The uncertainty in the assessment objectives is considered to be negligible.

10.2. Exposure scenarios/Exposure model

In response to EFSA's request to submit PBB occurrence data in food, 6 member states submitted 5,643 analytical results covering 794 samples across five broad food categories. The UK and Belgium submitted around 80 % of the results. The food products for which data were provided varied between submissions from the different Member States, but most samples belonged to the fish and seafood category, followed by products of terrestrial animal origin and only a few samples of plant origin. Moreover, there are considerable differences in the number of PBB congeners reported by each country, with a maximum of 16 out of the 209 possible PBB congeners. There is uncertainty in possible regional differences in PBB contamination of food commodities, and the CONTAM Panel recognised that the data set is not representative of food on the EU market. Food processing has been

shown to have an influence on the PBB levels in the prepared food commodities. Because this is dependent on the type of food product and type of processing, this influence could not be considered. But taking into account, that the processed foods in general had lower PBB concentrations than the respective raw materials, this could have led to some overestimation of the overall PBB exposure.

The high proportion of samples having levels below the LOD may have introduced uncertainties to the overall estimate. The use of the UB in this opinion tends to overestimate the dietary exposure. Because of the high proportion of samples below the LOD, all the exposure calculations were based on the mean concentrations. It is generally accepted that the use of the mean contamination to represent the long term dietary exposure is expected to be an overestimation compared with the use of the median. Taken together, the uncertainties regarding the exposure estimates are considered to overestimate the exposure.

10.3. Model input parameters

There are no prescribed fixed official methods for the analysis of PBBs and laboratories can use any method of analysis, provided it can be demonstrated in a traceable manner that they strictly fulfil the requirements according to ISO 17025. This may have added to the uncertainty in the analytical results. The lack of certified reference materials and proficiency tests are clearly limitations when the method performance for the analytical methods for analysis of PBBs in food is assessed, and add thereby to the overall uncertainty in the analytical results.

10.4. Other uncertainties

Most of the toxicological data were gained from experiments with technical mixtures rather than purified individual congeners. As these technical mixtures are complex and only the major congeners or homologue groups are known and information on minor components such as non-*ortho* PBBs or impurities such as dioxin-like compounds in different mixtures and batches are limited, this adds a considerable uncertainty in the hazard characterization. Even in cases where levels of an individual contaminant are low, their concentration adds to the total body burden of different contaminants, thereby inducing uncertainty about the specific health impact of the PBB mixture studied. Moreover, the congener profile currently found in food does neither resemble the profiles found in the technical PBB mixtures nor in human specimens. While the most frequently found congeners in food seem to be BB-52 and -101, human samples are generally dominated by BB-153 which might be an indication of the different half-lives in humans.

10.5. Summary of uncertainties

In Table 23 a summary of the uncertainty evaluation is presented, highlighting the main sources of uncertainty and indicating an estimate whether the respective source of uncertainty might have led to an over- or underestimation of the exposure or the resulting risk.

Table 23: Summary of qualitative evaluation of the impact of uncertainties on the risk assessment of the dietary exposure to PBBs.

Sources of uncertainty	Direction[(a)]
Measurement uncertainty of analytical results	+/-
Limited number of food categories with varying number of congeners reported	+/-
Extrapolation of occurrence data from a few member states to whole Europe	+/-
Influence of upper-bounds for non-detects on exposure estimate	+
Non consideration of food processing	+
Limited information on the composition and purity of technical mixtures used in animal studies, and their relevance to the PBBs profile currently found in food.	+/-

(a): + = uncertainty with potential to cause over-estimation of exposure/risk; - = uncertainty with potential to cause under-estimation of exposure/risk.

The CONTAM Panel considered that the impact of the uncertainties on the risk assessment of exposure to PBBs is considerable and concluded that its assessment of the risk is likely to be conservative, i.e. more likely to overestimate than to underestimate the risk.

CONCLUSIONS AND RECOMMENDATION

CONCLUSIONS

General

- Polybrominated biphenyls (PBBs) are a class of hydrocarbons with a basic structure that consists of two phenyl rings to which the bromine atoms are attached. Depending on the number and positions of the bromine atoms at the two rings, 209 different compounds are possible, referred to as PBB congeners.
- PBBs are additive flame retardants which were specially applied in synthetic fibres 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 DecaBB which was produced up till around 2000.
- Dependent on structure, PBBs are persistent and lipophilic compounds with low vapour pressure and low water solubility. They are generally chemically stable and bioaccumulative.

Occurrence

- PBBs are present in the environment at low concentrations and likewise in biota and in food and feed.
- Following an advice of the Panel on Contaminants in the Food Chain (CONTAM Panel), a monitoring exercise was carried out from 2006 and results obtained from the analysis of 16 PBB congeners on 794 food samples were provided to EFSA by 6 Member States, covering the period from 2003 to 2009.
- The food category "Fish and other seafood (including amphibians, reptiles, snails and insects)" dominated the total samples, followed by "Meat and meat products (including edible offal)" and "Animal and vegetable fats and oils" and "Milk and dairy products". Less than 30 samples were reported for the remaining food categories.

- The data were characterised by a high proportion of non detects for the different congeners (more than 80 %) with some food categories, i.e. "Animal and vegetable fats and oils", "Milk and dairy products", close to 100 % non detects.

- The highest frequency of analytical results with the lowest proportion of non detects were reported for the food category of "Fish and other seafood (including amphibians, reptiles, snails and insects)". In a specific study on the sub-category of "Fish meat" for 9 out of 10 congeners (BB-15, -49, -52, -77, -80, -101, -126, -153 and -169) analysed, an increasing fat content corresponded with increasing PBB contamination levels (except for BB-209).

- In order to allow for a reliable application of the upper and lower bound approach and to prevent an unrealistic exposure estimate, congeners were selected in the respective food categories where the proportion of non detects was lower than 80 %.

- Recent data on the contamination of human milk with PBBs were only available from two European countries, indicating that BB-153 is by far the most frequently found and most abundant congener, with mean levels of 134 pg/g fat and 200 pg/g fat, respectively.

Human exposure

- Environmental occurrence and human exposure in Europe are due to historical production and use of PBBs.

- 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 b.w. per day, for lower and upper bound, respectively. Median dietary exposure to BB-52 across countries is between 1.2 and 1.3 pg/kg b.w. per 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 b.w. per day (lower bound) and 28.2 pg/kg b.w. per day (upper bound). Exposure to BB-52 is between 6.3 pg/kg b.w. per day (lower bound) and 6.4 pg/kg b.w. per 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 b.w. and 16.1 pg/kg b.w. per day (lower and upper bound, respectively), and between 0.41 pg/kg b.w. and 16.2 pg/kg b.w. (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.

- For a specific population group consisting of high and frequent fish consumers consuming fatty fish meat (>8 % fat) the dietary lower and upper bound intake of BB-153 was estimated to be about 4.3 and 89 pg/kg b.w. per day, respectively. Lower bound estimates for BB-52, -101, -49 and -77 were 34.4, 12.2, 9.6 and 0.06 pg/kg b.w. per day, respectively. The respective upper bound estimates were about 35.0, 14.1, 11.2 and 0.09 pg/kg b.w. per day. Thus, the upper bound median exposure estimate for the sum of these five PBBs is about 149 pg/kg b.w. per day.

- Another source of PBBs exposure is supplements, such as cod liver oil, containing special fatty acids (e.g. omega-3, essential fatty acids). Assuming a maximum daily intake of 15 ml of oil an additional intake of BB-153 up to 18.9 pg/g kg b.w. per day (upperbound), of BB-49 up

to 10.4 pg/g b.w. per day (upper bound), of BB-52 up to 4.5 pg/g b.w. per day (upper bound), of BB-101 up to 4.8 pg/g b.w. per day (upperbound) and of BB-77 up to 0.02 pg/g b.w. per day (upperbound), were estimated.

- As contamination of food samples of plant origin is generally lower than that of food samples of animal origin, it can be assumed that the dietary exposure to PBBs for vegetarians is lower than that for people consuming a mixed diet.

- Based on data from two countries, mean exposure to BB-153 through breast feeding for infants with an average milk consumption (800 mL per day) was calculated as 0.62 and 0.92 ng/kg b.w. per day, respectively. Mean exposure for infants with a high milk consumption (1,200 mL per day) was 0.92 and 1.4 ng/kg b.w. per day. When also the other PBB congeners that were detected in human milk are included, these values will be about 10-20 % higher.

- Based on data from two consumption surveys the exposure to BB-153 for infants from 0 to 1 year old eating "Ready-to-eat meal for infants and young children" was estimated to be zero across the two consumption surveys (lower bound estimate) and 0.17 and 0.64 ng/kg b.w. day (upper bound estimates) for the two consumptions surveys, respectively.

Hazard identification and characterization

- Gastrointestinal absorption was estimated to be approximately 90 % for BB-153, but no data were identified regarding absorption of other congeners. PBBs are lipophilic compounds which accumulate in adipose tissue.

- Debromination and hydroxylation are the major metabolic pathways of PBBs.

- The serum half-life for PBBs in humans varies between about 10 and 30 years. Lactation constitutes the most important route of excretion of PBBs in lactating women.

- Most toxicological studies in animals were carried out with technical PBB mixtures.

- PBBs have low acute oral toxicity, with lethal dose (LD_{50}) values > 1,000 mg/kg b.w. after single exposure. After repeated exposure (60 days), lethality was in the range of 65-150 mg/kg b.w.

- PBBs caused liver enlargement, hepatocellular hypertrophy and fatty degeneration of the liver in experimental animals. In some instances hepatic necrosis was also observed.

- Evidence from animal studies indicate that exposure to PBBs influences the thyroid hormone homeostasis. The observed effects include decreases in serum levels of thyroid hormones (thyroxine (T4) and triiodothyronine (T3)), increases in thyroid stimulating hormone (TSH) levels, thyroid enlargement and effects in follicular cells.

- There is evidence that PBBs affect neurobehavior and the immune system. These effects occur at slightly higher levels than those on liver and thyroid.

- The embryotoxicity and teratogenicity studies indicate that exposure to PBBs in early pregnancy can lead to resorbtion of foetuses, while administration later in pregnancy can give rise to offspring with lower birth weight and minor malformations.

- *In vitro* and *in vivo* genotoxicity studies indicate that PBBs are not directly genotoxic.

- 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. The no-observed-effect level (NOEL) is 0.15 mg/kg b.w. There is evidence that some congeners may cause cancer through interaction with nuclear receptors, whereas others appear to cause tumours as a consequence of cytotoxicity, presumably via stimulation of regenerative proliferation.

- 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 arylhydrocarbon receptor (AhR) receptor and a number of the toxic effects observed are consistent with dioxin-like activity.

- There is some evidence that *ortho*-substituted PBBs can activate other receptors such as constitutive androstane receptor (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.

- The CONTAM Panel noted that the results of epidemiological studies on associations between exposure to PBBs and health effects including neurodevelopmental effects, excess of site-specific cancer and effects on fertility and offspring, were limited and inconsistent.

- The CONTAM Panel identified the hepatic carcinogenic effects of PBBs as the critical effect for the derivation of a reference point for gauging the potential health risks of dietary exposure to PBBs. The Panel noted that this NOEL of 0.15 mg/kg b.w. represents a worst case situation as it was obtained in a study with a technical PBB mixture, the congener composition of which is not representative of the congener profiles currently found in food. Therefore, the CONTAM Panel concluded that it was inappropriate to use this NOEL to derive a health based guidance value for PBBs.

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 b.w.

- 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, even considering the difference in kinetics between experimental animals and humans, is of no concern.

RECOMMENDATION

- 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.

