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

First draft addendum to the 2015 COT Statement on potential risks from hexabromocyclododecanes (HBCDDs) in the infant diet.

Introduction

1. The Committee on Toxicity (COT) has been asked to consider the toxicity of chemicals in the infant diet and the diet of young children aged 1-5 years, in support of a review by the Scientific Advisory Committee on Nutrition (SACN) of Government recommendations on complementary and young child feeding. A discussion paper on hexabromocyclododecanes (HBCDDs) (TOX/2015/28) was presented to Members in July 2016. Members concluded that the availability of new HBCDD occurrence data required an update of the exposures in the statement on the potential risks from HBCDDs in the infant diet (COT, 2015) and an exposure assessment for the diet of young children aged 1-5 years. This would be in the form of an addendum to the 2015 statement.

2. Members are asked to comment on the draft statement addendum, attached as Annex A.

Secretariat
August 2016

This is a draft statement for discussion.
It does not reflect the views of the Committee and should not be cited.

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Background

1. The Scientific Advisory Committee on Nutrition (SACN) is undertaking a review of scientific evidence that will inform the Government's dietary recommendations for infants and young children. SACN is examining the nutritional basis of the advice. The Committee on Toxicity in Food, Consumer Products and the Environment (COT) was asked to review the risks of toxicity from chemicals in the diet of infants and young children. The reviews will identify new evidence that has emerged since the Government's recommendations were formulated, and will appraise that evidence to determine whether the advice should be revised.

2. In 2015 the COT issued a statement on the potential risks from the flame retardants hexabromocyclododecanes (HBCDDs) in the infant diet[1]. This addendum to the 2015 statement updates the exposures for infants aged 0-12 months as new data have become available and provides estimated HBCDD exposures for children in the UK aged one to five years. There are currently no Government dietary recommendations for infants and young children which relate to HBCDDs.

3. In its 2015 statement, the COT concluded that a Margin of Exposure approach should be taken for the risk assessment, in which estimated exposures to HBCDDs were compared to a reference point of 3 μg/kg bodyweight (bw)/day This was derived from a study in which neonatal mice were given a technical mixture of HBCDDs by a single gavage administration and behavioural changes were observed in adulthood (Eriksson *et al*., 2006), using a body burden approach taking into account the slower rate of elimination of HBCDDs in humans compared to rodents, in line with the approach taken in EFSA (2011).

4. EFSA (2011) had considered that the potential for kinetic differences between species had been taken into account. Furthermore, since the reference point was derived from neurobehavioural effects in mice induced during a relevant period for brain development, and the body burden applied to the entire life span in humans, EFSA (2011) took the view that individual

[1] http://cot.food.gov.uk/sites/default/files/HBCDDsstatementfinal.pdf

differences in susceptibility had been covered. EFSA thus concluded that the MOEs needed to cover inter-species differences in toxicodynamics (factor 2.5) and uncertainties in the elimination half-life in humans (factor 3.2). This implied that an MOE greater than 8 (2.5 x 3.2) would indicate that there was no concern for health. The COT agreed that inter-species differences in toxicokinetics were accounted for by the body burden approach, and that the use 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 8 to provide reasonable assurance of safety.

New toxicological data

5. Members considered new toxicological data that had become available since the 2015 COT statement. In particular, a paper of Maurice *et al.* (2016), indicated a possible lower toxicological reference point. The COT expressed a number of reservations about the study, possibly compromising the validity of the statistical analysis, and concluded that the new data required confirmation and were not sufficient to modify the reference point.

HBCDD exposures in infants aged 0-12 months and young children aged 1 to 5 years

New data on sources of HBCDD exposure

Breast milk

6. There were no new UK data for HBCDD levels in human milk. Occurrence data used previously for estimating exposure from human milk were used to estimate exposure from this route in this paper.

Infant formula and commercial infant foods.

7. Data on the concentrations of HBCDDs in infant formula were not available previously. The concentrations of α-, β- and γ-HBCDDs in different varieties of infant formula and commercial infant foods were investigated recently in an FSA survey (Rose *et al.,* 2015). HBCDDs were not detected in 30 infant formula samples. The limit of detection (LOD) of 0.01 µg/kg for each congener was used in an upper-bound (UB) approach[2] for estimating exposure.

