TOX/2014/35

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

First draft statement on the potential risks from hexabromocyclododecanes (HBCDDs) in the infant diet

Introduction

1) The Committee on Toxicity (COT) has been asked to consider aspects related to the toxicity of chemicals in food, in support of a review by the Scientific Advisory Committee on Nutrition (SACN) of Government recommendations on complementary and young child feeding. Members concluded that brominated flame retardants (BFRs) should be considered as part of that body of work. 1,2,5,6,9,10-Hexabromocyclododecanes (HBCDDs, sometimes also abbreviated as HBCDs) are widely used as an additive flame retardant in fabrics and polystyrene products. A scoping paper (TOX2014/24) was presented to Members in September 2014.

2) Annex A contains a first draft COT statement summarising the available information, taking into account the previous discussion. Members' attention is drawn to the proposal in paragraph 39, that a Margin of Exposure (MOE) of about 30 would be considered acceptable. This differs from the EFSA view that since the MOE is based on a body burden, it is not necessary to allow for inter- or intra-species differences in toxicokinetics and therefore a minimum MOE of 8, comprising the toxicodynamic adjustment factors of 2.5 for inter-species differences and 3.2 for intra-species differences.

Questions on which the views of the Committee are sought

3) Members are invited to comment on the content of the first draft statement.

Secretariat
October 2014

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

First draft statement on the potential risks from hexabromocyclododecanes (HBCDDs) 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. SACN asked COT to review the risks of toxicity from chemicals in the infant diet.

2. This statement gives an overview of the potential risks from 1,2,5,6,9,10-hexabromocyclododecanes (HBCDDs, sometimes also abbreviated as HBCDs) in the infant diet. None of Government's current dietary recommendations for infants and young children relates to HBCDDs.

3. HBCDDs are members of the large chemical class of bromochemicals called brominated cycloalkanes. All HBCDDs share the same structural formula but differ from one another in their isomeric arrangement of bromine atoms around the ring, giving rise to 16 structural isomers that can be grouped into 8 diastereomeric pairs of enantiomers. HBCDDs have been widely used as additive flame retardants in fabrics and polystyrene products in the building and electronics industries and the preparation used for this purpose is referred to as "technical HBCDD".

4. Technical HBCDD consists mainly of 3 diastereomeric pairs of enantiomers, designated α, β and γ, as shown in Figure 1, with a composition of approximately 9-13% α, <0.5-12% β and 72-90% γ (EFSA, 2011).

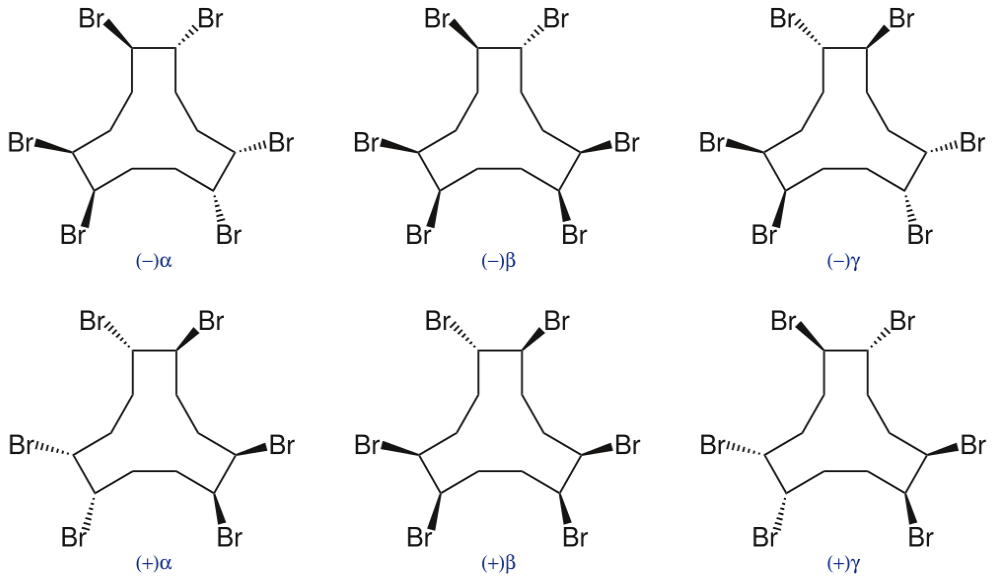

Figure 1: Structures of HBCDDs

5. The physicochemical properties of HBCDDs, especially their stability and lipophilicity, along with their large volume of annual production, ubiquitous use and the fact that they are not bound to the material they are intended to flame-proof, have all contributed to them becoming widely distributed in the environment and entering the food chain. HBCDDs have been added to Annex A of the Stockholm Convention on Persistent Organic Pollutants and their use for all but construction purposes will be banned in November 2014. (C.N.934.2013.TREATIES-XXVII.15 (Depositary Notification)) However since they are already widely distributed in the environment and consumer products, human exposure will persist despite the ban.