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APPENDICES

A. CURRENT OCCURRENCE DATA ON PBBS (FIGURES)

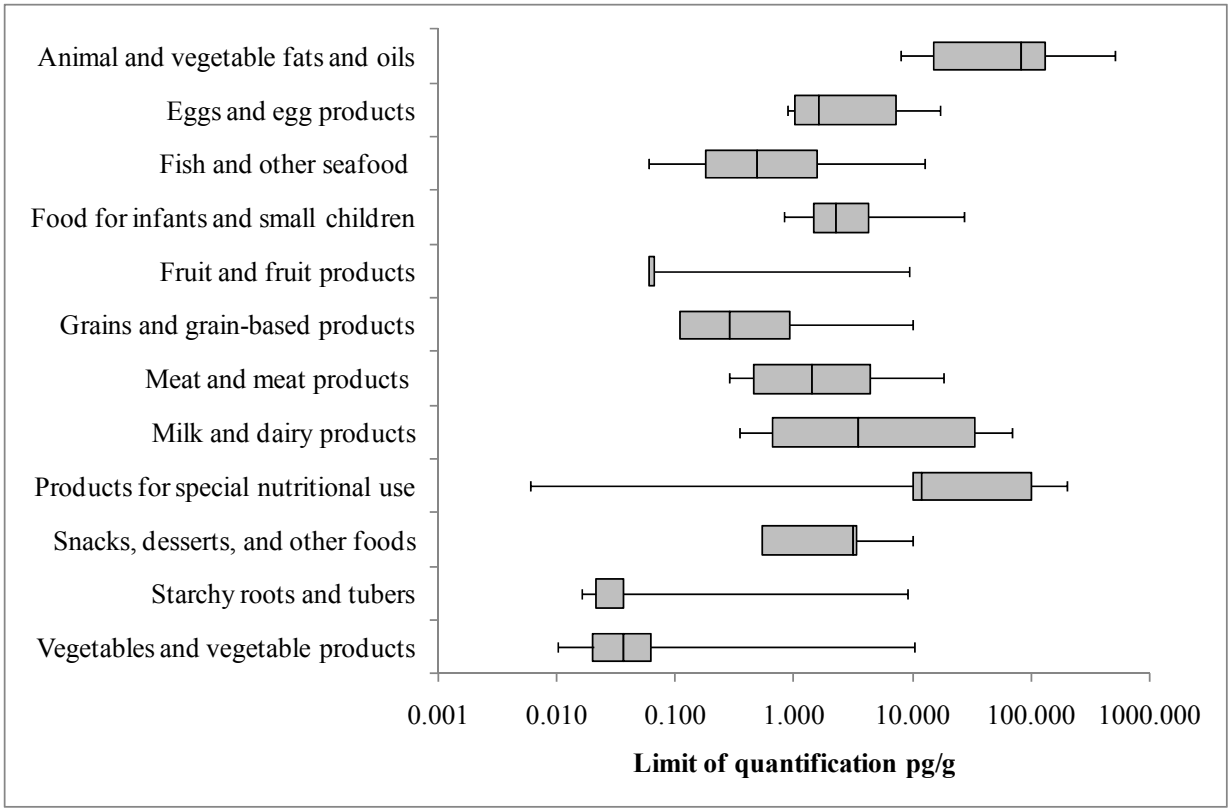

Figure A1: Distribution of the limit of quantification (LOQ) estimated from the LOQs reported for 12 PBB congeners (BB-3, -15, -29, -49, -52, -80, -101, -103, -153, -180, -194, -206 and -209) according to the first level of the FoodEx food categories.

B. PREVIOUSLY REPORTED PBBS OCCURRENCE RESULTS / LITERATURE DATA

Table B1: PBB levels (pg/g wet weight (w.w.) in fish samples reported in the literature. Data concerns individual samples, unless otherwise stated. p: pooled individuals.

Source	Matrix	Origin	Year (20xx)	n	Fat (%)	PBB congener (pg/kg w.w.)										
						BB-77	BB-126	BB-169	BB-15	BB-29	BB-49	BB-52	BB-80	BB-101	BB-153	BB-209
FSA, 2006a	Anchovy (canned)	UK[(a)]	02-04	1		<0.01	<0.01	<0.02	<1		<1	<1	<1	<1	<1	<3
FSA, 2006a	Cod	UK	02-04	1		0.01	<0.01	<0.01	<0.04		<0.1	<0.1	<0.04	<0.3	<0.3	<1
Gieron et al, 2010	Cod liver in oil	Poland	07	2p	56-59					20	99	134-443		93-313	93	
FSA, 2006a	Crab	UK	02-04	2		0.01-0.02	<0.01-<0.02	<0.01	<0.1-2		<0.1-1	<0.1-1	<0.1-1	<0.2-2	<0.2-10	<1-3
FSA, 2006a	Coley	UK	02-04	1		0.01	0.01	<0.01	<0.2		1	1	<0.2	0.4	<0.4	<10
FSA, 2006a	Crab	UK	02-04	2		0.01-0.02	<0.01-<0.02	<0.01	<0.1-2		<0.1-1	<0.1-1	<0.1-1	<0.2-2	<0.2-10	<1-3
FSA, 2006a	Dogfish	UK	02-04	1		0.02	<0.01	<0.01	<1		10	20	1	10	40	<0.7
FSA, 2006a	Eel	UK	02-04	1		0.01	<0.01	<0.01	<2		<2	4	<2	2	2	<10
FSA, 2006a	Fish paste	UK	02-04	1		0.02	<0.01	<0.02	<1		2	10	<1	2	<3	<4
Päpke et al., 2010	Fish	Europe	07-09	4								<2-7.6		<2-4.7	<2-1.3	<30-<100
Gieron et al., 2010	Grey Gurnard	North Sea	07	1p	17					7.3	33	57				
Gieron et al., 2010	Gilthead Sea Bream	North Sea	07	1p	17					2.4	15	56		17	179	
FSA, 2006a	Haddock	UK	02-04	1		<0.01	<0.01	<0.01	<0.1		<0.1	<0.1	<0.1	<0.3	<0.3	<1
FSA, 2006a	Hake	UK	02-04	1		0.01	<0.01	<0.01	<0.2		3	4	0.5	<0.5	1	20
FSA, 2006a	Halibut (farmed)	UK	02-04	1		0.02	<0.01	<0.01	<0.5		3	3	0.5	5	5	<10
FSA, 2006a	Halibut	UK	02-04	1		0.01	<0.01	<0.005	<0.4		10	10	<0.4	10	5	<10
FSA, 2006a	Herring	UK	02-04	2		0.04-0.08	<0.02-0.02	<0.02	<1-<2		3-10	11-20	<1-<2	4-10	2-4	<2-<4

Table B1: Continued.

Source	Matrix	Origin	Year (20xx)	n	Fat (%)	PBB congener (pg/kg w.w.)										
						BB-77	BB-126	BB-169	BB-15	BB-29	BB-49	BB-52	BB-80	BB-101	BB-153	BB-209
Gieron et al., 2010	Herring	Baltic Sea	07	2p	11-13							14		0.3	0.2	
Gieron et al., 2010	Herring	North Sea	07	1p	19					1.5		21				
Luross et al., 2002	Lake trout	USA	1997	4p	16-23					<1.3-5.2	6.8-125	8.4-191	<3.8	42-633	189-2083	
FSA, 2006a	Lemon sole	UK	02-04	1		0.01	0.01	<0.003	<0.1		0.3	1	<0.1	0.4	0.3	<10
FSA, 2006a	Mackerel	UK	02-04	2		0.05-0.06	<0.01-<0.02	<0.01	<1-<2		1-5	4-10	<1-<2	3-<10	<1-<5	<10
FSA, 2006a	Mussels	UK	02-04	1		0.05	<0.04	<0.04	<0.3		<1	3	<0.3	<1	<1	10
FSA, 2006a	Oysters	UK	02-04	1		0.13	<0.03	<0.03	1		2	10	<1	2	<4	30
FSA, 2006a	Pilchards	UK	02-04	1		0.01	<0.01	<0.01	<1		<1	<1	<1	<1	<1	<10
FSA, 2006a	Plaice	UK	02-04	1		0.01	<0.01	<0.01	<0.2		1	1	0	2	4	<1
FSA, 2006a	Prawns	UK	02-04	2		<0.01-0.01	<0.01	<0.01	<0.2		<0.3-10	<0.2-10	<0.2-1	<1-4	<0.3-4	<2
FSA, 2006a	Red snapper	UK	02-04	1		<0.01	<0.01	<0.005	<0.2		<0.4	<0.4	<0.2	<1	<1	<10
Gieron et al., 2010	Salmon	Baltic Sea	07	2p	20-43					0.95	14	15		11-14	2	
FSA, 2006a	Salmon canned	UK	02-04	1		<0.01	<0.01	<0.01	<1		<1	<1	<1	<1	<1	<2
FSA, 2006a	Salmon farmed	UK	02-04	1		0.03	<0.02	<0.01	<1		10	20	<1	10	10	<10
FSA, 2006a	Salmon	UK	02-04	2		0.01-0.02	<0.01-0.01	<0.01	<0.4-<1		<0.4-4	1-10	<0.4-<1	0.4-10	1-10	<10
Gieron et al., 2010	Salmon	North Sea	07	1p	23						29	20		18	11	
FSA, 2006a	Sardine / Pilchard	UK	02-04	1		0.02	0.01	<0.01	<1		3	10	<1	3	1	<10
FSA, 2006a	Sardine	UK	02-04	1		0.01	<0.01	<0.02	<1		<1	2	<1	<1	<1	<2
FSA, 2006a	Scallops	UK	02-04	1		0.01	<0.01	<0.01	<0.2		<0.2	<0.2	<0.2	<0.3	<0.3	<2
FSA, 2006a	Scampi	UK	02-04	1		0.01	<0.01	<0.01	<0.1		<0.3	<0.1	<0.2	<1	<0.2	20

Table B1: Continued.

Source	Matrix	Origin	Year (20xx)	n	Fat (%)	PBB congener (pg/kg w.w.)										
						BB-77	BB-126	BB-169	BB-15	BB-29	BB-49	BB-52	BB-80	BB-101	BB-153	BB-209
Gieron et al., 2010	Scarp	North Sea	07	1p	6							24				
FSA, 2006a	Sea Bass (farmed)	UK	02-04	1		0.01	<0.01	<0.01	<1		<1	<1	<1	<1	<1	<2
FSA, 2006a	Sea Bass	UK	02-04	1		<0.01	<0.01	<0.01	<1		3	10	<1	3	2	<10
FSA, 2006a	Sea Bream	UK	02-04	1		<0.01	<0.01	<0.01	<1		2	10	<1	10	3	<10
FSA, 2006a	Seat Trout	UK	02-04	1		0.03	<0.01	<0.01	<1		5	10	<1	10	4	<10
FSA, 2006a	Shark	UK	02-04	1		<0.01	0.01	<0.01	<0.1		0.4	0.4	<0.1	<0.4	1	10
FSA, 2006a	Sprat	UK	02-04	1		0.02	0.01	<0.01	<1		20	50	1	10	5	<10
FSA, 2006a	Surimi	UK	02-04	1		<0.01	<0.01	<0.01	<0.1		<0.1	<0.1	<0.1	<0.3	<0.3	<1
FSA, 2006a	Swordfish	UK	02-04	1		0.01	<0.01	<0.01	<1		<1	<1	2	2	2	<1
FSA, 2006a	Trout (farmed)	UK	02-04	1		0.03	<0.01	<0.01	<1		3	10	<1	3	3	10
Gieron et al., 2010	Trout	Poland	07	2p	6.4-12.8					0.45				1.4	0.42	
FSA, 2006a	Tuna	UK	02-04	2		<0.01	<0.01	<0.01	<0.1-<0.2		<0.1-<0.2	<0.1-<0.2	<0.1-<0.2	<0.2-<0.3	<0.2-0.4	<1
FSA, 2006a	Turbot (farmed)	UK	02-04			<0.01	<0.01	<0.01	<0.2		3	10	1	2	3	20
FSA, 2006a	Turbot	UK, Greenland	02-04	2		0.01-0.04	<0.01	<0.01	<0.3-<1		2-3	4-5	<1-1	3-4	3-4	<1-10
FSA, 2006a	Whitebait	UK	02-04	1		0.02	<0.01	<0.01	<0.5		5	20	<0.5	5	2	<10
FSA, 2006a	Whiting	UK	02-04	1		0.01	<0.01	<0.01	<0.1		<0.1	<0.4	<0.1	<0.4	<0.3	20

PBB: polybrominated biphenyl; w.w.: wet weight; p: pooled individuals; UK: The United Kingdom.

C. CURRENT OCCURRENCE DATA ON PBBS (TABLES)

Table C1: Statistical description of concentrations of BB-49, -52, -77, -101, -126, -153 and -169 (N: number of analysed samples; MEAN: mean; ND (%): percentage of not detected), across the food categories defined by Commission Directive 2006/13/EC. PBB levels are reported on fat (pg/g fat) or wet weight basis (pg/g w.w.) according to the different food categories as requested by the above mentioned legislation. The mean fat content calculated from the original samples is also reported (%).

