COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

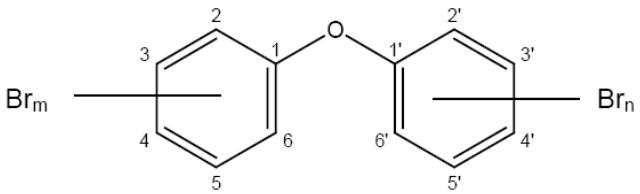
Statement on the potential risks from polybrominated diphenyl ethers (PBDEs) in the infant diet

Background

1. The Scientific Advisory Committee on Nutrition (SACN) is undertaking a review of scientific evidence that bears on the Government's dietary recommendations for infants and young children. The review will identify new evidence that has emerged since the Government's current recommendations were formulated, and will appraise that evidence to determine whether the advice should be revised. The recommendations cover diet from birth to age five years, but will be considered in two stages, focussing first on infants aged 0 – 12 months, and then on advice for children aged 1 to 5 years. SACN is examining the nutritional basis of the advice, and has asked that evidence on possible adverse effects of diet should be considered by other advisory committees with relevant expertise. COT was asked to review the risks of toxicity from chemicals in the infant diet.

2. This statement gives an overview of the potential risks from polybrominated diphenyl ethers (PBDEs) in the infant diet. PBDEs are brominated flame retardants (BFRs), which are used in the manufacture of a range of products to increase their fire-related safety. None of Government's current dietary recommendations for infants and young children relates to PBDEs.

3. PBDEs comprise two phenyl rings linked by an ether group with bromine atoms substituting different combinations of ring hydrogens. Their generic structure is shown in Figure 1. They include ten homologues with a total of 209 isomeric congeners (Table 1).



Where (m) plus (n) equal between 1 and 10 bromine atoms

Figure 1: Generic structure of the PBDEs

Table 1: PBDE homologues and congeners (from EFSA, 2011)

Homologues	Chemical formula	Molecular mass	Isomeric congeners	Number of congeners
monoBDEs	$C_{12}H_9BrO$	249.1	BDE-1 to BDE-3	3
diBDEs	$C_{12}H_8Br_2O$	328.0	BDE-4 to BDE-15	12
triBDEs	$C_{12}H_7Br_3O$	406.9	BDE-16 to BDE-39	24
tetraBDEs	$C_{12}H_6Br_4O$	485.8	BDE-40 to BDE-81	42
pentaBDEs	$C_{12}H_5Br_5O$	564.7	BDE-82 to BDE-127	46
hexaBDEs	$C_{12}H_4Br_6O$	643.6	BDE-128 to BDE-169	42
heptaBDEs	$C_{12}H_3Br_7O$	722.5	BDE-170 to BDE-193	24
octaBDEs	$C_{12}H_2Br_8O$	801.4	BDE-194 to BDE-205	12
nonaBDEs	$C_{12}HBr_9O$	880.3	BDE-206 to BDE-208	3
decaBDE	$C_{12}Br_{10}O$	959.2	BDE-209	1

4. Technical mixtures of PBDEs have been widely used as additive flame retardants in polymers and textiles, construction materials, furniture, and electrical equipment. Because PBDEs are not chemically bound to the materials in which they are incorporated, they can be dispersed into the environment and enter the food chain.

5. Table 2 lists the 8 congeners that were present in the largest amounts in commercial technical mixtures of pentaBDE, octaBDE and decaBDE (EFSA, 2011). International agreements on bans and regulations on production and use of technical mixtures of PBDEs have been introduced since 2004, leading to declining levels in the environment (EFSA, 2011). There are still some uses of commercial decaBDE (predominantly BDE-209), but it has been predicted that atmospheric concentrations of BDE-209 peaked in 2004 and will decline to negligible levels by 2025 (Earnshaw *et al*., 2015).

Table 2: Predominant congeners in commercial technical mixtures of PBDEs (EFSA, 2011)

Congener	Bromine substitution	CAS number
BDE-28	2,2’,4-triBDE	41318-75-6
BDE-47	2,2’,4,4’-tetraBDE	5436-43-1
BDE-99	2,2’,4,4’,5-pentaBDE	60348-60-9
BDE-100	2,2’,4,4’,6-pentaBDE	189084-64-8
BDE-153	2,2’,4,4’,5,5’-hexaBDE	68631-49-2
BDE-154	2,2’,4,4’,5,6’-hexaBDE	207122-15-4
BDE-183	2,2’,3,4,4’,5’,6-heptaBDE	207122-16-5
BDE-209	2,2’,3,3’,4,4’,5,5’,6,6’-decaBDE	1163-19-5

6. PBDE congeners are susceptible to photolysis, reductive debromination and free radical reactions in the environment. The chemical

stability of the PBDE congeners varies with their individual structure but in general congeners with up to three bromine substituents and those with nine and ten bromine substituents are more susceptible to abiotic transformation.

7. In 2004, the COT published a statement on PBDE residues in fish from two rivers in England[1]. Subsequently in 2006, the COT published a risk assessment for PBDE residues in a broader range of fish and shellfish[2]. The EFSA Panel on Contaminants in the Food Chain issued a comprehensive opinion on PBDEs in 2011 (EFSA, 2011). This statement draws on information from the EFSA review and from more recent publications. Literature searches were conducted from January 2011 to July 2014 using the term "PBDE" together with the terms "neurodevelopment", "neurotoxicity", "infant" and "neonatal", and focussing on studies relevant to infants.

Previous evaluations by COT and EFSA

COT

8. In its 2004 Statement, the COT noted that toxicity studies had been conducted mainly on commercial mixtures of PBDEs, the compositions of which were unclear and likely to differ from the profile of congeners in food and the environment. Because of the inadequacies of the toxicological databases it was not possible to establish a tolerable daily intake, and a Margin of Exposure (MoE) approach was adopted. The most sensitive effect of pentaBDE was considered to be neurodevelopmental, with a lowest observed adverse effect level (LOAEL) of 600 µg/kg bw, obtained from a study in which BDE-99 was administered by a single oral dose to mice on postnatal days (PNDs) 3 or 10. However, the focus of the 2004 Statement was on exposure to PBDEs from fish, and the available data did not allow an assessment of exposure to infants at a comparable developmental stage (up to one month). Therefore an MoE could not be calculated for neurodevelopmental effects.