Previous evaluations of COT and EFSA

COT

6. COT, in its statement on brominated flame retardants in fish from the Skerne-Tees rivers system (2004)[1] observed that the uncertainties and deficiencies in the toxicological databases for HBCDDs prevented establishment of tolerable daily intakes (TDIs) and so adopted a Margin of Exposure (MOE) approach to its risk assessment. The COT noted that HBCD is hepatotoxic. It had not shown evidence of developmental toxicity in routine studies, but one study, available in abstract form only, indicated that it might produce neurodevelopmental effects although there was insufficient detail to use the data in risk assessment. The lowest observed adverse effect level (LOAEL) of 100 mg/kg, for increased liver weights and disturbances in thyroid hormones, was used as the point of departure to calculate MOEs..

EFSA

[1] http://cot.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2004/cotstatementbfrfish2004

7. EFSA (2011) noted that orally administered HBCDD is easily absorbed with some differences between the stereoisomers. α-HBCDD was reported to concentrate in adipose tissue. Debromination and hydroxylation were the major routes of metabolism. Stereoisomerisation of γ-HBCDD to the α- and β-isomers was observed in mice, but stereoisomerisation of α–HBCDD had not been reported. Elimination half-lives in mice varied from 3-4 days for γ-HBCDD to 17 days for γ-HBCDD. The elimination half-life for humans was estimated to be 64 days (range 23-219 days).

8. Data related to the toxicity of the different stereoisomers were only available from an *in vitro* cytotoxicity study (Zhang *et al.,* 2008). These data are of limited relevance to the *in vivo* chronic effects of HBCDDs.

9. The main targets for HBCDD toxicity in experimental animals were the liver, thyroid hormone homeostasis, and the immune, reproductive and nervous systems. The two available epidemiology studies did not show any association between the level of HBCDDs in blood and bone mineral density in elderly women, or between HBCDD in human milk and effects on neonatal thyroid stimulating hormone (TSH). Like COT, EFSA concluded that due to limitations and uncertainties in the database, the derivation of a TDI was not appropriate, and an MOE approach was adopted (EFSA 2011).

10. In a 28-day study of HBCDD in rats (van der Ven *et al.,* 2006), the most sensitive effects were on the thyroid hormone axis, and these were observed at much lower doses than effects on thyroid homeostastis in other studies. The effects were restricted to females, which is consistent with the high liver concentrations of HBCD in females compared to males. EFSA noted that extrapolation of effects on thyroid hormone homeostasis observed in rodents to humans is complicated by species differences in transporting systems and feedback regulation, but that thyroid hormone insufficiency in both humans and experimental animals may lead to neurodevelopmental effects. The COT considered the above study and noted that the female specificity of effects contrasted to those reported by Chengelis *et al* (2001) who reported similar effects in both sexes, and that the effects of HBCDD on the thyroid hormone axis are considered to be secondary to increased hepatic clearance of T4 via glucuronidation

11. EFSA (2011) identified neurodevelopmental effects as the critical end-point and derived a benchmark dose lower confidence limit for a benchmark response of 10 % ($BMDL_{10}$) from the study of Eriksson et al. (2006). Eriksson et al. administered a single oral gavage dose of HBCDD (α-, β- and γ-HBCDD with a relative content of 3 %, 8 % and 89 %, respectively) at either 0.9 or 13.5 mg/kg bw to NMRI mouse pups at the age of 10 days, the peak time of brain growth activity in mice. At 3 months of age the mice were tested for changes in locomotion and memory. The mice treated with HBCDD at the higher dose initially scored lower than controls and low dose animals in the locomotion tests but maintained their level of activity so that after 40 minutes they were significantly more active than the other two groups ($p < 0.01$). The higher dose group also took significantly longer than the other groups to complete a swim maze test ($p < 0.05$), suggesting that spatial learning was impaired. EFSA modelled the dose-response data from this study to derive a $BMDL_{10}$ of 0.93 mg/kg bw