Food categories (Legal groups)	N	TYPE	PBB target congeners														Mean (%) fat in original sample
			BB-49		BB-52		BB-77		BB-101		BB-126		BB-153		BB-169		
			MEAN	ND (%)	MEAN	ND (%)	MEAN	ND (%)	MEAN	ND (%)	MEAN	ND (%)	MEAN	ND (%)	MEAN	ND (%)	
Meat and meat products ruminants – pg/g fat	35	LB	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.01	80%	0.00	100%	0.00	100%	11.78
	35	UB	10.00	100%	10.00	100%	0.06	100%	10.00	100%	0.07	80%	12.00	100%	0.10	100%	11.78
Meat and meat products poultry – pg/g fat	68	LB	5.42	96%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	5.42	96%	0.00	100%	6.44
	68	UB	156.79	96%	10.00	100%	0.08	100%	10.00	100%	0.04	100%	240.13	96%	0.11	100%	6.44
Meat and meat products pigs – pg/g fat	21	LB	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	10.33
	21	UB	10.00	100%	10.00	100%	0.07	100%	10.00	100%	0.08	100%	10.00	100%	0.11	100%	10.33
Liver and products terrestrial animals – pg/g fat	148	LB	0.00	100%	0.75	83%	0.01	90%	0.75	83%	0.19	65%	22.00	70%	0.00	100%	5.95
	148	UB	10.00	100%	9.08	83%	0.08	90%	9.08	83%	0.25	65%	33.00	70%	0.12	100%	5.95
Muscle meat fish and fish products excl. eel – pg/g w.w.	1009	LB	1.27	39%	3.64	28%	0.02	28%	1.30	60%	0.00	95%	0.61	80%	0.00	100%	4.95
	1009	UB	1.42	39%	3.74	28%	0.02	28%	1.60	60%	0.01	95%	15.15	80%	0.01	100%	4.95
Muscle meat eel – pg/g w.w.	38	LB	1.43	80%	18.64	20%	0.00	80%	5.35	20%	0.00	100%	1.94	63%	0.00	100%	26.46
	38	UB	3.48	80%	19.42	20%	0.02	80%	6.13	20%	0.01	100%	21.87	63%	0.02	100%	26.46
Raw milk and dairy products incl. butter – pg/g fat	498	LB	0.00	100%	0.48	68%	0.00	100%	0.56	68%	0.00	100%	0.00	100%	0.00	100%	21.17
	498	UB	69.49	100%	7.26	68%	0.06	100%	7.34	68%	0.05	100%	89.49	100%	0.08	100%	21.17
Hen eggs and egg products – pg/g fat	4	LB	0.00	100%	.	.	.	.	.	.	.	.	0.00	100%	.	.	6.58
	4	UB	110.00	100%	.	.	.	.	.	.	.	.	110.00	100%	.	.	6.58
Fat ruminants – pg/g fat	75	LB	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	86.16
	75	UB	93.33	100%	10.00	100%	0.06	100%	10.00	100%	0.05	100%	160.00	100%	0.07	100%	86.16

Table C1: Continued.

Food categories (Legal groups)	N	TYPE	PBB target congeners														Mean (%) fat in original sample
			BB-49		BB-52		BB-77		BB-101		BB-126		BB-153		BB-169		
			MEAN	ND (%)	MEAN	ND (%)	MEAN	ND (%)	MEAN	ND (%)	MEAN	ND (%)	MEAN	ND (%)	MEAN	ND (%)	
Fat poultry – pg/g fat	91	LB	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	84.92
	91	UB	10.00	100%	10.00	100%	0.06	100%	10.00	100%	0.05	100%	10.00	100%	0.05	100%	84.92
Fat pigs – pg/g fat	68	LB	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	82.24
	68	UB	63.74	100%	10.00	100%	0.07	100%	10.00	100%	0.05	100%	63.74	100%	0.07	100%	82.24
Mixed animal fats – pg/g fat	72	LB	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	86.92
	72	UB	54.55	100%	10.00	100%	0.05	100%	10.00	100%	0.04	100%	100.00	100%	0.06	100%	86.92
Vegetable oils and fats – pg/g fat	101	LB	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	99.03
	101	UB	97.67	100%	10.00	100%	0.07	100%	10.00	100%	0.08	100%	123.26	100%	0.09	100%	99.03
Fish liver and products – pg/g fat	10	LB	20.00	.00%	60.00	.00%	0.23	.00%	20.00	.00%	0.00	100%	0.00	100%	0.00	100%	18.27
	10	UB	20.00	.00%	60.00	.00%	0.23	.00%	20.00	.00%	0.13	100%	231.50	100%	0.19	100%	18.27
Fruits, vegetables and cereals – pg/g w.w.	119	LB	0.00	100%	0.00	100%	0.00	88%	0.00	100%	0.00	100%	0.00	100%	0.00	100%	1.03
	119	UB	0.10	100%	0.10	100%	0.00	88%	0.11	100%	0.00	100%	0.11	100%	0.00	100%	1.03
Other products – pg/g w.w.	749	LB	5.69	92%	8.24	32%	0.03	77%	6.08	32%	0.01	97%	10.80	88%	0.00	100%	18.21
	749	UB	29.89	92%	11.52	32%	0.11	77%	9.47	32%	0.14	97%	42.32	88%	0.14	100%	18.21
Infant and baby food – pg/g w.w.	40	LB	0.00	100%	.	.	.	.	.	.	.	.	0.00	100%	.	.	6.19
	40	UB	162.85	100%	.	.	.	.	.	.	.	.	222.85	100%	.	.	6.19

N: number of analysed samples; MEAN: mean; ND (%): percentage of not detected; w.w.: wet weight.
The number of figures after the decimal point is the same for all food categories and does not reflect precision.

D. CONSUMPTION DATA

Table D1: Basic information on the dietary surveys included in the "Comprehensive European Food Consumption Database".

Country	Name of the dietary survey	Institution providing the data	Reference publication
Austria	Austrian Study On Nutritional Status	Institute of Nutritional Sciences - University of Vienna	Elmadfa et al., 2008
Belgium	Diet National 2004	Scientific Institute of Public Health	de Vriese et al., 2005
Bulgaria	National Survey Of Food Intake And Nutritional Status	National Centre of Public Health Protection	Petrova and Angelova, 2006
Bulgaria II	NUTRICHILD	National Centre of Public Health Protection	Petrova et al., 2009
Czech Republic	SISP04	National Institute of Public Health	Ruprich et al., 2006
Denmark	Danish National Survey of Dietary Habits and Physical Activity	National Food Institute, Technical University of Denmark	Lyhne et al., 2005
Estonia	NDS 1997	National Institute for Public Health Development	Pomerleau et al., 1999
Finland	FINDIET 2007	National Public Health Institute - Nutrition Unit[(a)]	Paturi et al., 2008.
France	INCA2	French Agency for food, environmental and occupation health safety (ANSES)	ANSES, 2009; Lioret et al., 2010; Dubuisson et al,. 2010
Germany	German National Nutrition Survey II (NVS II)	Bundesforschungsinstitut für Ernährung und Lebensmittel (Max Rubner-Institut)	MRI, 2008; Krems et al., 2006
Hungary	National Repr Surv	Hungarian Food Safety Office	Rodler et al., 2005.
Ireland	NSIFCS	Food Safety Authority of Ireland	Kiely et al., 2001; Harrington et al., 2001
Italy	INRAN-SCAI 2005–06	National Research Institute for Food and Nutrition (INRAN)	Leclercq et al., 2009
Latvia	EFSA_TEST	Food Centre Food and Veterinary Service of Latvia	Šantare et al., 2008
Netherlands	VCP 2003	National Institute of Public Health and the Environment, TNO Quality of Life	Ocké et al., 2005
Poland	IZZ-FAO-2000	National Food and Nutrition Institute	Sekula et al., 2005; Szponar et al., 2001, 2003
Slovakia	SK MON 2008	Food Research Institute	Not available
Slovenia	CRP-2008	National Institute of Public Health of Slovenia	Gabrijelčič Blenkuš et al., 2009
Spain	AESAN -Fiab	Universidad Complutense de Madrid	Requejo et al., 2002
Spain II	AESAN	Universidad Complutense de Madrid	Ortega et al., 2010
Spain	Nutrition Survey of Basque population	Administración de la Comunidad Autónoma del País Vasco; Departamento de Sanidad	Larrañaga Larrañaga et al., 2006
Sweden	RIKSMATEN 1997-98	Swedish National Food Administration	Becker and Pearson, 2002
UK	National Diet & Nutrition Survey (NDNS)	Food Standards Agency (FSA)	Henderson et al., 2002

Table D2: Information on the dietary method used within the dietary surveys.

Country	Method	Number of replicates	Average distance between non consecutive replicates[a] (days)	Additional food frequency (FFQ) or propensity (FPQ) questionnaire[b]
Austria	24 h dietary recall	1	Not applicable	No
Belgium	24 h dietary recall	2	23	Yes
Bulgaria	24 h dietary recall	1	Not applicable	Yes
Bulgaria II	24 h dietary recall	2	3	Yes
Czech Republic	24 h dietary recall	2	79	Yes
Denmark	Food record	7	Consecutive days	No
Estonia	24 h dietary recall	1	Not applicable	Yes
Finland	48 h dietary recall	1	Not applicable	Yes
France	Food record	7	Consecutive days	No
Germany	24 h dietary recall	2	16	Dietary history
Hungary	Food record	3	2 consecutive days and 1 non consecutive day[c]	No
Ireland	Food record	7	Consecutive days	Yes, only focused on meat
Italy	Food record	3	Consecutive days	No
Latvia	24 h dietary recall	2	68	Yes
Netherlands	24 h dietary recall	2	11	Yes
Poland	24 h dietary recall	1	Not applicable	No
Slovakia	24 h dietary recall	1	Not applicable	No
Slovenia	24 h dietary recall	1	Not applicable	Yes
Spain	Food record	3	Consecutive days	Yes
Spain II	24 h dietary recall	2	3	Yes
Spain III	24 h dietary recall	2	7-10	Yes
Sweden	Food record	7	Consecutive days	No
United Kingdom	Food record	7	Consecutive days	No

E. DIETARY EXPOSURE

Table E1: Exposure (pg/kg b.w. per day) to 7 PBB congeners for average (mean) consumers of fish and other seafood (including amphibians, reptiles, snails and insects) across a number of subjects (N) in European countries. The dietary intake was estimated using the lower (LB) and upper (UB) bound PBBs concentrations across five broad food categories of the FoodEx food classification system.

European Country	N	Average exposure to 7 PBB congeners (pg/kg b.w. per day) from fish and other seafood (including amphibians, reptiles, snails and insects)													
		BB-49		BB-52		BB-77		BB-101		BB-126		BB-153		BB-169	
		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
AT	2123	0.27	0.31	0.86	0.89	0.00	0.00	0.32	0.38	0.00	0.00	0.17	3.89	0.00	0.00
BE	1356	0.47	0.54	1.48	1.53	0.01	0.01	0.55	0.66	0.00	0.00	0.29	6.67	0.00	0.00
BG	691	0.39	0.46	1.26	1.29	0.01	0.01	0.46	0.56	0.00	0.00	0.24	5.65	0.00	0.00
CZ	1666	0.30	0.34	0.95	0.98	0.00	0.01	0.35	0.42	0.00	0.00	0.18	4.26	0.00	0.00
DE	10419	0.30	0.34	0.95	0.98	0.00	0.01	0.35	0.42	0.00	0.00	0.18	4.27	0.00	0.00
DK	2821	0.33	0.38	1.05	1.08	0.00	0.01	0.39	0.47	0.00	0.00	0.20	4.73	0.00	0.00
EE	1858	0.40	0.46	1.27	1.31	0.01	0.01	0.47	0.56	0.00	0.00	0.24	5.73	0.00	0.00
ES[(a)]	982	1.49	1.72	4.74	4.88	0.02	0.03	1.75	2.10	0.00	0.01	0.91	21.32	0.00	0.01
ES[(b)]	418	1.19	1.38	3.81	3.92	0.02	0.02	1.41	1.69	0.00	0.01	0.73	17.12	0.00	0.01
ES[(c)]	61	0.87	1.00	2.76	2.84	0.01	0.01	1.02	1.22	0.00	0.01	0.53	12.43	0.00	0.01
FI	1575	0.45	0.52	1.44	1.48	0.01	0.01	0.53	0.64	0.00	0.00	0.28	6.47	0.00	0.00
FR	2276	0.59	0.69	1.89	1.94	0.01	0.01	0.70	0.84	0.00	0.00	0.36	8.50	0.00	0.00
GB	1724	0.48	0.56	1.54	1.58	0.01	0.01	0.57	0.68	0.00	0.00	0.30	6.91	0.00	0.00
HU	1074	0.16	0.18	0.51	0.52	0.00	0.00	0.19	0.23	0.00	0.00	0.10	2.29	0.00	0.00
IE	952	0.38	0.44	1.20	1.24	0.00	0.01	0.45	0.53	0.00	0.00	0.23	5.41	0.00	0.00
IT	2314	0.90	1.04	2.87	2.96	0.01	0.02	1.06	1.27	0.00	0.01	0.55	12.93	0.00	0.01
LV	1382	0.32	0.36	1.00	1.03	0.00	0.01	0.37	0.44	0.00	0.00	0.19	4.52	0.00	0.00
NL	750	0.16	0.18	0.51	0.52	0.00	0.00	0.19	0.22	0.00	0.00	0.10	2.28	0.00	0.00
PL	2527	0.33	0.38	1.05	1.08	0.00	0.01	0.39	0.47	0.00	0.00	0.20	4.73	0.00	0.00

Table E1: Continued.