9. Based on studies described in an EU Risk Assessment Report (European Commission, 2000), the COT concluded that liver toxicity was the most relevant and sensitive effect in older children and adults. The European Commission (2000) had reported that the effects of pentaPBDE included increases in liver weight, hepatocytomegaly, induction of a range of liver enzymes, and disturbances in the synthesis of cholesterol and porphyrin. The COT agreed with the no observed adverse effect level (NOAEL) for liver effects induced by a pentaBDE formulation in the rat (450 µg/kg bw/day) that had been identified in the EU Risk Assessment Report, and used that NOAEL as a reference point (point of departure).

10. In 2006, the COT considered exposure to PBDEs in fish and shellfish (using data collected during 2003-2004 (Fernandes, 2005a)), and from the

[1] http://cot.food.gov.uk/pdfs/bfrstatement.pdf
[2] http://multimedia.food.gov.uk/multimedia/pdfs/cotstatementfishsurveys.pdf

rest of the diet (using data from the 2003 Total Diet Study (Fernandes, 2005b)). An MoE approach was again taken, with the same reference point for liver effects.

EFSA

11. EFSA noted that following oral exposure, BDE-209 was absorbed to a limited extent (<25% of dose), whereas absorption of other congeners for which data were available was higher (50-80%), with distribution primarily into fatty tissues. Debromination and hydroxylation were the major metabolic pathways. Elimination half-lives for individual congeners in the rat ranged from about 2 to 20 days, whereas much larger values had been reported in humans for lower brominated congeners (e.g. 556-926 days for BDE-47, 1300-4,530 days for BDE-153). The elimination half-life of BDE-209 was reported as 2.5-8.6 days for rats, and about 15 days for humans. (EFSA, 2011).

12. The main targets of PBDE toxicity were identified as the liver, thyroid hormone homeostasis, and the reproductive and nervous systems. EFSA (2011) reviewed a number of epidemiological studies relating tissue levels of PBDEs to levels of thyroid hormones, neurodevelopmental effects, cancer, diabetes and metabolic syndrome, and effects on fertility and offspring. Limitations in the study designs, inconsistencies between the outcomes of different studies, and co-exposure to other halogenated contaminants prevented firm conclusions.

13. EFSA concluded that relevant toxicological data were available for only four individual congeners (BDE-47, BDE-99, BDE-153 and BDE-209) of the eight identified as being predominant in PBDE technical mixtures (Table 2). From studies of neurodevelopmental behavioural changes, mainly in mice, following a single administration by gavage in neonatal animals, EFSA calculated benchmark dose lower confidence limits for a 10% increase in different outcome measures ($BMDL_{10}$s). The critical neurodevelopmental effect of BDE-47 was on locomotor activity, whilst those for BDE-99, -153 and -209 were on total physical activity.

14. For BDE-47, -99 and -153, the much slower rate of elimination in humans compared to rodents led EFSA to take differing toxicokinetics into account by estimating the daily human intake which, after attainment of steady state, would produce the same body burden as might occur in rodents following a single dose by gavage at the $BMDL_{10}$ (assuming 75% uptake from the gut). These human intakes were then used as reference points in an MOE approach. In the case of BDE-209, the elimination half-life did not differ markedly between humans and rodents, and EFSA took the $BMDL_{10}$ value as the reference point without adjustment for body burden.

15. However, the COT considered that it would be appropriate to perform the same calculation for BDE-209 as for BDE-47, -99 and -153, in order to allow for extrapolation from a single dose to chronic exposure. The estimated

human intakes corresponding to the $BMDL_{10}$s for BDE-47, -99, -153 and BDE-209, are set out in table 3.

Table 3: BMDLs and references points based on EFSA (2011)

Congener	**Critical endpoint**	**$BMDL_{10}$** (µg/kg bw)	**Body burden at $BMDL_{10}$** (µg/kg bw)	**Reference point** (ng/kg bw/day)	**Reference**
BDE-47	Locomotion (mouse, PND 10)	309	232 [a]	172 [b]	Eriksson et al. (2001)
BDE-99	Total activity (mouse, PND 10)	12	9 [a]	4.2 [b]	Viberg, et al. (2004)
BDE-153	Total activity (mouse, PND 10)	83	62 [a]	9.6 [b]	Viberg et al. (2003)
BDE-209	Total activity (rat, PND 3)	1700	425 [c]	19640 [d]	Viberg et al. (2007)

[a] Estimated by EFSA (2011) assuming 75% bioavailability
[b] Daily human intake estimated by EFSA to result in the body burden occurring at the rodent $BMDL_{10}$.
[c] Estimated by COT assuming 25% bioavailability, as reported by EFSA (2011)
[d] Value for BDE-209 estimated by COT, using the same approach as EFSA took for BDE-47, -99 and -153, i.e.body burden x elimination rate constant, assuming bioavailability is similar in rodents and humans

16. EFSA expressed some reservations about the methods of the studies in neonatal animals and the relevance of their findings. Limitations included the use of only a single dose, not taking into account litter effects, and that most studies were conducted in a single laboratory with no independent verification. However, EFSA also noted that the studies identified the lowest doses that had been found to cause neurobehavioural effects, covered a relevant neurodevelopmental period in experimental animals, and that the half-lives and the lipophilic nature of a number of PBDE congeners were such that even a single dose would maintain internal exposures for an appreciable period of time. Thus on balance, EFSA considered it appropriate to use the studies for their risk assessment.

17. The potential for additive toxicity of PBDEs was considered by EFSA (2011) but the limited information that was available indicated divergent effects. Thus, it was not possible to identify a common mode of action between congeners, and a cumulative risk assessment was not performed.

New toxicological and epidemiological data

18. The literature search for 2011-14 found one new toxicological study of neurodevelopmental effects of BDE-47 that had been published since those included in the EFSA evaluation. Groups of nine male and nine female 10-day old rats were given a single administration by gavage of 1, 5 or 10 mg/kg bw BDE-47 (He *et al*., 2011). Serum/plasma concentrations of BDE-47 and thyroid hormones, organ to body weight ratios and performance in tests for

learning and memory were assessed when the rats were two months old. Relative uterine weights were significantly decreased at all doses of BDE-47, relative ovarian weights were increased at 5 and 10 mg/kg bw and relative thyroid weight was decreased at the top dose. Plasma thyroxine (T4) concentration was significantly increased at 5, but not 1 or 10 mg/kg bw BDE-47. Tri-iodothyronine (T3) and thyroid stimulating hormone (TSH) did not differ significantly from control. BDE-47 was detected in the serum of control animals at the age of 2 months, but was significantly higher in those that received doses of 5 and 10 mg/kg bw. Performance in learning and memory tests was reported to be impaired at all doses. The lowest dose in this study was higher than the BMDL calculated by EFSA.