12. The much slower rate of elimination in humans compared to rodents led EFSA to take body burden into account by estimating human intake associated with the body burden at the $BMDL_{10,}$ assuming 85% uptake of the single oral dose). The body burdens were then converted into a human intake of 3 µg/kg bw/day estimated to result, following attainment of steady state, in the body burden at the $BMDL_{10}$. EFSA concluded that, due to the limitations and uncertainties in the available data on HBCDDs, a MOE approach for the risk characterisation of HBCDDs should be taken using the estimated human intake at the $BMDL_{10}$, of 3 µg/kg bw/day, as the reference point.

13. EFSA also noted that effects on bone mineral density were observed with a $BMDL_{10}$ of 0.056 mg/kg bw (van der Ven *et al*., 2009) but that the ratio between the $BMDL_{10}$ and the benchmark dose upper confidence limit ($BMDU_{10)}$ indicated a large variation in the dose response data. EFSA therefore concluded that the $BMDL_{10}$ for effects on bone mineral density should not be used as the reference point for the MOE, and that further studies were needed to confirm the effect.

New toxicological and epidemiological data

14. The toxicokinetic data published since EFSA (2011) confirm that ≥ 85% of an oral dose of β-HBCDD is absorbed in mice, with a T_{max} of 3 hours (Sanders *et al*., 2013). An in vitro human colon model yielded similar results for all of the isomers (α 92%, β 80% and γ 72%) from ingested domestic dust (Abdallah *et al*., 2012). Similarly further studies have confirmed the widespread distributions and metabolism by debromination and hydroxylation (Malarvannan *et al*., 2013; Hakk *et al*., 2012; Sanders *et al*., 2013). Approximately 90% of an oral dose of β-HBCDD is excreted in urine and faeces within 24h, primarily as β-HBCDD-derived metabolites, with 9% excreted in faeces as γ-HBCDD (Sanders *et al*., 2013).

15. In Canadian studies, low but measurable concentrations of HBCDDs were reported in human sera (geometric mean 0.851 ng/g lipid, Rawn *et at.,* 2014a), placenta (median 48 ng/g lipid) and in fetal liver (median 29 ng/g lipid) (Rawn *et al*., 2014b).

16. Changes in neuronal migration in the dentate gyrus of rat pups (Saegusa *et al,* 2012) and rat fetal glial cell development (Fujimoto *et al* 2013), possibly resulting from effects of HBCDDs on the thyroid gland, were observed following dietary exposure of pregnant dams to >1000 – 10 000ppm HBCDDs. Rasinger *et al.* (2014) fed juvenile BALB/c mice a diet containing 1.3 g/kg HBCDD, resulting in a dose of 200 mg HBCDD/kg bw per day, for 28 days. HBCDD appeared to induce 90 genes in the brain with the overall effect being alterations in calcium and zinc homeostasis leading to excitotoxicity. Dietary administration of HBCDDs to mice at 199 mg/kg bw/day for 28 days resulted in increased liver weight and fat content (Maranghi *et al*., 2013). Sensitivity to this effect appeared to be increased when dietary fat content is raised, leading to significant increases in liver- and body-weight following weekly bolus gavage doses of 35 or 700 µg/kg/week (Yanagisawa *et al*., 2014). This study suggests that diet induced obese individuals may be more susceptible to HBCDD

than lean individuals, but is not suitable for deriving a reference point for the risk characterisation.

17. Recent in vitro studies have provided information on possible modes of action for HBCDDs, including oestrogenic activity (Dorosh et al., 2011) and production of reactive oxygen species (Al-Mousa & Michaelangeli, 2014). HBCDDs reduced splenocyte viability but enhanced the differentiation of bone marrow cells into dendritic cells (Koike *et a*l., 2013). HBCDDs inhibited cAMP production and the expression of several cAMP-dependent steroidogenesis genes in rat Leydig cells ,but increased basal steroidogenesis. (Fa *et al*., 2013). HBCDDs potentiated FSH-stimulated EGF receptor phosphorylation and activated ERK1/2 and PKB (AKT) but decreased FSH-induced luteinizing hormone receptor expression (Fa et al., 2014). HBCDDs suppressed thyroid hormone (TH) stimulated transcription and dendrite arborisation of new-born rat Purkinje cells (Ibhazehiebo et al., 2011a) and TH-induced neurite extension of cerebellar granule cells (Ibhazehiebo et al., 2011b), possibly by inhibiting the production of bone-derived neurotrophic factor, which promotes granule cell development. Both An *et al.* (2014) and Fa *et a*l. (2013) found that HBCDDs reduced mitochondrial membrane potential in cells in vitro .