European Country	N	Average exposure to 7 PBB congeners (pg/kg b.w. per day) from fish and other seafood (including amphibians, reptiles, snails and insects)													
		BB-49		BB-52		BB-77		BB-101		BB-126		BB-153		BB-169	
		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
SE	1081	0.49	0.56	1.55	1.60	0.01	0.01	0.57	0.69	0.00	0.00	0.30	6.98	0.00	0.00
SI	400	0.21	0.24	0.67	0.69	0.00	0.00	0.25	0.30	0.00	0.00	0.13	3.01	0.00	0.00
SK	2758	0.17	0.19	0.53	0.55	0.00	0.00	0.20	0.24	0.00	0.00	0.10	2.39	0.00	0.00
Minimum		**0.16**	**0.18**	**0.51**	**0.52**	**0.00**	**0.00**	**0.19**	**0.22**	**0.00**	**0.00**	**0.10**	**2.28**	**0.00**	**0.00**
Median		**0.39**	**0.45**	**1.23**	**1.26**	**0.00**	**0.01**	**0.45**	**0.54**	**0.00**	**0.00**	**0.24**	**5.53**	**0.00**	**0.00**
Maximum		**1.49**	**1.72**	**4.74**	**4.88**	**0.02**	**0.03**	**1.75**	**2.10**	**0.00**	**0.01**	**0.91**	**21.32**	**0.00**	**0.01**

N: Number of subjects; b.w.: body weight; PBB: polybrominated biphenyl; LB: lower bound; UP: upper bound; AT: Austria; BE: Belgium; BG: Bulgaria; CZ: Czech Republic; DE: Germany; DK: Denmark; EE: Estonia; ES: Spain; FI: Finland; FR: France; GB: Great Britain; HU: Hungary; IE: Ireland; IT: Italy; LV: Latvia; NL: The Netherlands; PL: Poland; SE: Sweden; SI: Slovenia; SK: Slovak Republic.
(a): Dietary survey AESAN-Fiab, Universidad Complutense de Madrid (Requejo et al., 2002).
(b): Dietary survey AESAN, Universidad Complutense de Madrid, (Ortega et al., 2010).
(c): Nutrition Survey of Basque population, Administración de la Comunidad Autónoma del País Vasco; Departamento de Sanidad, Larrañaga Larrañaga et al., 2006.
The number of figures after the decimal point is the same for all congeners and for all food categories and does not reflect precision.

Table E2: Exposure (pg/kg b.w. per day) to 7 PBB congeners for high consumers (95th percentiles) of fish and other seafood (including amphibians, reptiles, snails and insects) across a number of subjects (N) in European countries. The dietary intake was estimated using the lower (LB) and upper (UB) bound PBBs concentrations across five broad food categories of the FoodEx food classification system.

European Country	N	95th percentiles exposure to 7 PBB congeners (pg/kg b.w. per day) from of fish and other seafood (including amphibians, reptiles, snails and insects)													
		BB-49		BB-52		BB-77		BB-101		BB-126		BB-153		BB-169	
		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
AT	2123	2.53	2.93	8.07	8.30	0.03	0.04	2.99	3.57	0.00	0.02	1.55	36.28	0.00	0.02
BE	1356	2.14	2.47	6.82	7.01	0.03	0.04	2.52	3.02	0.00	0.01	1.31	30.66	0.00	0.01
BG	691	3.20	3.70	10.20	10.49	0.04	0.05	3.78	4.52	0.00	0.02	1.96	45.88	0.00	0.02
CZ	1666	1.94	2.24	6.17	6.34	0.02	0.03	2.28	2.73	0.00	0.01	1.19	27.74	0.00	0.01
DE	10419	1.81	2.09	5.76	5.92	0.02	0.03	2.13	2.55	0.00	0.01	1.11	25.89	0.00	0.01
DK	2821	0.98	1.13	3.11	3.20	0.01	0.02	1.15	1.38	0.00	0.01	0.60	13.97	0.00	0.01
EE	1858	2.83	3.28	9.03	9.29	0.04	0.05	3.34	4.00	0.00	0.02	1.74	40.62	0.00	0.02
ES[a]	982	3.84	4.43	12.22	12.57	0.05	0.07	4.52	5.41	0.00	0.03	2.35	54.97	0.00	0.03
ES[b]	418	3.79	4.38	12.06	12.41	0.05	0.06	4.46	5.34	0.00	0.02	2.32	54.26	0.00	0.03
ES[c]	61	2.55	2.95	8.13	8.37	0.03	0.04	3.01	3.60	0.00	0.02	1.56	36.59	0.00	0.02
FI	1575	2.00	2.31	6.37	6.56	0.03	0.03	2.36	2.82	0.00	0.01	1.23	28.67	0.00	0.01
FR	2276	1.64	1.90	5.23	5.38	0.02	0.03	1.94	2.32	0.00	0.01	1.01	23.52	0.00	0.01
GB	1724	1.49	1.72	4.75	4.88	0.02	0.03	1.76	2.10	0.00	0.01	0.91	21.35	0.00	0.01
HU	1074	1.21	1.39	3.84	3.95	0.02	0.02	1.42	1.70	0.00	0.01	0.74	17.28	0.00	0.01
IE	952	1.31	1.52	4.19	4.31	0.02	0.02	1.55	1.85	0.00	0.01	0.81	18.84	0.00	0.01
IT	2314	2.94	3.40	9.37	9.64	0.04	0.05	3.47	4.15	0.00	0.02	1.80	42.14	0.00	0.02
LV	1382	1.73	2.00	5.52	5.68	0.02	0.03	2.04	2.44	0.00	0.01	1.06	24.82	0.00	0.01
NL	750	1.21	1.40	3.85	3.96	0.02	0.02	1.42	1.70	0.00	0.01	0.74	17.31	0.00	0.01
PL	2527	2.65	3.06	8.44	8.68	0.03	0.05	3.12	3.74	0.00	0.02	1.62	37.95	0.00	0.02

Table E2: Continued.

European Country	N	95th percentiles exposure to 7 PBB congeners (pg/kg b.w. per day) from of fish and other seafood (including amphibians, reptiles, snails and insects)													
		BB-49		BB-52		BB-77		BB-101		BB-126		BB-153		BB-169	
		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
SE	1081	1.30	1.50	4.15	4.27	0.02	0.02	1.54	1.84	0.00	0.01	0.80	18.66	0.00	0.01
SI	400	2.03	2.35	6.48	6.67	0.03	0.03	2.40	2.87	0.00	0.01	1.25	29.15	0.00	0.01
SK	2758	1.46	1.69	4.66	4.79	0.02	0.03	1.72	2.06	0.00	0.01	0.90	20.96	0.00	0.01
Minimum		**0.98**	**1.13**	**3.11**	**3.20**	**0.01**	**0.02**	**1.15**	**1.38**	**0.00**	**0.01**	**0.60**	**13.97**	**0.00**	**0.01**
Median		**1.97**	**2.27**	**6.27**	**6.45**	**0.03**	**0.03**	**2.32**	**2.78**	**0.00**	**0.01**	**1.21**	**28.20**	**0.00**	**0.01**
Maximum		**3.84**	**4.43**	**12.22**	**12.57**	**0.05**	**0.07**	**4.52**	**5.41**	**0.00**	**0.03**	**2.35**	**54.97**	**0.00**	**0.03**

N: Number of subjects; b.w.: body weight; PBB: polybrominated biphenyl; LB: lower bound; UP: upper bound; AT: Austria; BE: Belgium; BG: Bulgaria; CZ: Czech Republic; DE: Germany; DK: Denmark; EE: Estonia; ES: Spain; FI: Finland; FR: France; GB: Great Britain; HU: Hungary; IE: Ireland; IT: Italy; LV: Latvia; NL: The Netherlands; PL: Poland; SE: Sweden; SI: Slovenia; SK: Slovak Republic.
(a): Dietary survey AESAN-Fiab, Universidad Complutense de Madrid (Requejo et al., 2002).
(b): Dietary survey AESAN, Universidad Complutense de Madrid, (Ortega et al., 2010).
(c): Nutrition Survey of Basque population, Administración de la Comunidad Autónoma del País Vasco; Departamento de Sanidad, Larrañaga Larrañaga et al., 2006.
The number of figures after the decimal point is the same for all congeners and for all food categories and does not reflect precision.

Table E3: Exposure (pg/kg b.w. per day) to 5 PBBs for average (mean) consumers of meat and meat products (including offal) across a number of subjects (N) in European countries. The dietary intake was estimated using the lower (LB) and upper (UB) bound PBBs concentrations across five broad food categories of the FoodEx food classification system.

European Country	N	Average exposure to 5 PBB congeners (pg/kg b.w. per day) from meat and meat products (including offal)									
		BB-52		BB-77		BB-101		BB-126		BB-169	
		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
AT	2123	0.10	0.71	0.00	0.01	0.10	0.71	0.01	0.02	0.00	0.01
BE	1356	0.09	0.65	0.00	0.01	0.09	0.65	0.01	0.02	0.00	0.01
BG	691	0.09	0.62	0.00	0.01	0.09	0.62	0.01	0.02	0.00	0.01
CZ	1666	0.13	0.95	0.00	0.01	0.13	0.95	0.01	0.03	0.00	0.02
DE	10419	0.08	0.55	0.00	0.01	0.08	0.55	0.01	0.02	0.00	0.01
DK	2821	0.10	0.71	0.00	0.01	0.10	0.71	0.01	0.02	0.00	0.01
EE	1858	0.12	0.87	0.00	0.01	0.12	0.87	0.01	0.02	0.00	0.02
ES[(a)]	982	0.15	1.05	0.00	0.01	0.15	1.05	0.01	0.03	0.00	0.02
ES[(b)]	418	0.12	0.82	0.00	0.01	0.12	0.82	0.01	0.02	0.00	0.02
ES[(c)]	61	0.16	1.15	0.00	0.02	0.16	1.15	0.01	0.03	0.00	0.02
FI	1575	0.09	0.66	0.00	0.01	0.09	0.66	0.01	0.02	0.00	0.01
FR	2276	0.11	0.76	0.00	0.01	0.11	0.76	0.01	0.02	0.00	0.01
GB	1724	0.08	0.54	0.00	0.01	0.08	0.54	0.01	0.01	0.00	0.01
HU	1074	0.14	1.01	0.00	0.01	0.14	1.01	0.01	0.03	0.00	0.02
IE	952	0.13	0.89	0.00	0.01	0.13	0.89	0.01	0.02	0.00	0.02
IT	2314	0.09	0.64	0.00	0.01	0.09	0.64	0.01	0.02	0.00	0.01
LV	1382	0.10	0.68	0.00	0.01	0.10	0.68	0.01	0.02	0.00	0.01
NL	750	0.10	0.72	0.00	0.01	0.10	0.72	0.01	0.02	0.00	0.01
PL	2527	0.22	1.58	0.00	0.02	0.22	1.58	0.02	0.04	0.00	0.03

Table E3: Continued.

European Country	N	Average exposure to 5 PBB congeners (pg/kg b.w. per day) from meat and meat products (including offal)									
		BB-52		BB-77		BB-101		BB-126		BB-169	
		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
SE	1081	0.06	0.45	0.00	0.01	0.06	0.45	0.01	0.01	0.00	0.01
SI	400	0.13	0.90	0.00	0.01	0.13	0.90	0.01	0.02	0.00	0.02
SK	2758	0.12	0.82	0.00	0.01	0.12	0.82	0.01	0.02	0.00	0.02
Minimum		0.06	0.45	0.00	0.01	0.06	0.45	0.01	0.01	0.00	0.01
Median		0.10	0.74	0.00	0.01	0.10	0.74	0.01	0.02	0.00	0.01
Maximum		0.22	1.58	0.00	0.02	0.22	1.58	0.02	0.04	0.00	0.03

N: Number of subjects; b.w.: body weight; PBB: polybrominated biphenyl; LB: lower bound; UP: upper bound; AT: Austria; BE: Belgium; BG: Bulgaria; CZ: Czech Republic; DE: Germany; DK: Denmark; EE: Estonia; ES: Spain; FI: Finland; FR: France; GB: Great Britain; HU: Hungary; IE: Ireland; IT: Italy; LV: Latvia; NL: The Netherlands; PL: Poland; SE: Sweden; SI: Slovenia; SK: Slovak Republic.
(a): Dietary survey AESAN-Fiab, Universidad Complutense de Madrid (Requejo et al., 2002).
(b): Dietary survey AESAN, Universidad Complutense de Madrid, (Ortega et al., 2010).
(c): Nutrition Survey of Basque population, Administración de la Comunidad Autónoma del País Vasco; Departamento de Sanidad, Larrañaga Larrañaga et al., 2006.
The number of figures after the decimal point is the same for all congeners and for all food categories and does not reflect precision.

Table E4: Exposure (pg/kg b.w. per day) to 5 PBBs for high consumers (95th percentile) of meat and meat products (including offal) across a number of subjects (N) in European countries. The dietary intake was estimated using the lower (LB) and upper (UB) bound PBBs concentrations across five broad food categories of the FoodEx food classification system.