19. Two main modes of action have been proposed for the neurodevelopmental effects of PBDEs: an indirect effect mediated by modulation of thyroid hormone homeostasis; and direct toxicity of PBDEs to neuronal and glial cells through oxidative stress (Dingemans *et al*., 2011; Gilbert *et* al., 2012; Costa *et al*., 2013).

20. A recent developmental neurotoxicity study, conducted according to international guidelines, found no evidence of adverse effects of BDE-209 on neurodevelopment following repeated administration by oral gavage to dams from gestation day 6 to weaning, at doses of 0, 1, 10, 100 and 1000 mg/kg bw/day. No treatment-related neurobehavioural changes were observed in detailed clinical observations, startle response, learning and memory tests, or assessments of motor activity up to 6 months of age. Furthermore, there were no treatment-related neuropathological or morphometric alterations, and the authors concluded that the NOAEL was 1000 mg/kg bw/day, the highest dose tested (Biesemeier *et al*., 2011). It should be noted that this NOAEL applies to a maternal dose, whereas the $BMDL_{10}$ of 1700 µg/kg bw/day relates to direct exposure of the neonatal animal, and is therefore more relevant to the assessment of risk from the infant diet.

21. Roth and Wilks (2014) conducted a systematic review of the epidemiological literature since January 2006 relating neurodevelopmental and neurobehavioural outcomes to exposure to polybrominated and polyfluorinated chemicals. The review identified 10 reports concerning PBDEs that met the specified inclusion criteria, of which only 3 were judged to be high quality. The studies addressed various endpoints including reduced head circumference, motor function, cognitive development, attention and hyperactivity disorders, internalising and externalising behaviour, socio-emotional skills, and social competence. The authors noted the difficulty in appraising the body of evidence for specific neurodevelopmental and neurobehavioural outcomes because of inconsistencies across studies. However, they concluded that the epidemiological evidence did not support a strong causal association between PBDEs and adverse neurodevelopmental or neurobehavioural outcomes in infants and children.

22. The literature search did not identify any additional epidemiological studies concerning post-natal exposure (via breastfeeding) to PBDEs that

were not included in either the systematic review of Roth and Wilks (2014) or the EFSA opinion.

23. Overall, the COT concluded that the new data did not call into question the reference points identified by EFSA for BDE-47, BDE-99 and BDE-153, and therefore these were used as reference points also by COT, again in an MoE approach. As regards BDE-209, COT concluded that the daily human intake of 19640 ng/kg bw/day that it had calculated in an equivalent manner (Table 3) was the most appropriate reference point. The new studies did not provide a basis on which to establish reference points for other congeners.

Sources of exposure to PBDEs

Environmental occurrence of PBDEs

24. Because of their low vapour pressure, PBDEs preferentially partition to dust in the indoor environment (Law *et al*., 2014). Concentrations of PBDEs have been measured in dust sampled from homes, offices and cars in the UK. Results have varied widely depending on the specific compounds measured and the location of sampling, but generally have shown higher levels of BDE-209 and the nonaBDEs than of other congeners. For most compounds, concentrations were in the order cars > offices ≥ homes. It is likely, however, that the levels of specific PBDE congeners have changed over time due to progressive reductions in usage of PBDE products and environmental degradation.

25. Table 4 presents results from samples of dust that were vacuumed from carpets or bare floors in UK homes. Household dust is likely to be more relevant to the long-term exposures of infants than dust in offices or cars. Particularly highly concentrations of BDE-209 were found in the dust from two homes (0.22 and 0.14%). In an effort to verify the second highest concentration of 1,400,000 µg/kg, dust was resampled approximately nine months after the original sample had been taken. There was only a slight decline in concentration to 900,000 µg/kg BDE-209. Between the two sampling times, the furniture, television, video recorder, and DVD player had been replaced, which suggests that these were not the source of the elevated BDE-209 levels. The origin appeared to be either two items of electronic equipment (a music system and a digital television receiver) that had been present in the room at both times, or the carpet or curtains. These results indicate that high concentrations of BDE209 can occur in the dust of UK homes, but their prevalence is uncertain.

Table 4: Concentrations of eight PBDEs in dust (30 samples) collected in UK homes during 2006 (Harrad *et al*., 2008)

Congener	PBDE concentrations in dust (µg/kg)		
	Median	Mean	Range

BDE-28	<0.5 [a]	0.70	<0.5 – 2.10
BDE-47	10	15	1.2 – 58
BDE-99	20	36	2.8 – 180
BDE-100	3.4	5.6	<0.5 – 17
BDE-153	5.0	14	<0.5 – 110
BDE-154	2.8	4.4	<0.5 – 16
BDE-183	4.2	71	<2 – 550
BDE-209	8100	260,000	12 – 2,200,000

Thirty samples were analysed for tri-hexa-BDEs; 18 samples were analysed for tri-deca-BDEs, DBDPE, and TBE.

[a] below the limit of detection (LOD) - number of samples <LOD not reported

26. The median summed concentration of BDEs 28, 47, 49, 66, 99, 100, 153, and 154, in air sampled in the 31 UK homes (reported in 2006), was 24 pg/m^3 (range 4-245 pg/m^3), which was higher than in outdoor air (median 8.7, range 0.49-30 pg/m^3) (Harrad *et al*., 2010). Concentrations of BDE-209 were not reported.

Dietary occurrence of PBDEs

Breast milk

27. Fürst (2006) noted that PBDE levels in milk samples collected in the early 2000s were approximately 60% higher than those sampled 10 years earlier. A review by Costa *et al*. (2008) reported that levels of PBDEs in breast milk had increased in the past 20-30 years, along with serum levels in the general population, although a slight decline had started to emerge towards the end of the period. The more recent review by EFSA did not find a consistent trend (EFSA, 2011).

28. Data from the two available studies of breast milk sampled in the UK are summarised in Table 5. BDE-47 was the congener with the highest reported concentrations in both studies. In contrast to the findings in dust and food (tables 4 and 7), BDE-209 was not detected at markedly higher levels than the other congeners, which is consistent with its being less bioaccumulative. In one of these studies, Bramwell *et al.* (2014), analysed samples from six individuals. They found no association of body mass index (BMI) with the sum of PBDEs in breast milk, whereas there were significant positive associations for both BDE-49 and BDE-66. Weak negative associations were found between the sum of PBDEs in breast milk and parity, and also with total months breast-feeding, the latter result apparently being based apparently on only two individuals.