18. Kim & Oh (2014) reported a statistically significant ($p < 0.05$) negative correlation between exposure to β-HBCDD and the level of triiodothyronine (T3) in the mothers of children with congenital hypothyroidism. The authors concluded that although the findings were suggestive of effects on human thyroid function, the small number of subjects tested (26 mother-infant pairs) meant that a larger study would be needed to confirm these results. COT noted limitations in the reporting and agreed that further studies would be needed to verify these data.

19. The HBCDD concentration in house dust has been correlated ($p = 0.004$, Spearman's $r = 0.46$, $n = 28$) with decreased sex hormone binding globulin and increased free androgen index in men (Johnson *et al*., 2013), but exposure was not estimated. Meijer *et al*. (2012) found HBCDDs at 0.7 ng/g fat in the serum of 34 women at the 35th week of pregnancy but no correlation with testes volume or penile length of their infants postnatally.

20. Overall, the COT concluded that the new data did not call into question the reference point identified by EFSA for HBCDD.

Sources of exposure to HBCDDs

21. HBCDDs have been found in food, breast milk, indoor dust and soil particles Temporal measurement trends seem to be variable (Law *et al*., 2014; Dietz *et al*., 2013).

Environmental occurrence of HBCDDs

Dust

22. Searches for HBCDDs in the air found a number of papers where there was some ambiguity as to whether the phase analysed was atmospheric gas or particles suspended in it and therefore the distinction between “air” and “dust” was unclear. Abdallah *et al* (2008a) found a mean concentration of 250 pg Σ HBCDD/m^3 (range 67 – 1300 pg/m^3) in the vapour and airborne particulate phase of indoor air from 33 homes in Birmingham UK and the authors suggested that inhalation constituted only a minor route of exposure. Both air and dust showed isomeric proportions had shifted from those in technical HBCDD (α:β:γ 3:8:89) with air being 22% α: 11% β: 65% γ and dust being 33% α: 11% β: 56% γ. Table 1 shows measurements of HBCDD in dust from houses and cars.

Table 1. HBCDD in dust from houses and cars in the UK

Sampling date where given	Environment	ΣHBCDD (ng/g)	Reference
March – December 2007	House (n = 21) Car (n=12)	228 – 140774 (range) 10021 (mean) 194 – 55822 (range) 18488 (mean)	Abdallah *et al*., 2009
	House (n = 45)	1 300 (median) 250 (mean)	Abdallah *et al.,* 2008a
	House (n = 31)	730 (median) 6000 (mean)	Abdallah *et al*., 2008b
2009	Car (n = 14)	9200 (mean)	Harrad and Abdallah., 2011

23. A study investigating spatial and temporal enantiomeric shifts in ΣHBCDD (the sum of the total amounts of each isomer) in household dust revealed a rapid photolytically-mediated shift from γ-HBCDD to α-HBCDD that was complete after one week of exposure, and a slower degradative loss of HBCDDs via elimination of HBr. When exposed to light the decay of ΣHBCDD was faster than in light-shielded samples ($t_{1/2}$ =12 weeks and 24 weeks respectively) Spatial variation within sampled rooms was substantial and in one room correlated negatively with distance from a television that was identified as the source of HBCDDs. The Σ HBCDD concentration within the TV was 540,000 ng/g, it was 24,000 ng/g at 1 metre, falling to 5,700 ng/g at 4 metres. Significant negative correlation was observed in one room between concentrations of ΣHBCDD and dust loading (g dust/m^2 floor), implying that "dilution" occurs at higher dust loadings. (Harrad *et al*., 2009).