European Country	N	95th percentiles exposure to 5 PBB congeners (pg/kg b.w. per day) from meat and meat products (including offal)									
		BB-52		BB-77		BB-101		BB-126		BB-169	
		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
AT	2123	0.26	1.81	0.00	0.03	0.26	1.81	0.02	0.05	0.00	0.04
BE	1356	0.22	1.53	0.00	0.02	0.22	1.53	0.02	0.04	0.00	0.03
BG	691	0.25	1.77	0.00	0.03	0.25	1.77	0.02	0.05	0.00	0.03
CZ	1666	0.29	2.05	0.00	0.03	0.29	2.05	0.02	0.06	0.00	0.04
DE	10419	0.20	1.38	0.00	0.02	0.20	1.38	0.02	0.04	0.00	0.03
DK	2821	0.18	1.29	0.00	0.02	0.18	1.29	0.01	0.04	0.00	0.03
EE	1858	0.34	2.42	0.00	0.03	0.34	2.42	0.03	0.07	0.00	0.05
ES[(a)]	982	0.28	1.98	0.00	0.03	0.28	1.98	0.02	0.05	0.00	0.04
ES[(b)]	418	0.26	1.85	0.00	0.03	0.26	1.85	0.02	0.05	0.00	0.04
ES[(c)]	61	0.29	2.05	0.00	0.03	0.29	2.05	0.02	0.06	0.00	0.04
FI	1575	0.21	1.47	0.00	0.02	0.21	1.47	0.02	0.04	0.00	0.03
FR	2276	0.20	1.45	0.00	0.02	0.20	1.45	0.02	0.04	0.00	0.03
GB	1724	0.15	1.06	0.00	0.02	0.15	1.06	0.01	0.03	0.00	0.02
HU	1074	0.28	1.98	0.00	0.03	0.28	1.98	0.02	0.05	0.00	0.04
IE	952	0.24	1.67	0.00	0.02	0.24	1.67	0.02	0.05	0.00	0.03
IT	2314	0.18	1.27	0.00	0.02	0.18	1.27	0.01	0.03	0.00	0.02
LV	1382	0.25	1.74	0.00	0.02	0.25	1.74	0.02	0.05	0.00	0.03
NL	750	0.23	1.60	0.00	0.02	0.23	1.60	0.02	0.04	0.00	0.03
PL	2527	0.54	3.85	0.00	0.05	0.54	3.85	0.04	0.11	0.00	0.08

Table E4: Continued.

European Country	N	95th percentiles exposure to 5 PBB congeners (pg/kg b.w. per day) from meat and meat products (including offal)									
		BB-52		BB-77		BB-101		BB-126		BB-169	
		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
SE	1081	0.12	0.88	0.00	0.01	0.12	0.88	0.01	0.02	0.00	0.02
SI	400	0.31	2.16	0.00	0.03	0.31	2.16	0.02	0.06	0.00	0.04
SK	2758	0.32	2.23	0.00	0.03	0.32	2.23	0.03	0.06	0.00	0.04
Minimum		0.12	0.88	0.00	0.01	0.12	0.88	0.01	0.02	0.00	0.02
Median		0.25	1.75	0.00	0.02	0.25	1.75	0.02	0.05	0.00	0.03
Maximum		0.54	3.85	0.00	0.05	0.54	3.85	0.04	0.11	0.00	0.08

N: Number of subjects; b.w.: body weight; PBB: polybrominated biphenyl; LB: lower bound; UP: upper bound; AT: Austria; BE: Belgium; BG: Bulgaria; CZ: Czech Republic; DE: Germany; DK: Denmark; EE: Estonia; ES: Spain; FI: Finland; FR: France; GB: Great Britain; HU: Hungary; IE: Ireland; IT: Italy; LV: Latvia; NL: The Netherlands; PL: Poland; SE: Sweden; SI: Slovenia; SK: Slovak Republic.
(a): Dietary survey AESAN-Fiab, Universidad Complutense de Madrid (Requejo et al., 2002).
(b): Dietary survey AESAN, Universidad Complutense de Madrid, (Ortega et al., 2010).
(c): Nutrition Survey of Basque population, Administración de la Comunidad Autónoma del País Vasco; Departamento de Sanidad, Larrañaga Larrañaga et al., 2006.
The number of figures after the decimal point is the same for all congeners and for all food categories and does not reflect precision.

Table E5: Exposure (pg/kg b.w. per day) to 5 PBBs for average (mean) consumers of milk and dairy products across a number of subjects (N) in European countries. The dietary intake was estimated using the lower (LB) and upper (UB) bound PBBs concentrations across five broad food categories of the FoodEx food classification system.

European Country	N	Average exposure to 5 PBB congeners (pg/kg b.w. per day) from milk and dairy products									
		BB-52		BB-77		BB-101		BB-126		BB-169	
		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
AT	2123	0.04	1.63	0.00	0.01	0.04	1.64	0.00	0.01	0.00	0.02
BE	1356	0.03	1.45	0.00	0.01	0.04	1.46	0.00	0.01	0.00	0.02
BG	691	0.03	1.32	0.00	0.01	0.03	1.32	0.00	0.01	0.00	0.02
CZ	1666	0.03	1.35	0.00	0.01	0.03	1.36	0.00	0.01	0.00	0.02
DE	10419	0.03	1.47	0.00	0.01	0.04	1.47	0.00	0.01	0.00	0.02
DK	2821	0.06	3.01	0.00	0.03	0.08	3.02	0.00	0.02	0.00	0.04
EE	1858	0.05	2.43	0.00	0.02	0.06	2.44	0.00	0.02	0.00	0.03
ES[(a)]	982	0.07	3.32	0.00	0.03	0.08	3.33	0.00	0.02	0.00	0.04
ES[(b)]	418	0.06	2.92	0.00	0.03	0.07	2.93	0.00	0.02	0.00	0.04
ES[(c)]	61	0.08	3.59	0.00	0.03	0.09	3.60	0.00	0.03	0.00	0.04
FI	1575	0.07	3.48	0.00	0.03	0.09	3.49	0.00	0.03	0.00	0.04
FR	2276	0.04	1.74	0.00	0.02	0.04	1.75	0.00	0.01	0.00	0.02
GB	1724	0.04	2.07	0.00	0.02	0.05	2.08	0.00	0.02	0.00	0.03
HU	1074	0.05	2.14	0.00	0.02	0.05	2.14	0.00	0.02	0.00	0.03
IE	952	0.05	2.39	0.00	0.02	0.06	2.40	0.00	0.02	0.00	0.03
IT	2314	0.03	1.61	0.00	0.01	0.04	1.61	0.00	0.01	0.00	0.02
LV	1382	0.02	1.05	0.00	0.01	0.03	1.06	0.00	0.01	0.00	0.01
NL	750	0.06	2.94	0.00	0.03	0.07	2.95	0.00	0.02	0.00	0.04
PL	2527	0.03	1.37	0.00	0.01	0.03	1.38	0.00	0.01	0.00	0.02

Table E5: Continued.

European Country	N	Average exposure to 5 PBB congeners (pg/kg b.w. per day) from milk and dairy products									
		BB-52		BB-77		BB-101		BB-126		BB-169	
		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
SE	1081	0.06	2.89	0.00	0.03	0.07	2.90	0.00	0.02	0.00	0.04
SI	400	0.03	1.49	0.00	0.01	0.04	1.50	0.00	0.01	0.00	0.02
SK	2758	0.02	1.08	0.00	0.01	0.03	1.08	0.00	0.01	0.00	0.01
Minimum		0.02	1.05	0.00	0.01	0.03	1.06	0.00	0.01	0.00	0.01
Median		0.04	1.91	0.00	0.02	0.05	1.91	0.00	0.01	0.00	0.02
Maximum		0.08	3.59	0.00	0.03	0.09	3.60	0.00	0.03	0.00	0.04

N: Number of subjects; b.w.: body weight; PBB: polybrominated biphenyl; LB: lower bound; UP: upper bound; AT: Austria; BE: Belgium; BG: Bulgaria; CZ: Czech Republic; DE: Germany; DK: Denmark; EE: Estonia; ES: Spain; FI: Finland; FR: France; GB: Great Britain; HU: Hungary; IE: Ireland; IT: Italy; LV: Latvia; NL: The Netherlands; PL: Poland; SE: Sweden; SI: Slovenia; SK: Slovak Republic.
(a): Dietary survey AESAN-Fiab, Universidad Complutense de Madrid (Requejo et al., 2002).
(b): Dietary survey AESAN, Universidad Complutense de Madrid, (Ortega et al., 2010).
(c): Nutrition Survey of Basque population, Administración de la Comunidad Autónoma del País Vasco; Departamento de Sanidad, Larrañaga Larrañaga et al., 2006.
The number of figures after the decimal point is the same for all congeners and for all food categories and does not reflect precision.

Table E6: Exposure (pg/kg b.w. per day) to 5 PBBs for high consumers (95th percentile) of milk and dairy products across a number of subjects (N) in European countries. The dietary intake was estimated using the lower (LB) and upper (UB) bound PBB concentrations across five broad food categories of the FoodEx food classification system.

European Country	N	95th percentiles exposure to 5PBB congeners (pg/kg b.w. per day) from of milk and dairy products									
		BB-52		BB-77		BB-101		BB-126		BB-169	
		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
AT	2123	0.10	4.80	0.00	0.04	0.12	4.82	0.00	0.04	0.00	0.06
BE	1356	0.09	4.08	0.00	0.04	0.10	4.09	0.00	0.03	0.00	0.05
BG	691	0.09	4.28	0.00	0.04	0.11	4.30	0.00	0.03	0.00	0.05
CZ	1666	0.08	3.90	0.00	0.03	0.10	3.92	0.00	0.03	0.00	0.05
DE	10419	0.09	4.27	0.00	0.04	0.11	4.28	0.00	0.03	0.00	0.05
DK	2821	0.16	7.39	0.00	0.07	0.19	7.42	0.00	0.05	0.00	0.09
EE	1858	0.16	7.31	0.00	0.06	0.19	7.34	0.00	0.05	0.00	0.09
ES[(a)]	982	0.14	6.69	0.00	0.06	0.17	6.71	0.00	0.05	0.00	0.08
ES[(b)]	418	0.13	5.89	0.00	0.05	0.15	5.92	0.00	0.04	0.00	0.07
ES[(c)]	61	0.17	8.00	0.00	0.07	0.20	8.03	0.00	0.06	0.00	0.10
FI	1575	0.18	8.34	0.00	0.07	0.21	8.38	0.00	0.06	0.00	0.10
FR	2276	0.10	4.45	0.00	0.04	0.11	4.47	0.00	0.03	0.00	0.05
GB	1724	0.10	4.51	0.00	0.04	0.11	4.53	0.00	0.03	0.00	0.06
HU	1074	0.11	5.33	0.00	0.05	0.14	5.35	0.00	0.04	0.00	0.07
IE	952	0.12	5.54	0.00	0.05	0.14	5.56	0.00	0.04	0.00	0.07
IT	2314	0.08	3.60	0.00	0.03	0.09	3.62	0.00	0.03	0.00	0.04
LV	1382	0.07	3.16	0.00	0.03	0.08	3.17	0.00	0.02	0.00	0.04
NL	750	0.15	7.14	0.00	0.06	0.18	7.17	0.00	0.05	0.00	0.09
PL	2527	0.10	4.75	0.00	0.04	0.12	4.77	0.00	0.04	0.00	0.06

Table E6: Continued.

European Country	N	95th percentiles exposure to 5PBB congeners (pg/kg b.w. per day) from of milk and dairy products									
		BB-52		BB-77		BB-101		BB-126		BB-169	
		LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
SE	1081	0.14	6.42	0.00	0.06	0.16	6.45	0.00	0.05	0.00	0.08
SI	400	0.10	4.88	0.00	0.04	0.12	4.90	0.00	0.04	0.00	0.06
SK	2758	0.09	4.13	0.00	0.04	0.11	4.14	0.00	0.03	0.00	0.05
Minimum		0.07	3.16	0.00	0.03	0.08	3.17	0.00	0.02	0.00	0.04
Median		0.10	4.84	0.00	0.04	0.12	4.86	0.00	0.04	0.00	0.06
Maximum		0.18	8.34	0.00	0.07	0.21	8.38	0.00	0.06	0.00	0.10

N: Number of subjects; b.w.: body weight; PBB: polybrominated biphenyl; LB: lower bound; UP: upper bound; AT: Austria; BE: Belgium; BG: Bulgaria; CZ: Czech Republic; DE: Germany; DK: Denmark; EE: Estonia; ES: Spain; FI: Finland; FR: France; GB: Great Britain; HU: Hungary; IE: Ireland; IT: Italy; LV: Latvia; NL: The Netherlands; PL: Poland; SE: Sweden; SI: Slovenia; SK: Slovak Republic.
(a): Dietary survey AESAN-Fiab, Universidad Complutense de Madrid (Requejo et al., 2002).
(b): Dietary survey AESAN, Universidad Complutense de Madrid, (Ortega et al., 2010).
(c): Nutrition Survey of Basque population, Administración de la Comunidad Autónoma del País Vasco; Departamento de Sanidad, Larrañaga Larrañaga et al., 2006.
The number of figures after the decimal point is the same for all congeners and for all food categories and does not reflect precision.