Table 5. PBDE congeners in breast milk sampled in the UK in 2010 (Abdallah and Harrad, 2014) and 2011-2012 (Bramwell *et al*., 2014)

Location Sampling date (number of samples) Reference	Congener (% >LOD)	Concentration in breast milk (ng/kg whole weight)[a]		
		Median	Minimum	Maximum
Birmingham Jan-Feb 2010 (n=35 primiparous women aged 22-35 years) Abdallah and Harrad, 2014	BDE-47 (100)	98	5.95	513
	BDE49 (20)	<1.75	<1.75	15.8
	BDE-85 (45)	<1.75	<1.75	29.1
	BDE-99 (94)	24.2	<2.1	120
	BDE-100 (89)	13.3	<1.75	65.1
	BDE-153 (97)	31.9	<2.1	156
	BDE-154 (77)	7.35	<2.1	389
	BDE-209 (69)	8.75	<2.1	32.2
North-East England April 2011-Feb 2012 (n=6 women aged 26-43 years) Bramwell et al., 2014	DBE28 (100)	3.15	0.7	10.9
	BDE-47 (100)	67.2	11.2	458
	BDE-49 (67)	1.05	<0.7	<3.85
	BDE-66 (67)	1.05	<1.05	4.55
	BDE-85 (83)	1.4	<0.35	12.3
	BDE-99 (100)	30.8	4.2	131
	BDE-100 (100)	22.4	2.45	76.7
	BDE-138 (100)	0.7	<0.35	1.4
	BDE-153 (67)	35.4	24.5	58.8
	BDE-154 (100)	2.45	0.35	6.3
	BDE-183 (100)	1.75	0.7	8.05
	BDE-209 (100)	18.2	<7	36.4

[a] Data converted to whole milk basis from fat weight basis assuming breast milk contains 3.5% fat.

Infant formulae and complementary foods

29. Table 6 presents mean occurrence data for eight PBDE congeners in foods classified as being “for infants and small children”, as reported by EFSA (2011). These were derived from 42 samples, of which 29 were ready-to-eat meals for infants and young children, eight were infant and follow-on formulae, two were cereal-based foods for infants and young children, and one was unspecified. Data are not available for infant formula or commercially-produced infant foods purchased in the UK.

Table 6: Mean concentrations of eight PBDEs in foods "for infants and small children" reported in EFSA (2011)

	Mean occurrence (ng/kg food)							
	BDE-28	BDE-47	BDE-99	BDE-100	BDE-153	BDE-154	BDE-183	BDE-209
Lower bound [a]	1	207	76	21	2	5	2	115
Upper bound [b]	2	208	78	23	6	7	5	127

[a] In the lower bound, values <LOD are treated as 0,
[b] In the upper bound, values <LOD are treated as the LOD

Food

30. The most recent measurements of PBDEs in food sampled in the UK are for the composite food groups of the 2012 Total Diet Study (TDS) (Fernandes *et al.*, 2012). The congeners measured in the 2012 TDS were BDE-17, -28, -47, -49, -66, -71, -77, -85, -99, -100, -119, -126, -138, -153, -154, -183 and -209. Table 7 shows the concentrations of the PBDE congeners for which reference points are available.

Table 7. Levels of selected and summed PBDE congeners in food expressed on a whole weight basis

Food group	PBDE concentrations in food (ng/kg food)[a]				
	BDE-47	BDE-99	BDE-153	Total excluding BDE-209[b]	BDE-209
Bread	5.38	5.71	1.66	24.6-26.6	<200[c]
Canned vegetables	0.65	0.47	<0.14	1.34-2.07	20.1
Carcase meat	17.9	22.5	7.06	61.4-62.1	<130
Cereals	6.31	7.63	2.07	20.9-22.6	<190
Dairy products	23.1	25.4	5.83	64.8-66.9	21.0
Eggs	12.8	16.2	4.97	45.0-45.7	89.8
Fats+oils	36.9	34.7	8.12	97.4-103	<391
Fish	134	22.7	7.08	304	170
Fresh fruit	1.22	0.91	0.24	3.19-3.66	142
Fruit products	1.25	0.99	0.41	2.86-4.42	30.2
Green vegetables	1.54	1.48	0.16	4.07-4.21	50.2
Meat products	17.7	19.2	4.01	52.0-52.8	<140
Milk	1.79	1.95	0.49	5.30-54.8	120
Nuts	5.86	4.60	1.26	13.4-20.1	100
Offal	7.34	8.83	2.98	25.4-27.4	<120
Other vegetables	5.13	7.75	1.37	21.1-21.2	50.2
Potatoes	4.67	5.19	0.67	12.9-13.4	49.8
Poultry	5.34	5.86	1.39	18.0-19.0	220
Sugar and preserves[d]	121	62.1	7.08	263	1948

[a] Concentrations in food were calculated from values for concentrations in fat and for the fat content of food, which were both reported in Fernandes *et al*., 2012.
[b] Total BDE-17, -28, -47, -49, -66, -71, -77, -85, -99, -100, -119, -126, -138, -153, -154, -183, Where a range is given it represents lower bound to upper bound (treating values <LOD as 0 and the LOD, respectively)
[c] Below the limit of detection (LOD), which varied with food group and congener.
[d] Includes sugar, sugar confectionery, jam, syrup, honey, jelly and chocolate.

Drinking water

31. Concentrations of PBDEs in water were not reported in EFSA (2011). In a series of international studies (Crookes *et al*., 2009), the only findings for PBDEs in water in the EU were from Sweden, and all were below the limits of detection (LOD), which ranged from 0.6 to 2.9 ng/L for different congeners. If PBDEs occur in water, levels are likely to be low because of their lipophilicity.

Exposure to PBDEs

32. The assessments that are presented in this section are for external exposures from dust, air and the diet. Data on bodyweights were taken from the UK Dietary and Nutrition Survey of Infants and Young Children (DNSIYC) (DH, 2013), with average values of 7.8, 8.7 and 9.6 kg for infants aged >4.0-6.0, >6.0-9.0 and >9.0-12.0 months, respectively. Since DNSIYC did not include infants younger than 4 months, a value of 5.9 kg for infants aged 0-3 months from an earlier survey (DH, 1994), was assumed for infants aged 0-4 months.

Environmental exposure to PBDEs

Dust and air

33. Table 8 shows potential exposures of infants to PBDEs through ingestion of dust, assuming ingestion of 100 mg dust/day (WHO, 2007), and based on the occurrence data in Table 4. The assessment focuses on infants aged 9-12 months because they are likely to have more contact with floors and other surfaces than younger infants. Since the dust was sampled in 2006, and there have been changes in usage of PBDEs since then, it is possible that these estimates are not representative of current exposures.