Soil

24. Atmospheric dust in the internal and external environment may contain a variable amount of soil contaminated from industrial sources that may be ingested as wind-blown particles. Most papers found in a search for levels in soil relate to polluted industrial sites in China and other Far East countries. These are unlikely to have any relevance to the exposure of UK infants to HBCDDs in soils

Dietary occurrence of HBCDD

Breast milk

25. A study conducted in Birmingham, UK, found HBCDDs in 34 samples of human milk, collection period unspecified, (mean ΣHBCDDs = 5.95 ng/kg lipid weight, equivalent to 208 pg/kg whole weight assuming 3.5% fat content) where α-HBCDD comprised 62-95% of ΣHBCDDs while β- and γ-HBCDD were 2-18% and 3-33% respectively (see Table 2). Enantioselective enrichment of (-)-α-HBCDD (average enantiomer fraction = 0.29) was observed indicating potential enantioselectivity associated with HBCDD absorption, metabolism and/or excretion (Abdallah & Harrad, 2011). These values were in broad agreement with a comprehensive study from Ireland that covered HBCDDs and other halogenated flame retardants in breast milk and found the mean sum of HBCDD enantiomers to be 3.52 ng/kg lipid weight with α-HBCDD representing over 70% of the total (Pratt *et al*., 2013).

Table 2. HBCDD in breast milk sampled in the UK.

Reference	Isomer	HBCDD concentration in breast milk (pg/kg whole weight) [a]			
		Mean	Minimum	Median	Maximum
Abdallah & Harrad 2011	α	172	26.3	110	690
	β	11.2	2.8	10.5	26.3
	γ	25.6	4.6	19.6	80.2
	Σ	208	36.4	134	784

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

Infant formula and complementary foods

26. Measurements of HBCDDs in infant formula or commercially available infant foods in the UK are not available

27. Total HBCDD was not detected in 3 samples of infant formula (limit of detection not stated) It was detected in 38% of 13 samples described as “Ready-to-eat meal for infants and small children”. The lower and upper bound means for these 16 samples were 0.01 and 0.03 ng/g w/w respectively EFSA (2011)

Food

28. The most recent measurements of HBCDD in food sampled in the UK are in the composite food groups of the 2012 Total Diet Study (TDS) (Fernandes *et al*., 2012). The three major diastereomers were measured individually. The levels were mostly below the limits of detection, as shown in Table 3.

Table 3. Concentrations of individual HBCDD isomers in food expressed on a whole weight basis

Food group	Mean concentration of HBCDD isomer in food item (µg/kg)		
	α-HBCDD	β-HBCDD	γ-HBCDD
Bread	0.03	<0.02	0.03
Cereals	0.03	<0.02	<0.02
Carcase meat	0.25	<0.01	<0.01
Offal	0.03	<0.01	<0.01
Meat products	0.1	0.02	<0.02
Poultry	<0.01	<0.01	<0.01
Fish	0.08	<0.01	<0.01
Fats & oils	0.16	<0.03	<0.05
Eggs	<0.01	<0.01	<0.01
Sugar and Preserves	<0.02	<0.01	<0.02
Green vegetables	0.01	<0.01	<0.01
Potatoes	<0.01	<0.01	<0.01
Other vegetables	<0.01	<0.01	<0.01
Canned Vegetables	<0.01	<0.01	<0.01
Fresh Fruit	<0.01	<0.01	<0.01
Fruit Products	0.04	<0.02	<0.03
Milk	<0.01	<0.01	<0.01
Dairy Products	0.03	<0.02	<0.02
Nuts	<0.06	<0.10	0.06

29. EFSA (2011) noted that HBCDD had been reported in dietary supplements containing fish oil. The lower bound (LB) and upper bound (UB) of the mean of the sum of the three stereoisomers in ten fish oil samples were 1.21 and 1.86 ng/g fat respectively, with a high proportion of α-HBCDD, which was detected more frequently than the β or γ isomers.

Drinking Water

30. Measurements of HBCDDs in drinking water in the UK are not available.

Exposure to HBCDDs

31. The exposure assessments for air, soils and dust and the diet presented here are based on external exposure. Bodyweight data are from the UK Dietary and Nutrition Survey of Infants and Young Children (DNSIYC, DH, 2013), with average bodyweights of 7.8, 8.7 and 9.6 kg for infants aged >4 – 6.0, >6.0 – 9.0 and >9.0 – 12.0 months old respectively. Since DNSIYC did not include infants younger than 4 months, in this statement a value of 5.9 kg for infants ages 0 – 3 months from an earlier survey (DH, 1994) is assumed for infants aged 0 – 4 months.