F. GENOTOXICITY (TABLE)

Table F1: Summary of *in vitro* and *in vivo* genotoxicity studies of PBBs.

Test method and endpoint		Test conditions	PBBs	Result	Reference
In vitro	Bacterial reverse mutation assay	*S. typhimurium* TA98, TA100, TA1535, TA1537, S9(+/-)	2-bromobiphenyl; 3- bromobiphenyl; 4- bromobiphenyl; HexaBB	Negative	Haworth et al., 1983
		S. typhimurium TA98, TA100, TA1535, TA1537, S9(+/-)	4- bromobiphenyl	Positive with S9	Kohli et al., 1978
		S. typhimurium TA98, TA100, TA1535, TA1537, S9(+/-)	FireMaster FF-1	Negative	Tennant et al, 1986
	Gene mutation in mammalian cells	Chinese hamster V79 cell (HGPRT locus), S9 (+/-)	3,3',4,4'-tetraBB; 2,2',4,4',55'-hexaBB; 3,3',4,4',5,5'-hexaBB; FireMaster BP-6;	Negative	Kavanagh et al., 1985
		Rat liver cells WB-F344 (HGPRT locus)	2,2',4,4',5,5'-hexaBB; 3,3',4,4',5, 5'-hexaBB		
		Rat hepatocyte (HGPRT locus) and Co-incubation system using rat liver epithelial cells (HGPRT locus) and human fibroblast cell D-550	FireMaster FF-1	Negative	Williams et al., 1984
		Mouse lymphoma L5178Y cells (TK locus)	FireMaster FF-1	Negative	Myhr and Caspary, 1991
	DNA repair synthesis	Primary culture of mouse, rat and hamster hepatocytes	FireMaster FF-1	Negative	Williams et al., 1984
	Chromosomal aberrations	CHO cells	PBBs (technical mixture or individual congeners not specified)	Negative	Galloway et al., 1987
	Sister chromatide exchange	CHO cells	PBBs (technical mixture or individual congeners not specified)	Negative	Galloway et al., 1987
	DNA adduct formation	Covalent binding to salmon DNA	2,2',4,4',5,5'-hexaBB; 2, 2',3,4,4',5,5'-heptaBB	Negative	Dannan et al., 1978

Table F1: Continued.

Test method and endpoint		Test conditions	PBBs	Result	Reference
In vivo	Micronuclei	Continuous *i.p.* administratiton (500, 1,000, 2,000 mg/kg per day) to male B6C3F1 mice for 3days.	PBBs (technical mixture or individual congeners not specified)	Negative	Shelby et al., 1993
		Oral exposure total doses 5, 10, 20 g/kg administered to mice in two equal doses 24 hours apart.	DecaBB (comercial mixture, not details known)	Negative	Millischer et al., 1979
	Chromosome aberration	Single oral administration (50, 500 mg/kg/day) to male Swiss mice.	FireMaster (details are unknown)	Negative	Wertz and Fiscor, 1978
		Administration (100 mg/kg/day) 6 times every other day starting from day GD6 to pregnant rats by oral gavage. Bone marrow cells were analyzed on GD19.	PBBs (technical mixture or individual congeners not specified)	Negative	Fiscor and Wertz, 1978
		Dietary exposure (5, 50, 500 ppm) of rats for 5 weeks. Bone marrow and spermatogonia were analyzed.	Firemaster BP-6	Negative	Garthhoff et al., 1977
	Unscheduled DNA syntesis	Single administration (50 -1,000 mg/kg) by gavage to male and female B6C3F1 mice and male Fischer-344 rats.	FireMaster FF-1	Negative	Mirsalis et al., 1985, 1989

PBB: polybrominated biphenyl; CHO: Chinese hamster ovary; GD: gestational day; *i..p.*: intraperitoneal.

G. OBSERVATIONS ON HUMANS (TABLES)

Table G1: Studies on effects on thyroid and endocrine disruption.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
South-eastern China 2008	Serum thyroid hormones (T3 and T4) and TSH	Impact of electronic waste exposure during recycling and dismantling activities on thyroid hormone levels	236 occupational-exposed people, 89 non-occupational-exposed people in electronic waste recycling sites; 117 subjects in the control group.	BB-209, -77, -103 and their sum	People having worked on an electronic waste recycling and dismantling had significantly lower TSH compared to the control group ($p<0.01$). A weak negative relation was found between the levels of BB-103 and T3.	Exposure to BFRs released from primitive electronic waste handling may contribute to the changes of thyroid hormones and TSH.	Wang et al., 2010

Table G1: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established in 1976	Immunologic disfunction Clinical Symptoms	To study the impact of PBBs on immunologic function	336 adult Michigan farm residents, 117 general consumers 75 dairy farm residents in Wisconsin, who had not eaten PBB-contaminated food, 79 healthy subjects in New York City 101 family units in New York	The prevalence of multiple clinical symptoms and immuno-biological abnormalities were examined among farm residents and within family units. Cluster analyses of clinical data and immunological parameters (T, B lymphocytes without surface markers. T and B lymphocyte function (PHA, ConA and PWM) and levels of immunoglobulins (IgG, IgA, IgM) were performed.	Abnormalities in the Michigan groups included hypergammaglobulinemia, exaggerated hypersensitive response to streptococci, significant decrease in absolute numbers and percentage of T- and B-lymphocytes, and increased number of lymphocytes with no detectable surface markers ("null cells"). Significant reduction of *in vitro* immune function was noted in 20-25 % of the Michigan farm residents who had eaten food containing PBBs.	The investigation suggested a "Human Toxic PBB Syndrome" characterised by effects on neurological and musculo-skeletal systems and persistence of a PBB-induced immune deficiency.	Bekesi et al., 1987

Table G1: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established in 1976 Survey in 1981	Immunologic disfunction	To evaluate the effects of PBBs on the function and on the synthesis of immunoglobulins by peripheral blood lymphocytes	Cases = 18 Michigan dairy farm residents, controls = 18 adult Wisconsin dairy farmers who were not exposed to PBB-contaminated meat and/or dairy products.	Standard laboratory methods	Concentrations of PBBs as low as 0.001 p,g/loS cells decreased lymphocyte response to pokeweed mitogen. PBBs had no effect on the quantity of E-rosette-forming cells, the total T or B cells, or the ratio of helper to suppressor T-cell subpopulations. Enhanced release of IgG was identified in lymphocyte cultures obtained from blood specimens of PBB-exposed Michigan farmers.	The data from this study suggest that PBB exerted an adverse effect on cell function, but produced a nonspecific activation of B lymphocytes.	Lipson, 1987

Table G1: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan and Wisconsin, USA, 1978	Hypothyroidism	To study hypothyroidism in workers exposed to PBBs	36 men employed at a chemical manufacturing firm. Controls = 89 subjects chosen from two other occupational group (steelworkers and wiremen) and from a group of volunteers from the community.	Serum T3 and thyrotropin were measured. The T4 resin-uptake ratio was determined. The free T3 index was calculated. Thyroid antimicrosomal and antithyroglobul in antibodies were measured.	4 cases of primary hypothyroidism in the 35 workers exposed to PBBs but none in the 89 control subjects. In the PBB workers, markedly elevated titles of thyroid antimicrosomal antibody (1:6400 or above) were found. An elevated title of Antithyroglobulin antibodies was found in one. The PBB group had significantly more subjects with elevated serum concentrations of thyrotropin (P = 0.006). The free T3 indexes (P = 0.06) and serum T4 concentrations (P = 0.11) did not differ significantly. Although more PBB workers than controls had antimicrosomal antibody titles greater than l:100, the difference between groups was not significant (P = 0.06).	This study documented primary hypothyroidism in four of 35 men (11.4 %) employed in the production of BB-209 or decabromo-biphenyl oxide. The laboratory findings of a low free thyroxine index in association with a high serum thyrotropin indicate that the hypothyroidism is primary. The high titles of thyroid antimicrosomal antibodies found in these subjects are consistent with a direct effect on the thyroid gland.	Bahn et al., 1980

Table G1: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established in 1976	Impaired immune function	PBBs and impaired immune function	55 exposed Michigan farm residents 11 Michigan chemical workers 46 non-exposed Wisconsin farmers	Tests on blood	In Michigan farmers and chemical workers: decreased number of T-lymphocytes, increase of "null cell" lymphocytes, altered lymphocyte function. PBBs and immunologic abnormalities were not detected in non-exposed Wisconsin dairy farm residents.	Immunological abnormalities were detected in PBB-exposed Michigan farmers and chemical workers, but not in non-exposed Wisconsin farmers .	Bekesi et al., 1979b

Table G1: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established in 1976	Impaired immune function	To study lymphocites and cell abnormalies in humans exposed to PBBs	45 exposed Michigan dairy farm residents and members of their families 46 not exposed Wisconsin dairy farm residents and members of their families 79 healthy subjects from the New York area	Tests on blood	In Michigan farmers lymphocytes functions abnormalities were detected, including decreases in the numbers and percentages of peripheral blood lymphocytes that form rosettes with either sheep erythrocytes alone or with sheep erythrocytes sensitised with antibody and complement, increases in lymphocytes with no detectable surface markers ("null" cells), and altered responses to tests designed to evaluate functional integrity of the cells. There appears to be no consistent correlation between the concentration of PBBs in the plasma and the altered lymphocytes. In Wisconsin dairy farm residents and healthy individuals in the New York area who were not exposed to PBBs there were no such abnormalities.	Immunological abnormalities were detected in PBB-exposed Michigan farmers and chemical workers, but not in non-exposed comparison groups.	Bekesi et al. 1979a,1978

Table G1: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established in 1976	Immunologic disfunction	To study lymphocyte in humans exposed to PBBs	36 PBB-highly exposed subjects (serum PBB values > 300 ppb) 59 subjects with 1 ppb <PBB level <11ppb	High vs. low exposure groups were compared with respect to T and B lymphocytes numbers and traformations to 3 mitogens.	No significant differences in percentages of T and B lymphocytes in different exposure groups. No significant depression of lymphocyte mitogenic responsiveness.	No correlation was found between serum PBB levels and lymphocyte number or function.	Silva et al., 1979

PBB: polybrominated biphenyls; T3: Thyroxine. T4: Triiodothyronine. TSH: thyroid stimulation hormone.

Table G2: Studies on neurodevelopmental effects.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established in 1976	Neuropsychological development of children	To investigate whether ingestion of PBBs has an adverse effect on the neuro-psychological development of young children exposed *in utero* and in infancy	19 Michigan children exposed to PBBs	Five tests of the McCarthy Scales of Children's Abilities (Block Building, Puzzle Solving, Word Knowledge, Draw-A-Design, Draw-A-Child)	Multivariate analysis showed the existence of a significant main effect for fat PBB levels, controlling for parental education. Children with higher body burdens of PBBs (> 0.100 ppm) scored significantly lower than exposed children with lower body burdens on the same tests, and on a composite score representing overall performance.	These results suggest the existence of an inverse relationship between body levels of PBBs and some developmental abilities in young children	Walker Seagull, 1983
Michigan, USA. PBB cohort established in 1976	Neurobehavioral symptoms	To study the prevalence of neurological symptoms in males and in females in the Michigan population exposed to PBBs (with comparison to similar data in the Wisconsin, non-PBB-exposed group.	626 adults from Michigan and 153 from Wisconsin. The sub-sample examined by means of performance tests consisted of 95 males and 67 females from Michigan and 50 males and 4 females from Wisconsin.	Performance tests used in order to obtain an objective assessment of brain functions were Block Design, Digit Symbol, and Embedded Figures	In Michigan (particularly among males) those who exhibited the most marked symptoms tended to show diminished performance as assessed by special tests, although population differences in performance were not as marked. Low indices of performance were also significantly correlated with intake of home-produced foodstuffs, particularly during the years 1972- 1974 and store-bought products during the years 1975-1976.	Serum PBB levels were not found to be significantly higher in Michigan males and females exhibiting the most prominent neurological symptoms. Serum PBB levels were negatively correlated with performance test scores, particularly in males in older age groups.	Valciukas et al., 1979

Table G2: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan PBB cohort established in 1976	Neurobehavioral effects	To evaluate neurobehavioral complaints	46 persons (37 men and 9 women) with known exposure to PBBs and incapacitating health complaints were identified from previous studies	Physical examinations and psychological-psychiatric tests. The patients' complaints were grouped into 5 categories: general, musculoskeletal, skin, gastro-intestinal, neurological.	Findings were hepatomegaly (72 %), skin abnormalities (28 %), objective joint abnormalities (13 %), neurologic abnormalities (15 %). 31 patients (67 %) were depressed Nerve conduction studies were abnormal in 19 patients (41 %). There was no relationship between the presence of these abnormalities and serum or fat PBB levels.	In this group of patients with known exposure to PBBs and incapacitating health care complaints, there was a high prevalence of hepatomegaly (72 %), sensory neuropathies (41 %), and reactive depression (67 %). There was no evidence of changes suggestive of organic brain syndromes.	Stross et al., 1979