Table 8: Potential exposures of infants aged 9-12 months to PBDEs in dust in UK homes

Congeners [a]	Potential exposures to PBDE from consumption of dust (ng/kg bw/day)	
	Congener present at mean measured concentration	Congener present at maximum measured concentration

BDE-28	0.007	0.022
BDE-47	**0.16**	**0.60**
BDE-99	**0.38**	**1.88**
BDE-100	0.058	0.18
BDE-153	**0.15**	**1.15**
BDE-154	0.046	0.17
BDE-183	0.74	5.73
BDE-209	**2,700**	**22,900**

[a] Congeners for which reference points have been derived are highlighted in bold

34. Potential exposures of UK infants to PBDEs in air, assuming a ventilation rate of 3 m^3/day (US EPA, 1989), and the median reported occurrence of 24 pg/m^3 for the sum of BDEs 28, 47, 49, 66, 99, 100, 153, and 154 in domestic air (paragraph 26), are much lower: 0.012, 0.009, 0.008 and 0.008 ng/kg bw/day at ages 0-4, 4-6, 6-9 and 9-12 months respectively.

Dietary exposure to PBDEs

Breast milk

35. Table 9 shows estimated exposure to PBDEs from exclusive breastfeeding by infants, based on the maximum concentrations identified from the data of Abdallah and Harrad (2014) and Bramwell *et al*. (2014), and assuming average (800 mL) or high-level (1200 mL) daily consumption of breast milk. Data from two subjects in the study by Bramwell *et al.* 2014) indicate that PBDE concentrations in breast milk decrease with the duration of breastfeeding. Bramwell *et al.* (2014) also reported a decrease in serum concentrations of most PBDEs compared with measurements from serum sampled in 2003 by Thomas *et al.* (2006), suggesting decreasing exposure over this period.

Table 9 PBDE exposure from exclusive breastfeeding by infants, estimated for average and high-level consumption of breast milk

Congener(s) (concentration in µg/L whole weight)	Exposures to PBDE from exclusive breastfeeding (ng/kg bw/day)			
	Ages 0-4.0 months (800 mL milk)	Ages 0-4.0 months (1200 mL milk)	Ages >4-6.0 months (800 mL milk)	Ages >4-6.0 months (1200 mL milk)
BDE-28 (10.9) [b]	1.47	2.21	1.11	1.67
BDE-47[a] (513) [c]	**69.5**	**104**	**52.6**	**78.9**
BDE-49 (15.8) [c]	2.14	3.20	1.62	2.42
BDE-66 (4.55) [b]	0.62	0.93	0.47	0.70
BDE-85 (29.1) [c]	3.94	5.91	2.98	4.47
BDE-99 (131) [b]	**17.8**	**26.6**	**13.4**	**20.1**
BDE-100 (76.7) [b]	10.4	15.6	7.86	11.8

BDE-138 (1.4) [b]	0.19	0.28	0.14	0.22
BDE-153 (156) [c]	**21.2**	**31.7**	**15.9**	**24.0**
BDE-154 (389) [c]	52.7	79.0	39.9	59.8
BDE-183 (8.05) [b]	1.09	1.64	0.83	1.24
BDE-209 (36.4) [b]	**4.94**	**7.40**	**3.73**	**5.60**

[a] Congeners for which reference points have been derived are highlighted in bold
[b] Bramwell *et al*. (2014)
[c] Abdallah and Harrad (2014)

Food

36. No UK data on PBDE in infant formula or commercially-produced infant foods are available. Table 10 summarises lower and upper bound total infant dietary exposures to PBDEs, estimated using the 19 composite food groups of the 2012 TDS (see Table 7) together with consumption data from the DNSIYC (DH, 2013). The differences between lower and upper bounds are minimal. The detailed data are presented in Annex 1. In almost all cases, the food group contributing most to total exposure was dairy products.

Table 10: Estimated exposure of infants to PBDEs from food

Congener(s)	Lower to upper bound[a] dietary exposure to PBDEs (ng/kg bw/day)					
	Age 4-6 months (n=102 [b])		Age 6-9 months (n=602 [b])		Age 9-12 months (n=684 [b])	
	Mean	P97.5 [c]	Mean	P97.5 [c]	Mean	P97.5 [c]
BDE-47	1.00	3.39	1.04	3.29	1.00	2.48
BDE-99	1.10	3.73	1.09	3.50	1.01	2.66
BDE-153	0.24	0.86	0.25	0.83	0.23	0.61
BDE-209	1.34-1.49	4.09-4.16	2.20-2.93	5.25-7.70	3.16-4.47	8.26-10.9

[a] Treating occurrence data < LOD as 0 and as the LOD, respectively. If there is only one figure all data were > LOD
[b] Number of infants in the survey
[c] 97.5th percentile

Risk characterisations for PBDEs

37. The MOEs for exposure via dust, calculated as the ratios of the reference points for BDE-47, 99, 153 and 209 (Table 3) to estimated exposures for the corresponding congeners, are highly variable depending on whether the mean or maximum reported concentration is used in calculation of the exposure (Table 11). The MOEs for potential exposure from air based on the median reported occurrence of 24 pg/m^3 for the sum of BDEs 28, 47, 49, 66, 99, 100, 153, and 154 in domestic air are larger, being in the region of 350-525 when compared with the lowest reference point of 4.2 ng/kg bw/day (for BDE-99).

Table 11: MoEs for exposure to PBDEs from consumption of dust in homes

Congener(s)	Margin of Exposure	
	Congener present at mean measured concentration.	Congener present at maximum measured concentration
BDE-47	1,075	287
BDE-99	11	2.2
BDE-153	64	8
BDE-209	7.3	0.86

38. Table 12 shows MoEs for exclusively breastfed infants for each of the four congeners for which reference points are available. The MOEs are less than 1 for BDEs-99 and BDE-153 and for BDE-47 they are less than 5. The MOEs for BDE-209 all exceed 2000

Table 12. MoEs for exclusively breastfed infants

Congener(s)	MoEs for PBDEs for exclusive breastfeeding for age 0-4 and 4-6 months			
	Ages 0-4.0 months (800 mL milk)	Ages 0-4.0 months (1200 mL milk)	Ages >4-6.0 months (800 mL milk)	Ages >4-6.0 months (1200 mL milk)
BDE-47	2.5	1.7	3.3	2.2
BDE-99	0.2	0.2	0.3	0.2
BDE-153	0.5	0.3	0.6	0.4
BDE-209	3976	2654	5265	3507

39. Table 13 shows that the MoEs for infants' dietary exposure to PBDEs are lowest for BDE-99, followed by BDE-153. MOEs for BDE-47 exceed 50, and those for BDE-209 all exceed 1000.