8. α-HBCDD was reported at a level of 0.03 µg/kg in two out of 120 individual commercial infant food samples, resulting in a UB mean concentration of 0.01 µg/kg (equivalent to the LOD). The LOD value was similarly used for the other congeners in an UB approach to estimating exposure.

[2] Using the value of the LOD concentration for data that were < LOD

Other food

9. The most recent measurements of HBCDDs in other foods sampled in the UK were for the composite food groups of the 2012 Total Diet Study (TDS) (Fernandes *et al.,* 2012).

Air

10. There were no new UK data on HBCDD levels in indoor air. Occurrence data used previously (COT 2015) for estimating exposure from air were used to estimate exposure from this route in this paper.

Dust and soil

11. A concentration range of 95-27477 µg/kg was reported for the sum of α-, β- and γ-HBCDDs in household dust from the living room of 29 UK homes in the West Midlands area during 2015 by Kuang *et al.* (2016). These levels are considerably lower than those reported previously by Abdallah *et al.* (2008) in 45 different homes from the same region of the UK (range: 228 – 140774 µg/kg). The catchment area and methodology used by Kuang *et al.* (2016) were the same as those used by Abdallah *et al.* (2008), and in the absence of an explanation for the difference in levels, the two data sets have been combined in this paper[3]. The median and 97.5th percentile concentrations for the sum of α-, β- and γ-HBCDDs in the combined dataset were 725 and 140774 µg/kg, respectively. There were no UK data for HBCDD levels in soil.

Exposure

12. Consumption data from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) (DH, 2013), and from years 1-4 of the National Diet and Nutrition Survey Rolling Programme years 1-4 (NDNS) (Bates *et al*., 2014) have been used for the estimation of dietary exposures. Average body weight data used in the estimation of exposures are shown in Table 1 below.

[3] The COT is grateful to Professor Stuart Harrad, University of Birmingham UK, for provision of the individual data for this analysis.

Table 1: Body weights used in exposure assessments

Age bands (months)	Weighted bodyweight
0 - <4	5.9 kg[a]
4 - <6	7.8 kg[b]
6 - <9	8.7 kg[b]
9 - <12	9.6 kg[b]
12 - <15	10.6 kg[b]
15 - <18	11.2 kg[b]
18 - <24	12.0 kg[c]
24 - <60	16.1 kg[c]

[a] *DH, 1994.*
[b] *DH, 2013.*
[c] *Bates et al., 2014.*

Dietary exposure to HBCDDs

Breast milk

13. The estimated exposures of exclusively breast-fed infants, aged 0 to 6 months for HBCDDs (Table 2) are those in the 2015 COT statement. Data on breast milk consumption were used in estimating exposure from breast milk in the 6 - <18 months age groups (Table 2). There were too few records of breast milk consumption for children older than 18 months in NDNS to allow a reliable exposure assessment, and breast milk is expected to contribute minimally in this age group. Mean and high level estimates of exposure to α-, β- and γ-HBCDDs were 0.0020-0.11 ng/kg bw/day and 0.0041-0.16 ng/kg bw/day, respectively. High-level exposure to the sum of α-, β- and γ-HBCDDs from human milk was up to 0.16 ng/kg bw/day; α-HBCDD was the main contributor to total exposure.

Table 2: Estimated exposure to HBCDDs from breastmilk

Isomer (maximum concentrations in ng/kg whole weight)		HBCDD exposure from breast milk (ng/kg bw/day) by age group (months)					
		0 - <4[a]	4 - <6[a]	6 -<9[b]	9 - <12[b]	12 - <15[b]	15 - <18[b]
α (0.69)	Mean	0.094	0.071	0.046	0.026	0.020	0.017
	High level	0.14	0.11	0.11	0.080	0.052	0.036
β (0.26)	Mean	0.035	0.027	0.017	0.0099	0.0076	0.0066
	High level	0.053	0.040	0.041	0.030	0.020	0.013
γ (0.080)	Mean	0.011	0.0082	0.0053	0.0030	0.0023	0.0020
	High level	0.016	0.012	0.013	0.0093	0.0060	0.0041
Sum (0.78)[c]	Mean	0.11	0.080	0.052	0.030	0.023	0.020
	High level	0.16	0.12	0.12	0.090	0.059	0.040