Table G2: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan PBB cohort established in 1976	Effects on personality and cognitive functioning	To evaluate neurobehavioral complaints	21 persons exposed to PBB were compared with 21 hospital volunteers. Patients exposed to PBBs were selected for this study only if they had persistent medical complaints	Battery of tests measuring memory, motor strength and coordination, cortical-sensory perception, personality, and higher cognitive functioning	The PBB adipose levels did not correlate with performance on any test in the battery. The two groups did differ on the Minnesota Multiphasic Personality Inventory, suggesting an adjustment reaction with depressive symptoms and somatizing defenses. Persons exposed to PBBs were also impaired relative to control subjects on tests of prose recall, short-term memory, concentration, and cognitive flexibility. However these differences vanished when results were controlled for group differences on education and personality.	The PBB adipose levels did not correlate with performance on any test in the battery.	Brown and Nixon, 1979.
Michigan, USA. PBB cohort established in 1976	Neurobehavioral symptoms	To study the prevalence of neurological symptoms in males and in females in the Michigan population exposed to PBBs (with comparison to similar data in the Wisconsin, non-PBB-exposed)	644 adults from Michigan and 153 from Wisconsin. A sub-sample (102 males and 68 females from Michigan and 50 males and 43 females from Wisconsin) was chosen at random during comprehensive cross-sectional clinical surveys in the two states.	Neurobehavioral tests (Block Design, Digit Symbol and Embedded Figures) were used in the assessment of performance of the populations studied.	A significant constellation of neurological symptoms and neurobehavioral test scores occurred among dairy farmers during the period 1972-1976, when compared to a non-PBB-exposed-dairy farm population.	A significant constellation of neurological symptoms and neurobehavioral test scores occurred among dairy farmers during the period 1972-1976, when compared to a non-PBB-exposed-dairy farm population.	Valciukas et al., 1978

PBB: polybrominated biphenyl.

Table G3: Studies on cancer.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Zhejiang, China 2007 - 2008	Burdens of PBBs and PBDE in cancer patients	To explore the burdens of PBBs, PBDEs, (and PCBs) among cancer patients living in the electronic waste disassembly sites	Kidney (n=19), liver (n=55), and lung (n=7) tissue samples from surgical patients who were newly diagnosed for cancer	The contents of 23 PBBs, 12 PBDEs, and 27 PCBs in kidney, liver, and lung samples were measured	Low-brominated PBBs and BB-153 were the predominant congeners. PBB levels (181-192 ng/g fat) were higher than those reported in the general USA population (3-8 ng/g fat).	High burdens of PBBs, PBDEs and PCBs were detected in tissues samples of cancer patients living in electronic waste disassembly sites.	Zhao et al., 2009
Michigan, USA. PBB cohort established in 1976 1976-1993	Risk for 12 site-specific cancer	To evaluate the association between site-specific cancer risk and serum PBB levels	Nested case-control study: 195 primary cancers in 187 persons. 696 controls not affected by cancer	18 years follow-up data adjusted for age, smoking, family cancer history, alcohol drinking and baseline serum PCB level. Serum PBB distribution categorized into 4 groups using cutpoints corresponding to the median and 90th and 95th percentiles.	Digestive system cancer: OR = 8.23 [95 % CI = 1.27-53-3]. OR = 12.3 [95 % CI = 0.80-191]. OR = 22.9 [95 % CI = 1.34-392] in categories of exposure levels of 4-20 ppb, 21-50 ppb, and >50 ppb. Lymphoma: OR = 3.24 [95 % CI = 0.24-95.9]. OR = 20.5 [95 % CI = 1.51-608]. OR = 32.6 [95 % CI = 3.33-861] for the same exposure categories.	A risk is suggested for cancer of digestive system and lymphoma.	Hoque et al., 1998

Table G3: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA 1976 - 1993	Breast cancer	To examine the association between breast cancer and serum PBBs	Case-control study based on 1,925 women enrolled in a PBB registry. 20 women who developed breast cancer were matched to 290 control subjects on sex, race, and age.	Case-control study	Women with serum PBB levels of 2.0-3.0 ppb [odds ratio (OR) = 3.5; 95 % confidence interval (CI) = 0.9-13] or 4.0 ppb or greater (OR = 3.1; 95 % CI = 0.8-12) had a higher estimated risk for breast cancer than women with less than 2.0 ppb. The odds ratios were unchanged when available breast cancer risk factors were included in the analysis.	Women with higher serum PBB levels had an increased risk for developing breast cancer compared with women with lower serum PBB levels. No dose-response relation was observed. The excess risk was not limited to cases diagnosed ten or more years after exposure. The broad confidence intervals make it difficult to exclude chance as an explanation for these findings.	Henderson et al., 1995

Table G3: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, Arkansas USA 1935-1976	Mortality	To evaluate all - causes and cause-specific mortality	3,579 white male workers employed at 3 manufacturing plants (2 in Michigan and 1 in Arkansas)	Historical cohort mortality study	Of the 91 workers potentially exposed on a "routine" basis, none died during the study period; among the 237 "non-routinely" exposed male workers, two deaths were observed versus 6.4 expected, one of which was due to cancer of the large intestine (1 observed versus 0.1 expected).	No significant overall or cause-specific mortality excess was detected.	Wong et al., 1984

PBB: polybrominated biphenyl; PBDE: polybrominated biphenyl ether; PCB: polychlorinated biphenyl; OR: odds ratio; CI: confidence interval.

Table G4: Studies on diabetes and metabolic syndrome.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
CARDIA (Coronary Artery Risk Development in Young Adults) Birmingham, Chicago, Minneapolis, Oakland, USA 1985-2006	diabetes	To evaluate several POPs (including BB-153) as predictors of type 2 diabetes	5,115 African American and white participants recruited at baseline in 1985-1986 (year 0). 90 new cases of diabetes. 90 controls randomly selected among diabetes free subjects	Case-control study nested in the CARDIA cohort. Follow-up examinations completed at years 2, 5, 7, 10, 15, and 20 (2005-06) in 91 %, 86 %, 81 %, 79 %, 74 %, and 72 % respectively, of survivors. Serum samples stored were available for measuments of POPs.100 % sera had detectable rate for PBB-153: quartile of serum concentrations (pg/g of lipid) were <=9, 10-16, 17-23, >23.	The highest risk was observed in the 2nd quartiles of trans-nonachlor, oxychlordane, mirex, highly chlorinated PCBs, suggesting low dose effects. The adjusted odds ratios among subjects in the 2nd sextile was 5.3 compared to the lowest sextile; and 20.1 among those with BMI ≥30 kg/m^2. Odds ratios (sex, age, ethnic group, BMI, triglyceride, total cholesterol adjusted) for PBB-153 quartiles were 1.0, 2.5 (95 % CI 0.9-6.9), 2.5 (0.8-7.6) and 1.8 (0.6-5.8).	Several POPs at low doses similar to current exposure levels may increase the risk of diabetes, possibly through endocrine disruption. Certain POPs may play a role in the current epidemic of diabetes, which has been attributed to obesity. A statistically non-significant excess risk, with no dose response for BB-153 was found.	Lee et al., 2010

Table G4: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
National Health and Examination Survey (NHANES), USA	Diabetes, metabolic syndrome	To study cross-sectional associations of serum concentrations of BFRs with diabetes and metabolic syndrome	Diabetes (n=1367) Metabolic syndrome (n=637) among NHANES 2003-2004. NHANES is an ongoing survey designed since 1999 to measure the health and nutritional status of the civilian non-institutionalised U.S. population.	Cross-sectional Study: 1,367 adults were examined with respect to diabetes status. Five PBDEs and one PBB were selected, detectable in _60 % of participants. For the outcome metabolic syndrome, analyses were restricted to 637 participants with a morning fasting sample. PBDEs and PBBs were measured in serum. 100 % sera had detectable rate for PBB-153: quartile of serum concentrations (pg/g of lipid) were 1.2, 2.3, 3.8, 13.1.	Compared with subjects with serum concentrations below the LOD, prevalent diabetes had differing dose-response associations with serum concentrations of BB-153. Adjusted odds ratios across not detectable/ quartiles of serum concentrations were 1.0/ 0.7, 1.4, 1.6, and 1.9 (*P* for trend _0.01) and 1.0, 1.6, 2.6, 2.7, and 1.8 (*P* for quadratic term _0.01), respectively. BB-153 was also positively associated with the prevalence of metabolic syndrome with adjusted odds ratios of 1.0, 1.5, 3.1, 3.1, and 3.1 (*P* for trend=0.01).	Pending confirmation in prospective studies, lipophilic xenobiotics, including brominated POPs stored in adipose tissue, may be involved in the pathogenesis of diabetes and metabolic syndrome	Lim et al., 2008

Table G4: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA, 1976-1991-1993-2001 Michigan, USA. PBB cohort established 1976, surveyed 1991-1993 and 2001.	Incidence of diabetes	To determine the incidence of adult-onset diabetes in subjects exposed to PBBs	N=1384 Age ≥ 20y, no diabetes at enrolment	25years follow-up data. Self-reported diagnosis of diabetes. PBB serum concentrations were grouped into 4 levels, based on their concentrations within the study group (one group below LODs, and tertiles for the remainders): <=1 ppb, 1.1-3.0, 3.1-7, >7 ppb.	The study confirmed the increased risk of diabetes related to PCB exposure. Analysing 25 years of follow-up data, the study did not find that higher PBB serum levels were a risk factor for the incidence of diabetes mellitus ORs ranged from 0.5 to 1.5 with no dose response and wide confidence intervals.	Higher PBB serum levels were not a risk factor for incidence of diabetes.	Vasiliu et al., 2006

CARDIA: Coronary Artery Risk Development in Young Adults; NHANES: National Health and Examination Survey; PBB: polybrominated biphenyl; BMI: body mass index; POP: persistent organic pollutant; LOD: limit of detection; PBDE: polybrominated diphenyl ether.

Table G5. Studies on fertility or offspring.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established in 1976	Genitourinary (GU) conditions in male offspring	Relationship between maternal serum levels of PBBs and GU conditions among male offspring exposed *in utero*	464 sons of mothers exposed to PBBs	Self-reported data on GU conditions among male offspring in relation to maternal serum PBB levels controlling for gestational age at birth.	33 reported any GU condition (13 hernias, 10 hydroceles, 9 cryptorchidism, 5 hypospadias, and 1 varicocele). Four reported both hernia and hydrocele, and one both hernia and cryptorchidism. Sons of highly exposed women (> 5 ppb) were twice as likely to report any GU condition compared with sons of the least exposed women [≤ 1 ppb; OR = 2.0; 95 % confidence interval (CI), 0.8–5.1]. This risk was increased when sons born after the exposure but before the mother's serum PBB measurement were excluded (OR = 3.1; 95 % CI, 1.0–9.1). We found evidence of a 3-fold increase in reported hernia or hydrocele among sons with higher PBB exposure (test of trend *p*-value = 0.04). Neither hypospadias nor cryptorchidism was individually associated with PBB exposure.	Although cryptorchidism and hypospadias were not associated with *in utero* exposure to PBBs, this study suggests that other GU conditions may be associated with exposure to endocrine-disrupting chemicals during development.	Small et al., 2009

Table G5: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established in 1976 1975-1988	Parental exposure offspring sex ratio	To study the association between parental exposures to PBBs and offspring sex ratio.	865 Michigan born offspring to 479 PBB cohort mothers. Of these, 300 offspring had mothers and fathers who were both in the cohort (n = 171 pairs of mothers and fathers).	Gender of offspring of female PBB cohort participants (born 1975-1988) linked to parental serum PBB and PCB concentrations collected at enrollment into the cohort. Major potential confounders were taken into account in the analysis.	Proportion of male offspring among 865 live births to cohort mothers was 0.542. This was higher than the national male proportion of 0.514 (binomial test: p = 0.10). When both parents were in the cohort (n = 300), increased odds of a male birth with combined parents' enrolment. Exposure above the median concentrations (3 microg/L for mothers; 6 for fathers) compared to combined parents' PBB exposure below the median concentrations gave an OR = 1.43, 95 % CI: 0.89-2.29, although this did not reach statistical significance.	In this population, combined parental exposure to PBBs (or PCBs) suggested an increase in the odds of a male birth. Even if many potential confounders were considered in the analysis, in this study it was not possible to separate exposure to PBBs and PCBs, limiting the interpretation of this potential association.	Terrell et al., 2009