Table 13. MoEs for upper bound dietary exposure of infants

Congener(s)	Age 4-6 months		Age 6-9 months		Age 9-12 months	
	Mean	P97.5 [a]	Mean	P97.5 [a]	Mean	P97.5 [a]
BDE-47	172	50	165	52	172	69
BDE-99	3.8	1.1	3.8	1.2	4.2	1.6
BDE-153	40	11	38	12	42	16
BDE-209	13181	4721	6703	2550	4393	1801

[a] 97.5th percentile

40. EFSA (2011) noted that usually an MOE of 100, covering uncertainties and variability with respect to kinetic and dynamic differences between animal species and humans (factor 4 for kinetics × 2.5 for dynamics = 10) and within the human population (factor 3.2 × 3.2 = 10), is considered sufficient to conclude that there is no health concern. This breakdown of the uncertainty factors is consistent with the COT Report on Variability and Uncertainty in Toxicology (COT, 2007)[3]. Since for PBDEs, the MOE approach was based on a body burden comparison between animals and humans, using the higher end of the reported range for elimination half-life in humans, EFSA (2011) considered that the potential inter and intra-species kinetic differences had been accounted for. Similarly, by focussing on the body burden associated with a BMDL10 for neurobehavioural effects in mice induced during a relevant period for brain development, and applying this body burden to the entire life span in humans, EFSA (2011) took the view that individual differences in susceptibility has been covered. Therefore, they sought reassurance that the calculated MOEs were sufficient to cover toxicodynamic differences between species in sensitivity to the effects observed. This would imply that an MOE larger than 2.5 might indicate that there was no health concern (EFSA, 2011).

41. The COT agreed that inter-species differences in toxicokinetics were accounted for by the body burden approach, and that the use of a relatively high elimination half-life for humans, and of data relating to a critical period of development, reduced uncertainties in the risk assessment. However, they considered that MOEs should be rather higher than 2.5 to provide assurance of safety.

42. Many of the MOEs summarised in this section give no cause for concern. However, others are less satisfactory, in particular, those for exposure to BDE-99, and -209 via consumption of dust, to BDE-47, -99 and -153 via breast milk and to BDE-99 and -153 from food. This does not necessarily imply that toxicity is occurring and the absence of clear evidence for adverse effects in epidemiological studies gives some reassurance. Nevertheless the risk assessment does not give the assurance of safety that would normally be expected.

Uncertainties

43. Data on the toxicity of specific PBDEs are available for only a small number of congeners, and cover only a limited range of toxic end-points. The toxicity studies used by EFSA to derive reference points for MOEs involved a single gavage administration to neonatal mice (or rats in the case of BDE-209). There is uncertainty about the relevance of these studies to risk assessment for longer term repeated exposures in humans (see paragraph 15), but because they found neurobehavioural effects at lower doses than in other studies, and covered a relevant neurodevelopmental period in experimental animals, they could not be discounted. The long half-lives of PBDEs mean that after a single administration, systemic exposure would continue over a prolonged period. Furthermore, when the body burden

[3] http://cot.food.gov.uk/cotreports/cotwgreports/cotwgvut

following single administration matches that in steady state from repeated exposures, most tissue concentrations are likely to be higher as there will have been limited redistribution to adipose tissue. This would tend to make derivation of reference points from the single dose studies conservative.

44. On the other hand, if adverse effects depended on the exposure of tissues at a critical time point which did not coincide exactly with that at which the maximum level was reached following single administration, it is possible that the single dose studies may have overestimated the body burden needed to produce toxicity.

45. Occurrence data for PBDEs are limited to a relatively small proportion of the 209 possible congeners. Whilst different research groups have measured and reported different subsets of congeners, they have generally focussed on those that were most likely to be present, based on their prevalence in technical mixtures of PBDEs that have been used as BFRs. However, the profile of congeners now present in food and the environment differs from that in the original mixtures. There is uncertainty about the full profile of exposure to PBDEs, and the effects of this combined exposure.

46. In addition, no data were available on levels of PBDEs in infant formula and commercially produced infant foods in the UK.

Conclusions

47. There are 209 PBDE congeners, most of which have not been tested for their toxicological properties. Toxicity tests conducted with formerly available commercial technical mixtures are of limited relevance to the profile of PBDEs in the environment and in food, due to differing persistence of individual congeners.

48. In animal studies, the main targets of PBDE toxicity are the liver, thyroid hormone homeostasis, and the reproductive and nervous systems. Epidemiological data on possible adverse effects in human populations are inconsistent, and cannot be used as a basis for quantitative risk assessment.

49. The available data are insufficient to establish health-based guidance values, such as Tolerable Daily Intakes, for PBDEs. Therefore the COT adopted a Margin of Exposure (MOE) approach to risk assessment, in which estimated exposures of infants to specific PBDEs or combinations of PBDEs were compared to reference points derived from toxicity studies for those compounds.

50. Suitable reference points for use in the MOE approach were available for only four congeners: BDE-47, BDE-99, BDE-153 and BDE-209. These reference points were derived from studies in which neonatal rodents were given the PBDE congeners via a single gavage administration, and behavioural changes were observed in adulthood. The Committee had some

reservations about the studies, but in the context of a limited database, concluded that they provided a reasonable basis for risk assessment.

51. Overall the analysis indicated possible concerns regarding the exposures of infants to BDE-99 and -209 via ingestion of dust, to BDE-47, -99 and -153 via breast milk, and BDE-99 and -153 from food.

52. There are uncertainties because of the limited toxicological database, and no data are available on potential exposures in the UK from infant formula and commercially produced infant foods.

53. Given that with the exception of some continuing applications for commercial decaBDE, use of PBDEs has been phased out, and that the main dietary sources of exposure to residual environmental PBDEs are breast milk and dairy products, options for risk management are limited. Thus generation of further toxicological data to refine the risk assessment may not be of great practical value. A higher priority is continued monitoring of PBDEs in breast milk and food to check that levels are declining as expected. It would also be useful to measure levels in infant formula and commercially produced infant foods.

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Abbreviations

COT	Committee on Toxicity of Chemicals in Food Consumer Products and the Environment
BDE	Brominated diphenyl ether
BMDL	Benchmark dose lower confidence limit
BFR	Brominated flame retardant
bw	Body weight
DH	Department of Health
DNSIYC	Dietary and Nutrition Survey of Infants and Young Children
EFSA	European Food Safety Authority
FERA	Food and Environment Research Agency
LOAEL	Lowest observed adverse effect level
LOD	Limit of detection
MoE	Margin of Exposure
NOAEL	No observed adverse effect level
PBDE	Polybrominated diphenyl ether
PND	Postnatal day
SACN	Scientific Advisory Committee on Nutrition
T3	Tri-iodothyronine
T4	Thyroxine
TSH	Thyroid stimulating hormone

Additional abbreviations can be found within Tables 1 and 2.