[a] *Mean and high level HBCDD exposures were based on exclusive breastfeeding and consumption of 800 and 1200mL of milk for mean and high level, respectively (COT, 2015).*
[b] *Consumption data from DNSYIC: high level is 97.5th percentile.*
[c] *Sum of $\alpha + \beta + \gamma$*
All values are rounded to 2 significant figures

Infant Formula

14. Possible UB HBCDD exposure from exclusive feeding on infant formulae were calculated for infants up to 6 months of age using the LOD for ready-to-feed 'first milk' infant formula (0.01 µg/kg) (Table 3). Exposures were up to 6 ng/kg bw/day.

Table 3: Estimated UB exposures to HBCDDs of infants aged 0 to 6 months from exclusively feeding on infant formula.

HBCDD isomer	UB HBCDD exposure (ng/kg bw/day) from exclusive infant formula (first milk) by age group (months)			
	0 - <4		4 - <6	
	800 mL[a]	1200 mL[a]	800 mL[a]	1200 mL[a]
α	1.4	2.0	1.0	1.5
β	1.4	2.0	1.0	1.5
γ	1.4	2.0	1.0	1.5
Sum[b]	4.2	6.0	3.0	4.5

[a] *Mean and high level exposures were based on exclusive feeding on infant formula and consumption of 800 and 1,200mL, respectively (COT, 2015).*
[b] *Sum of α, β and γ*
All values are rounded to 2 significant figures.

15. Possible UB exposures of infants and children aged 4.0 to <18 months from infant formula were also estimated using DNSIYC consumption data (DH 2013) (Table 4). UB exposures to the sum of α-, β- and γ-HBCDDs based on consumption of all varieties of infant formulae, were up 4.7 ng/kg bw/day.

Table 4: Estimated UB exposure to HBCDDs from infant formula as part of the diet at age 4 to <18 months.

HBCDD isomer	UB exposure to HBCDDs (ng/kg bw/day) by age group (months)									
	4 - <6		6 - <9		9 - <12		12 - <15		15 - <18	
	Mean	High[a]	Mean	High[a]	Mean	High[a]	Mean	High[a]	Mean	High[a]
α	0.73	1.9	0.80	1.9	0.66	1.8	0.22	1.2	0.12	0.74
β	0.65	1.4	0.52	1.1	0.38	0.91	0.15	0.69	0.083	0.50
γ	0.65	1.4	0.52	1.1	0.38	0.91	0.15	0.69	0.083	0.50
Sum[b]	2.0	4.7	1.8	4.1	1.4	3.6	0.52	2.6	0.29	1.7

[a] *High level is 97.5th percentile*
[b] *Sum of α, β and γ*
All values are rounded to 2 significant figures.

Commercial infant foods

16. Table 5 summarises the exposure to HBCDDs from commercial infant foods estimated for infants and young children up to 18 months using DNSIYC consumption data (DH 2013). UB exposures to the sum of α-, β- and γ-HBCDDs based on consumption of all varieties of commercial infant foods, were up to 1.6 ng/kg bw/day.

Table 5: Estimated UB exposures to HBCDDs from commercial infant foods at age 4 to <18 months.

HBCDD isomer	UB dietary exposure to HBCDDs (ng/kg bw/day) by age group (months)									
	4 - <6		6 - <9		9 - <12		12 - <15		15 - <18	
	Mean	High[a]	Mean	High[a]	Mean	High[a]	Mean	High[a]	Mean	High[a]
α	0.099	0.46	0.14	0.53	0.12	0.51	0.067	0.36	0.04	0.22
β	0.099	0.46	0.14	0.53	0.12	0.51	0.067	0.36	0.04	0.22
γ	0.099	0.46	0.14	0.53	0.12	0.51	0.067	0.36	0.04	0.22
Sum[b]	0.30	1.4	0.42	1.6	0.36	1.5	0.20	1.1	0.12	0.66

[a] *High level is 97.5th percentile*
[b] *Sum of α, β and γ*
All values are rounded to 2 significant figures.