Environmental Exposure to HBCDDs

Dust

32. Assuming the daily ingestion of 100 mg of dust per day (WHO, 2007), and the range of mean values for HBCDD in house dust in Table 1 (250-10,021 ng/g), infants aged 9-12 months, who are more likely to come into contact with floors and other surfaces than those in younger age groups could be exposed to 2.6 – 104 ng/kg bw/day ΣHBCDD.

Dietary exposure to HBCDDs

Breast milk

33. Table 4 shows estimated exposure of exclusively breast-fed infants based on the median and maximum values from the data of Abdallah and Harrad (2011) for average (800 mL) and high-level (1200 mL) daily consumption of breast milk.

Table 4. Estimated exposure of UK infants to HBCDD from exclusive breastfeeding.

Isomer	Exposure pg/kg bw/day							
	Average consumer 800 mL/day				High consumer 1200 mL/day			
	0 - 4 months		>4 – 6 months		0 - 4 months		>4 – 6 months	
	Median	Max	Median	Max	Median	Max	Median	Max
α	14.9	93.4	11.3	70.8	22.4	140	16.9	106
β	1.4	3.6	1.1	2.7	2.1	5.3	1.6	4.0
γ	2.7	10.9	2.0	8.2	4.0	16.3	3.0	12.3
Σ	18.2	106	13.7	80.4	27.3	159	20.6	121

Exposure values calculated from occurrence data from Abdallah and Harrad 2011.

Food

34. No UK data on HBCDD in infant formula and commercially-produced infant food are not available. Similarly, EFSA (2011) did not estimate infant's exposure to HBCDD from infant formula and "ready-to-eat meal for infants and small children" because the available data were too limited.

35. Table 5 summarises the UB mean and high level infant dietary exposure to HBCDD estimated using the 19 composite food groups of the 2012 TDS (see Table 3) together with consumption data from DNSIYC (DH, 2013). Since HBCDDs were not detected in most of the food groups, it is possible that the upper bound approach over-estimates actual exposure. The individual item data are in Annex 1.

Table 5 Estimated dietary exposure of infants to HBCDD in food

HBCDD isomer	**Upper bound dietary exposure to HBCDD isomers (ng/kg bw/day)**					
	4 – 6 months		6 – 9 months		9 – 12 months	
	Mean	P97.5	Mean	P97.5	Mean	P97.5
α	1.39	4.41	1.62	4.50	1.74	3.70
β	0.92	2.94	1.00	2.85	1.02	2.25
γ	0.93	2.94	1.01	2.85	1.05	2.29

Σ	3.24	9.29	3.63	10.2	3.81	8.24

Risk Characterisation for HBCDDs

36. MOEs for HBCDDs were calculated as the ratio of the reference point of 3 μg/kg bw/day, derived from a study on a technical mixture of HBCDDs to the estimated exposure values. For dust, the MOEs range from 29 to 1154.

37. Table 6 shows the MOEs for HBCDDs for exclusively breastfed infants, calculated for the maximum reported concentration of HBCDDs in breast milk.

Table 6. MOEs for HBCDD from exclusively breastfed UK infants.

Isomer	**MOE for HBCDDs in breast milk**			
	Average consumer 800 mL/day		High consumer 1200 mL/day	
	0 - 4 months	>4 – 6 months	0 - 4 months	>4 – 6 months
α	32,000	42,000	21,000	28,000
β	833,000	1111,000	566,000	750,000
γ	275,000	366,000	184,000	244,000
Σ	28,000	37,000	19,000	25,000

38. Table 7 show the MOEs for HBCDDs for infant exposure to HBCDDs via the diet and dust.

Table 7 MOEs for dietary exposure of infants to HBCDD

HBCDD isomer	**MOEs for upper bound dietary exposure to HBCDD isomers**					
	4 – 6 months		6 – 9 months		9 – 12 months	
	Mean	P97.5	Mean	P97.5	mean	P97.5
α	2158	671	1852	667	1724	809
β	3261	1020	3000	1053	2941	1333
γ	3226	1020	2970	1053	2857	1310
Σ	761	323	826	294	787	364

P97.5 = 97.5th percentile

39. For non-genotoxic compounds, an MOE of 100 is normally considered to provide adequate reassurance that there is no health concern regarding the toxic effect on which it is based. A margin of this magnitude covers uncertainties and variability in toxicokinetic and toxicodynamic differences between experimental animals and humans (factor 4 x 2.5 = 10), and within the human population (factor 3.2 x 3.2 = 10). The reference point for HBCDD took into account differences in toxicokinetics between humans and animals and therefore an MOE somewhat < 100 (say about 30) would be acceptable. An additional uncertainty is that the exposure and reference point relate to different profiles of HBCDD isomers.