Annex 1

Dietary exposure to PBDEs for different foods and infant age groups

Table A1: Estimated mean dietary exposures at age 4-6 months

Food group	Number of Consumers	4.00 to 5.99 months - PBDE LB-UB Mean Exposure (ng/kg bw/d)				
		BDE-47	BDE-99	BDE-153	Sum exc BDE-209	BDE-209
Bread	11	0.0041	0.0044	0.0013	0.0188-0.0204	0-0.1531
Canned vegetables	4	0.0013	0.0009	0-0.0003	0.0026-0.0040	0.0387
Carcase meat	10	0.0149	0.0187	0.0059	0.0510-0.0516	0-0.1080
Cereals	59	0.0072	0.0087	0.0023	0.0237-0.0257	0-0.2157
Dairy products	76	1.2842	1.412	0.3241	3.6024-3.7191	1.1674
Eggs	2	0.0079	0.0099	0.0031	0.0277-0.0281	0.0553
Fats+oils	14	0.0045	0.0042	0.0010	0.0119-0.0126	0-0.0478
Fish	6	0.1549	0.0262	0.0082	0.3514	0.1965
Fresh fruit	36	0.0046	0.0034	0.0009	0.0120-0.0138	0.5346
Fruit products	29	0.0028	0.0022	0.0009	0.0063-0.0097	0.0666
Green vegetables	33	0.0034	0.0032	0.0004	0.0089-0.0092	0.1098
Meat products	1	0.0132	0.0143	0.0030	0.0387-0.0393	0-0.1042
Milk	17	0.0055	0.006	0.0015	0.0163-0.1689	0.3698
Nuts	0	0	0	0	0	0
Offal	0	0	0	0	0	0
Other vegetables	57	0.0128	0.0193	0.0034	0.0526-0.0528	0.125
Potatoes	36	0.0108	0.012	0.0016	0.0299-0.031	0.1154
Poultry	11	0.0084	0.0093	0.0022	0.0285-0.0301	0.348
Sugar and preserves	10	0.0272	0.0139	0.0016	0.059	0.4374
Total	102	1.0049	1.0981	0.2418	2.7172-2.8925	1.3433-1.5512

Table A2: Estimated mean dietary exposures at age 6-9 months

Food group	Number of Consumers	6.00 to 8.99 months - PBDE Mean Exposure (ng/kg bw/d)				
		BDE-47	BDE-99	BDE-153	Sum exc BDE-209	BDE-209
Bread	242	0.0066	0.0070	0.0020	0.0300-0.0325	0-0.2441
Canned vegetables	131	0.0011	0.0008	0-0.0003	0.0022-0.0035	0.0335
Carcase meat	217	0.0267	0.0335	0.0105	0.0915-0.0926	0-0.1938
Cereals	496	0.0194	0.0235	0.0064	0.0634-0.0695	0-0.5847
Dairy products	535	1.0104	1.1110	0.2550	2.8343-2.9261	0.9185
Eggs	88	0.0163	0.0207	0.0063	0.0575-0.0584	0.1147
Fats+oils	282	0.0069	0.0065	0.0015	0.0183-0.0193	0-0.0733
Fish	175	0.1607	0.0272	0.0085	0.3646	0.2039
Fresh fruit	385	0.0050	0.0037	0.0010	0.0131-0.0150	0.5823
Fruit products	235	0.0023	0.0018	0.0007	0.0052-0.0080	0.0549
Green vegetables	338	0.0029	0.0028	0.0003	0.0076-0.0079	0.0938
Meat products	93	0.0267	0.0289	0.0060	0.0783-0.0795	0-0.2108
Milk	270	0.0100	0.0109	0.0027	0.0286-0.3061	0.6702
Nuts	19	0.0013	0.0010	0.0003	0.0029-0.0043	0.0215
Offal	6	0.0030	0.0036	0.0012	0.0104-0.0112	0-0.0491
Other vegetables	453	0.0178	0.0269	0.0048	0.0732-0.0736	0.1742
Potatoes	389	0.0130	0.0144	0.0019	0.0358-0.0372	0.1382
Poultry	252	0.0059	0.0065	0.0015	0.0200-0.0211	0.2440
Sugar and preserves	172	0.0449	0.0231	0.0026	0.0976	0.7231
Total	602	1.0419	1.0986	0.2523	2.9148-3.1311	2.2046-2.9320

Table A3: Estimated mean dietary exposures at age 9-12 months

Food group	Number of Consumers	9.00 to 11.99 months - PBDE Mean Exposure (ng/kg bw/d)				
		BDE-47	BDE-99	BDE-153	Sum exc BDE-209	BDE-209
Bread	502	0.0101	0.0107	0.0031	0.0460-0.0498	0-0.3742
Canned vegetables	271	0.0015	0.0011	0-0.0003	0.0031-0.0048	0.0463
Carcase meat	372	0.0280	0.0352	0.0111	0.0962-0.0973	0-0.2036
Cereals	656	0.0269	0.0326	0.0088	0.0892-0.0965	0.7221-0.8112
Dairy products	661	0.7943	0.8734	0.2005	2.2283-2.3004	0.7221
Eggs	207	0.0184	0.0233	0.0071	0.0646-0.0656	0.1290
Fats+oils	456	0.0106	0.0100	0.0023	0.0281-0.0297	0-0.1127
Fish	305	0.1998	0.0339	0.0106	0.4534	0.2535
Fresh fruit	574	0.0062	0.0046	0.0012	0.0163-0.0187	0.7253
Fruit products	322	0.0026	0.0021	0.0009	0.0060-0.0092	0.0630
Green vegetables	436	0.0028	0.0027	0.0003	0.0074-0.0076	0.0908
Meat products	262	0.0261	0.0283	0.0059	0.0767-0.0779	0-0.2065
Milk	426	0.0188	0.0205	0.0051	0.0557-0.5756	1.2604
Nuts	29	0.0020	0.0016	0.0004	0.0047-0.0070	0.0349
Offal	9	0.0072	0.0087	0.0029	0.0250-0.0270	0-0.1182
Other vegetables	595	0.0175	0.0264	0.0047	0.0718-0.0721	0.1708
Potatoes	546	0.0161	0.0179	0.0023	0.0444-0.0462	0.1715
Poultry	400	0.0075	0.0082	0.0019	0.0241-0.0265	0.3069
Sugar and preserves	297	0.0552	0.0283	0.0032	0.1200	0.8890
Total	684	1.0001	1.0136	0.2331-0.2333	2.7958-3.2012	3.1632-4.4659