Other foods

17. UB mean and high-level estimates of infant dietary exposure to HBCDDs were previously calculated using measurements for the 19 composite food groups analysed in the 2012 TDS in combination with data on the consumption of those foods from DNSIYC. Table 6 summarises UB dietary exposures to α-, β- and γ-HBCDDs for 12 to 60 month old children. These were also estimated using concentrations reported previously for the 2012 TDS (Fernandes *et al.,* 2012) together with consumption data from the DNSIYC (DH 2013) and NDNS (Bates *et al.,* 2014).

18. Mean and high level UB exposures in other foods were higher than those estimated from infant formula or commercial infant foods. The highest UB high-level exposure to the sum of α-, β- and γ-HBCDDs was 7.5 in 12 to <60 month old children. This exposure is slightly lower than the corresponding value (10 ng/kg bw/day) estimated for the 4 to 12 month old infants in the 2015 COT statement. As with infant formula and commercial foods, HBCDDs were not detected in most of the food groups in TDS and thus, it is possible that the UB estimates are substantially higher than actual exposures.

Table 6: Estimated exposure to HBCDDs from food at age 12 to 60 months.

HBCDD Isomer	UB dietary exposure to HBCDDs (ng/kg bw/day) by age group (months)							
	12 - <15		15 - <18		18 - <24		24 - <60	
	Mean	High[a]	Mean	High[a]	Mean	High[a]	Mean	High[a]
α	1.5	3.2	1.7	3.1	1.9	3.9	1.5	2.7
β	0.90	1.8	0.93	1.6	1.0	1.7	0.81	1.3
γ	0.95	1.9	0.99	1.7	1.1	1.9	0.90	1.6
Sum[b]	3.4	6.9	3.6	6.4	4.0	7.5	3.2	5.6

[a] *High level is 97.5th percentile*
[b] *Sum of α, β and γ*
All values are rounded to 2 significant figures.

19. Although dietary supplements like cod liver oil are not recommended for children under 3 years of age, there were five recorded cases in the DNSIYC in which infants aged 12 to 18 months were given daily doses of 9 to 45 mg fish oil /kg bw, either by spoon or from capsules. Assuming the highest UB concentration of HBCDDs (2.99 ng/g) reported by EFSA for bottled fish oil, 45mg fish oil /kg bw/day would lead to an exposure of 0.13 ng HBCDDs /kg bw/day. The NDNS recorded no cases of children aged 18 to 24 months being given fish oil dietary supplements like cod liver oil. There were six recorded cases in the NDNS in which children aged 24 to 60 months were given daily doses of 11 to 117 mg fish oil /kg bw, either by spoon or as capsules. Assuming the highest UB concentration of HBCDDs reported by EFSA, 117mg fish oil /kg bw/day would lead to an exposure of 0.35 ng HBCDDs /kg bw/day. The small number of consumers in DNSIYC and NDNS

and the incompleteness of the recorded data on consumption mean that there are large uncertainties in performing a risk assessment for HBCDDs in fish oil, and it is not clear how relevant the data reported by EFSA are to fish oil on the UK market.

Environmental exposures to HBCDD

Air

20. The estimated exposures to the sum of HBCDDs from air that were reported for infants previously (COT, 2015) are updated in Table 7, together with estimated exposure for 12 to 60 month old children, on the basis of ventilation rates for infants and young children (US EPA, 2011) using the total mean reported occurrence value of 250 pg/m^3 (range 67 – 1300 pg/m^3) in indoor air from 45 homes in Birmingham UK. The exposure to the sum of α-, β- and γ-HBCDDs via air ranged from 0.13 to 0.19 ng/k bw/day.