40. From the above tables the MOE values for dietary sources of HBCDDs are all considerably in excess of 30.

Conclusions

[To be drafted after COT discussion]

Secretariat
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Upper bound mean dietary exposure of infants to HBCDD isomers in food

Food group	Number of Consumers	4.00 to 5.99 months - HBCD Mean Exposure (ng/kg bw/d)		
		Alpha	Beta	Gamma
Bread	11	0.0230	0.0153	0.0230
Canned vegetables	4	0.0193	0.0193	0.0193
Carcase meat	10	0.2076	0.0083	0.0083
Cereals	59	0.0341	0.0227	0.0227
Dairy products	76	1.6678	1.1118	1.1118
Eggs	2	0.0062	0.0062	0.0062
Fats+oils	14	0.0196	0.0037	0.0061
Fish	6	0.0925	0.0116	0.0116
Fresh fruit	36	0.0376	0.0376	0.0376
Fruit products	29	0.0882	0.0441	0.0661
Green vegetables	33	0.0219	0.0219	0.0219
Meat products	1	0.0744	0.0149	0.0149
Milk	17	0.0308	0.0308	0.0308
Nuts	0	0.0000	0.0000	0.0000
Offal	0	0.0000	0.0000	0.0000
Other vegetables	57	0.0249	0.0249	0.0249
Potatoes	36	0.0232	0.0232	0.0232
Poultry	11	0.0158	0.0158	0.0158
Sugar and preserves[3]	10	0.0045	0.0022	0.0045
Total	102	1.3868	0.9200	0.9274

Food group	Number of Consumers	6.00 to 8.99 months - HBCD Mean Exposure (ng/kg bw/d)		
		Alpha	Beta	Gamma
Bread	242	0.0366	0.0244	0.0366
Canned vegetables	131	0.0167	0.0167	0.0167
Carcase meat	217	0.3727	0.0149	0.0149
Cereals	496	0.0923	0.0615	0.0615
Dairy products	535	1.3122	0.8748	0.8748
Eggs	88	0.0128	0.0128	0.0128
Fats+oils	282	0.0300	0.0056	0.0094
Fish	175	0.0959	0.0120	0.0120
Fresh fruit	385	0.0410	0.0410	0.0410
Fruit products	235	0.0727	0.0363	0.0545
Green vegetables	338	0.0187	0.0187	0.0187
Meat products	93	0.1506	0.0301	0.0301
Milk	270	0.0559	0.0559	0.0559
Nuts	19	0.0129	0.0215	0.0129
Offal	6	0.0123	0.0041	0.0041
Other vegetables	453	0.0347	0.0347	0.0347
Potatoes	389	0.0277	0.0277	0.0277
Poultry	252	0.0111	0.0111	0.0111
Sugar and preserves[3]	172	0.0074	0.0037	0.0074
Total	602	1.6220	0.9965	1.0113

Food group	Number of Consumers	9.00 to 11.99 months - HBCD Mean Exposure (ng/kg bw/d)		
		Alpha	Beta	Gamma
Bread	502	0.0561	0.0374	0.0561
Canned vegetables	271	0.0230	0.0230	0.0230
Carcase meat	372	0.3916	0.0157	0.0157
Cereals	656	0.1281	0.0854	0.0854
Dairy products	661	1.0316	0.6877	0.6877
Eggs	207	0.0144	0.0144	0.0144
Fats+oils	456	0.0461	0.0086	0.0144
Fish	305	0.1193	0.0149	0.0149
Fresh fruit	574	0.0511	0.0511	0.0511
Fruit products	322	0.0835	0.0418	0.0626
Green vegetables	436	0.0181	0.0181	0.0181
Meat products	262	0.1475	0.0295	0.0295
Milk	426	0.1050	0.1050	0.1050
Nuts	29	0.0209	0.0349	0.0209
Offal	9	0.0295	0.0098	0.0098
Other vegetables	595	0.0340	0.0340	0.0340
Potatoes	546	0.0344	0.0344	0.0344
Poultry	400	0.0140	0.0140	0.0140
Sugar and preserves[3]	297	0.0091	0.0046	0.0091
Total	684	1.7447	1.0233	1.0515