Table G5: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established in 1976 1975 - 1994	Parental exposure Birth weight – gestational lenght	This study examined the association between early age at exposure to PBBs and subsequent birth weight and gestational length in offspring among females	1111 births that occurred among 560 women enrolled in the Michigan PBB Cohort from 1975 to 1994	Maternal age at exposure was categorized into three groups: <10 years (n = 64), 11–16 years (n = 149), and 17-42 years (n = 347). Overall serum PBB levels ranged from 0 to 1490 ppb, with a median of 2, 3, and 2 ppb in the three age groups, respectively. Separate mixed-effects linear regression models were used to evaluate the effect of age at exposure (years) and initial PBB level (ppb) on birth weight and gestational age, controlling for gestational age (in the model examining effects on birth weight), BMI (kg/m^2) and serum PCB level at enrollment.	Relative to the oldest age group, age <10 years at exposure was the most important predictor of increased birth weight (estimated regression coefficient 225 g, p = 0.012). Infant birth weight increased approximately 16 g for every 10 ppb increase in serum PBBs (p = 0.004).	No association between initial PBB levels and gestational age	Sweeney and Symanski, 2007

Table G5: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established in 1976 1975 - 1997	Birth weight and gestational age	To evaluate the influence of maternal exposures on gestational age and birth weight	444 mothers and their 899 infants born between 1975 and 1997	Maternal serum PBB concentration at the time of conception was extrapolated from PBB measurement taken at the date of enrolment with correlation between predicted and measured level of 0.92.	No significant association was found between estimated maternal serum PBB at conception and gestational age or infant birth weight. However, a negative association with high levels of enrolment maternal serum PBB and birth weight was suggested. Birth weight and gestational age among offspring of women with the highest (10 %) PBB levels, showed no significant association.	No association between estimated maternal serum PBB at conception and gestational age or infant birth weight was found.	Givens et al., 2007
Michigan, USA. PBB cohort established in 1976 1997	Endometriosis	To study the association between endometriosis and exposure to PBBs (and PCBs)	943 women	Cox models to estimate the relative incidence of endometriosis in relation to PBB (and PCB) levels.	Seventy-nine of women (9 %) reported endometriosis. Compared to women with low PBB exposure (≤ ppb), women with moderate PBB (1-4 ppb) had a hazard ratio (HR) of 0.72; 95 % CI, 0.39–1.35. HR for women with high PBB (≥ 4 ppb) was 0.90; 95 % CI, 0.51- 1.59. Increased incidence of endometriosis was suggested among women exposed to PCB.	This study does not support an association between PBB exposure and endometriosis	Hoffman et al., 2007

Table G5: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established in 1976 1997	Spontaneous abortion	To study the association between spontaneous abortions and exposure to PBBs and PCBs	529 women with 1344 potentially exposed pregnancies	Adjustment for maternal age at conception, age at menarche, and prior infertility	Compared to pregnancies with PBB exposure below the limit of detection, those with levels above 2.9 ppb had a non-significant reduced odds of spontaneous abortion (adjusted OR=0.73; 95 % CI= 0.47-1.13).	PBB (and PCB) exposure were not associated with risk of spontaneous abortion	Small et al., 2007
Michigan, USA. PBB cohort established in 1976 1997 - 1998	Menstrual cycle length	To study the association between menstrual cycle length and exposure to PBBs and PCBs	337 women (age range: 24-56 years) with self-reported menstrual cycles of 20-35 days	All models were adjusted for serum PCB levels, age, body mass index, history of at least 10 % weight loss in the past year, physical activity, smoking, education, and household income.	Average cycle length did not differ among women when stratified by exposure to PBBs at enrolment or by exposure to PBBs estimated at the time of the interview. When women with weight loss in the highest decile of estimated current PBB exposure were considered, the interaction term was significant.	No overall association between current estimated PBBs and either menstrual cycle length or bleed length was found. However, these associations were found among the small number of women with recent weight loss suggesting either a chance finding or that mobilization of PBBs from lipid stores may be important.	Davis et al., 2005

Table G5: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established 1976 1997	Time to menopause	Time to menopause in women exposed orally to PBBs and PCBs	874 women aged 24 years and older	Women were asked whether they had had any menstrual periods in the previous year, why their menstrual periods had stopped (e.g. surgery), and age at their last menstrual period. Serum PBB and PCB taken at enrollment (1976-1978) into the Michigan PBB registry was used as the measure of exposure. Proportional hazard modeling was used to analyze the risk for menopause in relation to exposure.	No association between either PBB or PCB exposure and time to menopause was found.	No association between either PBB or PCB exposure and time to menopause was found.	Blanck et al., 2004
Michigan, USA. PBB cohort established in 1976 1997-98	Prenatal exposure and growth in girls	To study the association of estimated PBB and PCB exposure during pregnancy with current height and weight in daughters	308 daughters, 5-24 years of age (mean age 15.2 years), born to women in the cohort	Prenatal PBB exposure using maternal enrolment serum PBB and a model of PBB elimination. Self-reported height and weight were obtained from a 1997–1998 health survey.	No association between prenatal PBB exposure and either daughter's current height or daughter's weight adjusted for height was found. Prenatal PCB exposure above 5 parts per billion was associated with reduced weight adjusted for height.	No association between prenatal PBB exposure and either daughter's current height or daughter's weight adjusted for height was found.	Blanck et al., 2002

Table G5: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established in 1976 1997	Age at Menarche and Tanner Stage	Pubertal development in females who were exposed to PBB *in utero* and, in many cases, through breastfeeding	327 females 5–24 years of age	*In utero* exposure to PBBs using maternal serum PBB measurements taken after exposure (1976-1979) and extrapolated to time of pregnancy using a model of PBB decay.	Breastfed girls exposed to high levels of PBBs *in utero* (≥7 ppb) had an earlier age at menarche (mean age = 11.6 years) than breastfed girls exposed to lower levels of PBB *in utero* (mean age = 12.2-12.6 years) or girls who were not breastfed (mean age = 12.7 years). This association persisted after adjustment for potential confounders (menarche ratio = 3.4, 95 % confidence interval = 1.3-9.0). Perinatal PBB exposure was associated with earlier pubic hair stage in breastfed girls, but little association was found with breast development.	The associations observed here lend support to the hypothesis that pubertal events may be affected by pre- and postnatal exposure to organohalogens.	Blanck et al., 2000b

Table G5: Continued.

Location, Time period	Outcome	Aim	Study population	Methods	Results	Conclusions	Reference
Michigan, USA. PBB cohort established in 1976	Fetal mortality	To study fetal mortality in exposed groups	The high exposure group consisted of seven lower peninsula counties with between 6.8 per cent and 20.4 per cent of total farms quarantined per county. Comparison group: 13 upper peninsula counties with no quarantined farms.	Spontaneous abortions occurring after 20 weeks of gestation	The annual RRs fluctuate widely and range from 0.53 in 1968 to 1.69 in 1981; However, over all the pre-exposure years the RR is significantly lower in the lower peninsula counties (RR = 0.83, CI 0.71-0.97). Since counts of early (up to week 20) spontaneous abortions are lacking, a complete assessment of the possible impact on reproductive outcome cannot be made.	Comparison of fetal death rates among residents of Lower Peninsula counties with a high percentage of quarantined farms and among residents of Upper Peninsula counties with no quarantined farms reveals no important differences in rates or trends after the contamination.	Humble and Speizer, 1984
Michigan, USA Time period not specified	Spermatogenesis among PBB-exposed men	To evaluate spermatogenesis among PBB-exposed men	Cases: semen from 52 PBB-exposed men (41 PBB-exposed dairy farms residents and consumers, 11 PBB-exposed chemical workers) Controls: semen from 52 graduate students not exposed to PBB.	Analyses were controlled for potential confounders (past medical, drugs, smoking, alcohol, reproductive and chemical exposure histories).	No differences in the distribution of sperm counts, motility, or morphology.	No differences in the distribution of sperm counts, motility, or morphology.	Rosenman et al., 1979

GU: genitourinary; PBB: polybrominated biphenyl; OR: odds ratio; CI: confidence interval; PCB: polychlorinated biphenyl; BMI: body mass index; HR: hazard ratio; RR: relative risk.

ABBREVIATIONS

AhR	Arylhydrocarbon receptor
ABS	Acrylonitrilebutadiene-styrene copolymers
AHH	Aryl hydrocarbon hydroxilase
AT	Austria
ATSDR	Agency for Toxic Substances and Disease Registry
BE	Belgium
BFR	Brominated Flame Retardant
BG	Bulgaria
BMI	Body mass index
b.w.	body weight
BTBPE	Bis(2,4,6-tribromophenoxy)ethane
CAR	Constitutive androstane receptor
CARDIA	Coronary Artery Risk Development in Young Adults
CHO cells	Chinese hamster ovary cells
CI	Confidence interval
CLRTAP POP	Convention on Long-Range Transboundary Air Pollution on Persistent Organic Pollutants
CONTAM Panel	Panel on Contaminants in the Food Chain
COT	Committee on Toxicity
CZ	Czech Republic
DATEX	Data collection and Exposure Unit (EFSA)
DBDPE	Decabromodiphenyl ethane
DE	Germany
DecaBB	Decabromo biphenyl
DK	Denmark
DR-CALUX	Dioxin Responsive Chemical-Activated LUciferase gene eXpression
ECD	Electron capture detector

ECNI	Electron capture negative ionization
EE	Estonia
EFSA	European Food Safety Authority
EC	European Commission
EI	Electron impact
ES	Spain
EU	European Union
EXPOCHI	EFSA Article 36 project "Individual food consumption data and exposure assessment studies for children
FI	Finland
FFQ	Food frequency questionnaire
FPQ	Food propensity questionnaire
FR	France
GB	Great Britain
GC	Gas Chromatography
GC×GC	Comprehensive multidimensional GC
GC-ECNI-MS/MS	Gas Chromatography - Electron Capture Negative Ionization -Tandem Mass Spectrometry
GC-HRMS	Gas Chromatography - High Resolution Mass Spectrometry
GD	Gestational day
GEMS/Food	WHO-Global Environment Monitoring System-Food Contamination Monitoring and Assessment Programme
GGT	Gamma-Glutamyl Transpeptidase
GI	Gastrointestinal
GJIC	Gap Junctional Intercellular Communication
GPC	Gel Permeation Chromatography
GSTP	Glutathione S-Transferase P
GU	Genitourinary
HBCDD	Hexabromocyclododecane
HR	Hazard Ratio
HRMS	High resolution mass spectrometry

HU	Hungary
IARC	International Agency for Research on Cancer
IE	Ireland
IgC/G	Immunoglobulin C/G
IOM	Institute of Medicine of the U.S. National Academies of Sciences
i.p.	Intraperitoneal
IPCS	International Program on Chemical Safety
IT	Italy
IUPAC	International Union of Pure and Applied Chemistry
i.v.	Intravenous
LB	Lower bound
LD_{50}	Lethal Dose – the dose required to kill half the members of a tested animal population
LOEL	Lowest Observed Effect Level
LOAEL	Lowest Observed Adverse Effect Level
LOD	Limit of detection
Log K_{ow}	Octanol-water partitioning coefficient
LOQ	Limit of quantification
LV	Latvia
MLs	Maximum levels
MS	Mass spectrometry
MS/MS	Tandem mass spectrometry
MSs	Member States
n	Frequency of results
N	Number of subjects
nd	not detected
NHANES	National Health and Nutrition Examination Survey
NL	The Netherlands
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect level

ns	not specified
NTP	National Toxicology Program
NIEHS	National Institute of Environmental Health Sciences
OR	Odds/Risk Ratio
PBBs	Polybrominated biphenyls
PBDEs	Polybrominated diphenyl ethers
PBLs	peripheral blood lymphocytes
PBPK	Physiologically-based pharmacokinetic model
PCBs	Polychlorinated biphenyls
PHA	Phytohemaglutin
PL	Poland
PND	Postnatal day
POP	Persistent Organic Pollutant
PXR	Pregnane X receptor
p.o.	*per oral*
PTV	Programmable temperature vaporiser
RoHS	Restriction of the use of certain hazardous substances
RR	Relative risk
SAF	Sampling Adjustment Factors
SE	Sweden
SI	Slovania
SK	Slovak Republic
SRBC	Sheep Red Blood Cells
T3	Thyroxine hormone
T4	Triiodothyronine hormone
TBBP-A	Tetrabromobisphenol A
TCDD	2,3,7,8-tetrachlorodibenzo-*p*-dioxin
TDI	Tolerable daily intake
TDS	Todal Diet Study

TSH	Thyroid stimulation hormone
TTR	Transthyretin
TEF	Toxic equivalency factor
TEQ	Toxicity equivalent
UB	Upper bound
UDS	Unscheduled DNA synthesis
UK	United Kingdom
USA	United States of America
v/v	volume/volume
WEEE	Waste electrical and electronic equipment
WHO	World Health Organisation
w.w.	Wet weight