Table A4: Estimated high level (97.5th percentile) dietary exposures at age 4-6 months

Food group	Number of Consumers	4.00 to 5.99 months - PBDE 97.5 Percentile Exposure (ng/kg bw/d)				
		BDE-47	BDE-99	BDE-153	Sum exc BDE-209	BDE-209
Bread	11	0.0087	0.0093	0.0027	0.0400-0.0433	0-0.3252
Canned vegetables	4	0.0015	0.0011	0-0.0003	0.0031-0.0048	0.0465
Carcase meat	10	0.0412	0.0517	0.0162	0.1412-0.1428	0-0.2989
Cereals	59	0.0266	0.0322	0.0087	0.0881-0.0953	0-0.8009
Dairy products	76	3.4152	3.7552	0.8619	9.5802-9.8907	3.1047
Eggs	2	0.0174	0.0205	0.0068	0.0613-0.0622	0.1222
Fats+oils	14	0.0122	1.2000	0.0028	0.0338-0.0358	0-0.1358
Fish	6	0.2890	0.0490	0.0153	0.6558	0.3667
Fresh fruit	36	0.0166	0.0124	0.0033	0.0434-0.0498	1.9338
Fruit products	29	0.0113	0.0090	0.0037	0.0259-0.0400	0.2735
Green vegetables	33	0.0103	0.0099	0.0011	0.0272-0.0281	0.3355
Meat products	1	0.0132	0.0143	0.0030	0.0387-0.0393	0-0.1042
Milk	17	0.0248	0.0245	0.0062	0.0666-0.6881	1.5069
Nuts	0	0	0	0	0	0
Offal	0	0	0	0	0	0
Other vegetables	57	0.0399	0.0604	0.0107	0.01644-0.1652	0.3912
Potatoes	36	0.0261	0.0291	0.0038	0.0722-0.0750	0.2788
Poultry	11	0.0283	0.0310	0.0074	0.0954-0.1007	1.1657
Sugar and preserves	10	0.0591	0.0303	0.0035	0.1285	0.9520
Total	102	3.3923	3.7307	0.8562	9.5118-9.8199	4.0908-4.1620

Table A5: Estimated high level (97.5th percentile) dietary exposures at age 6-9 months

Food group	Number of Consumers	6.00 to 8.99 months - PBDE 97.5 Percentile Exposure (ug/kg bw/d)				
		BDE-47	BDE-99	BDE-153	Sum exc BDE-209	BDE-209
Bread	242	0.0235	0.0249	0.0072	0.1072-0.1161	0-0.8720
Canned vegetables	131	0.0045	0.0033	0-0.0010	0.0093-0.0144	0.1395
Carcase meat	217	0.1125	0.1414	0.0444	0.3858-0.3902	0-0.8168
Cereals	496	0.0781	0.0945	0.0256	0.2587-0.2798	0-2.3521
Dairy products	535	3.2813	3.6080	0.8281	9.2047-9.5030	2.9830
Eggs	88	0.0687	0.0869	0.0267	0.2414-0.2452	0.4817
Fats+oils	282	0.0281	0.0264	0.0062	0.0742-0.0784	0-0.2977
Fish	175	0.6028	0.1021	0.0318	1.3676	0.7647
Fresh fruit	385	0.0174	0.0130	0.0034	0.0455-0.0522	2.0237
Fruit products	235	0.0095	0.0076	0.0031	0.0218-0.0337	0.2306
Green vegetables	338	0.0116	0.0111	0.0012	0.0306-0.0316	0.3768
Meat products	93	0.0928	0.1006	0.0210	0.2725-0.2767	0.7338
Milk	270	0.0320	0.0349	0.0088	0.0947-0.9794	2.1448
Nuts	19	0.0040	0.0032	0.0009	0.0092-0.0138	0-0.0689
Offal	6	0.0038	0.0045	0.0015	0.0131-0.0141	0-0.0618
Other vegetables	453	0.0618	0.0933	0.0165	0.2541-0.2553	0.6045
Potatoes	389	0.0485	0.0539	0.0070	0.1340-0.1392	0.5173
Poultry	252	0.0243	0.0266	0.0063	0.0818-0.0863	0.9998
Sugar and preserves	172	0.1409	0.0723	0.0082	0.3063	2.2686
Total	602	3.2894	3.4974	0.8316	9.2499-9.5498	5.2466-7.6956

Table A6: Estimated high level (97.5th percentile) dietary exposures at age 9-12 months

Food group	Number of Consumers	9.00 to 11.99 months - PBDE 97.5 Percentile Exposure (ng/kg bw/d)				
		BDE-47	BDE-99	BDE-153	Sum exc BDE-209	BDE-209
Bread	502	0.0338	0.0359	0.0104	0.1546-0.1672	0-1.2565
Canned vegetables	271	0.0056	0.0040	0-0.0012	0.0115-0.0178	0.1729
Carcase meat	372	0.1263	0.1588	0.0498	0.4332-0.4338	0-0.9173
Cereals	656	0.0899	0.1087	0.0295	0.2977-0.3219	0-2.7064
Dairy products	661	2.3175	2.5482	0.5849	6.5009-6.7116	2.1068
Eggs	207	0.0707	0.0894	0.0274	0.2484-0.2523	0.4958
Fats+oils	456	0.0393	0.0370	0.0086	0.1037-0.1097	0-0.4164
Fish	305	0.7344	0.1244	0.0388	1.6662	0.9318
Fresh fruit	574	0.0208	0.0155	0.0041	0.0545-0.0625	2.4257
Fruit products	322	0.0125	0.0099	0.0041	0.0285-0.0440	0.3009
Green vegetables	436	0.0127	0.0122	0.0013	0.0336-0.0348	0.4148
Meat products	262	0.1029	0.1116	0.0233	0.3023-0.3070	0-0.8139
Milk	426	0.1065	0.1161	0.0292	0.3154-3.2615	7.1419
Nuts	29	0.0068	0.0054	0.0015	0.0156-0.0234	0.1165
Offal	9	0.0160	0.0193	0.0065	0.0554-0.0598	0-0.2619
Other vegetables	595	0.0512	0.0774	0.0137	0.2106-0.2116	0.5011
Potatoes	546	0.0532	0.0591	0.0076	0.1470-0.1527	0.5674
Poultry	400	0.0257	0.0282	0.0067	0.0867-0.0916	1.0602
Sugar and preserves	297	0.1996	0.1024	0.0117	0.4338	3.2131
Total	684	2.4809	2.6602	0.6119	6.9468-7.2501	8.2578-10.9306