Upper bound 97.5th percentile exposure of infants to HBCDD isomers in food

Food group	Number of Consumers	4.00 to 5.99 months - HBCD 97.5 Exposure (ng/kg bw/d)		
		Alpha	Beta	Gamma
Bread	11	0.0488	0.0325	0.0488
Canned vegetables	4	0.0231	0.0231	0.0231
Carcase meat	10	0.5748	0.0230	0.0230
Cereals	59	0.1265	0.0843	0.0843
Dairy products	76	4.4353	2.9569	2.9569
Eggs	2	0.0136	0.0136	0.0136
Fats+oils	14	0.0556	0.0104	0.0174
Fish	6	0.1726	0.0216	0.0216
Fresh fruit	36	0.1362	0.1362	0.1362
Fruit products	29	0.3623	0.1811	0.2717
Green vegetables	33	0.0668	0.0668	0.0668
Meat products	1	0.0744	0.0149	0.0149
Milk	17	0.1256	0.1256	0.1256
Nuts	0	0.0000	0.0000	0.0000
Offal	0	0.0000	0.0000	0.0000
Other vegetables	57	0.0779	0.0779	0.0779
Potatoes	36	0.0560	0.0560	0.0560
Poultry	11	0.0530	0.0530	0.0530
Sugar and preserves[3]	10	0.0098	0.0049	0.0098
Total	102	4.4067	2.9387	2.9387

Food group	Number of Consumers	6.00 to 8.99 months - HBCD 97.5 Exposure (ng/kg bw/d)		
		Alpha	Beta	Gamma
Bread	242	0.1308	0.0872	0.1308
Canned vegetables	131	0.0694	0.0694	0.0694
Carcase meat	217	1.5708	0.0628	0.0628
Cereals	496	0.3714	0.2476	0.2476
Dairy products	535	4.2614	2.8409	2.8409
Eggs	88	0.0536	0.0536	0.0536
Fats+oils	282	0.1218	0.0228	0.0381
Fish	175	0.3599	0.0450	0.0450
Fresh fruit	385	0.1425	0.1425	0.1425
Fruit products	235	0.3054	0.1527	0.2290
Green vegetables	338	0.0751	0.0751	0.0751
Meat products	93	0.5241	0.1048	0.1048
Milk	270	0.1787	0.1787	0.1787
Nuts	19	0.0413	0.0689	0.0413
Offal	6	0.0154	0.0051	0.0051
Other vegetables	453	0.1204	0.1204	0.1204
Potatoes	389	0.1039	0.1039	0.1039
Poultry	252	0.0454	0.0454	0.0454
Sugar and preserves[3]	172	0.0233	0.0116	0.0233
Total	602	4.5038	2.8475	2.8486

Food group	Number of Consumers	9.00 to 11.99 months - HBCD 97.5 Exposure (ng/kg bw/d)		
		Alpha	Beta	Gamma
Bread	502	0.1885	0.1257	0.1885
Canned vegetables	271	0.0860	0.0860	0.0860
Carcase meat	372	1.7640	0.0706	0.0706
Cereals	656	0.4273	0.2849	0.2849
Dairy products	661	3.0097	2.0065	2.0065
Eggs	207	0.0552	0.0552	0.0552
Fats+oils	456	0.1704	0.0319	0.0532
Fish	305	0.4385	0.0548	0.0548
Fresh fruit	574	0.1708	0.1708	0.1708
Fruit products	322	0.3985	0.1993	0.2989
Green vegetables	436	0.0826	0.0826	0.0826
Meat products	262	0.5814	0.1163	0.1163
Milk	426	0.5952	0.5952	0.5952
Nuts	29	0.0699	0.1165	0.0699
Offal	9	0.0655	0.0218	0.0218
Other vegetables	595	0.0998	0.0998	0.0998
Potatoes	546	0.1139	0.1139	0.1139
Poultry	400	0.0482	0.0482	0.0482
Sugar and preserves[3]	297	0.0330	0.0165	0.0330
Total	684	3.7047	2.2458	2.2903