Table 7: Estimated exposure to the sum of α–, β– and γ–HBCDDs from air

Sum HBCDD mean concentration	**Exposure to HBCDDs in air (ng/kg bw/day) by age group (months)**							
	0 - <4 (3.6)[a]	**4 - <6** (4.1)[a]	**6 to <9** (5.4)[a]	**9 to <12** (5.4)[a]	**12 - <15** (8.0)[a]	**15 - <18** (8.0)[a]	**18 - <24** (8.0)[a]	**24 - <60** (10.1)[a]
250pg/m^3	0.15	0. 13	0. 16	0.14	0.19	0.18	0.17	0.16

[a] *Ventilation rate in m^3/day.*
All values are rounded to 2 significant figures

Dust and soil

21. Exposure to HBCDDs through ingestion of dust and soil were estimated assuming ingestion of 60mg per day at age 6 to 12 months and 100 mg/day at age 12-60 months (US EPA, 2011), based on the median and maximum concentrations of dust reported in paragraph 11 (Table 8). Since there were no data for soil, it has been assumed that the levels could be comparable to those in dust, however this is a conservative assumption because the presence of HBCDDs in dust is likely to be due to their use as flame retardants. Estimated exposures were up to 1300 ng/kg bw/day for the sum of α-, β- and γ-HBCDDs when using the maximum concentration of 140774 µg/kg.

Table 8: Possible HBCDD exposure from dust and soil in infants and young children aged 6 to 60 months

Sum α+β+γ HBCDD (µg/kg)	Exposure to HBCDDs in dust and soil (ng/kg bw/day) by age group (months)					
	6 - <9	9 - <12	12 - <15	15 - <18	18 - <24	24 - <60
Median (725)	5.0	4.5	6.8	6.5	6.0	4.5
Maximum (140774)	970	880	1300	1200	1200	870

All values are rounded to 2 significant figures.

Risk characterisation

22. MOEs were calculated as the ratio of the reference point of 3 µg/kg bw/day to the estimated exposures to the sum of HBCDDs from different sources (Table 9). All MOEs are 400 or greater, with the exception of those calculated for exposure from dust and soil based on the highest reported concentration of HBCDD in household dust. Exposure from this source is likely to be overestimated due to the assumption that the concentration of HBCDD in soil could be similar to that in dust. Furthermore, the maximum reported concentration was very much higher than the median, and such exposure would therefore be expected to affect very few children. MOEs for fish oil were 9000 or more.

Conclusions

23. Exposure to HBCDDs arises from its use as a flame retardant, and subsequent release to the environment. The major sources of exposure for infants and young children are food and household dust.

24. The risks associated with exposure of infants and young children to HBCDDs are assessed in this addendum in relation to a reference value of 3 µg/kg bw/day, used previously by the COT. The new toxicological data were not sufficient to modify this reference point.

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25. The margins of exposure to HBCDDs by dietary intake of breast milk, infant formula, commercial infant food, fish oil and food in general are unlikely to be cause for concern for any age group

26. Data for household dust in the UK were available from two publications, with very different ranges reported. Because there was no clear explanation for the differences, the COT decided to combine the datasets in order to calculate an overall median value for use in the risk assessment. The

overall maximum level was also used since it is possible that this value is relevant for a small number of homes.

27. While the level of HBCDD in the diet of infants and young children is not a cause for concern, the possibility of high levels in household dust continues to be so. Levels should be monitored to determine whether they fall now that production and usage of HBCDDs has largely ceased.

Table 9. MOEs for exposure to the sum of HBCDDs from different sources

Source		MOEs by age group (months)							
		0 -<4	**4-<6**	**6-<9**	**9-<12**	**12-<15**	**15-<18**	**18-<24**	**24-<60**
Breast milk[a]	Mean	30000	40000	60000	100000	100000	200000	NR[b]	NR
	High level	20000	30000	30000	30000	50000	80000	NR	NR
Infant formula[a]	Mean	700	1000	2000	2000	6000	10000	NR	NR
	High level	500	700	700	800	1000	2000	NR	NR
Commercial infant food	Mean	NR	10000	7000	8000	20000	30000	NR	NR
	High level	NR	2000	2000	2000	3000	5000	NR	NR
Other foods	Mean	NR	NR	NR	NR	900	800	800	900
	High level	NR	NR	NR	NR	400	500	400	500
Air	Mean	20000	20000	20000	20000	20000	20000	20000	20000
Dust/soil	Mean	NR	NR	600	700	400	500	500	700
	High level	NR	NR	3	3	2	3	3	3

[a] *Based on exclusive feeding up to 6 months*
[b] *NR – not relevant*
All MOEs are rounded to 1 significant figure.

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