TOX/2017/38

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

Proposal for a breastmilk analysis study using pre-existing samples held by Imperial College London.

Introduction

1. The COT has recently been reviewing scientific evidence relating to the diets of infants and young children as part of a wider government review of infant feeding. This is being led by the Scientific Advisory Committee on Nutrition (SACN) who is examining the nutritional basis of dietary advice to this age group. The COT was asked to review the risks of toxicity from chemicals in the diet of infants. The reviews have identified 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. The recommendations cover diet from birth to age five years.

2. The SACN have examined the nutritional aspects and the 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. The recommendations cover diet from birth to age five years.

3. At the beginning of this process, the COT identified a number of chemicals which they considered should be looked at in detail[1]. For these chemicals, literature searching has been carried out in order to identify relevant toxicity and exposure data which can be used to determine the risk posed by these chemicals in the diets of infants and young children. During this process, it has become apparent that data on chemicals in UK breastmilk are sparse for many of the chemicals of interest.

4. The COT secretariat has been made aware of an ongoing project, co-ordinated by Imperial College London, where breastmilk samples are available for analysis. The FSA has been offered the opportunity to become involved in this work and part-fund this project. In return the FSA would receive access to the large amount of data already collected, and be able to help direct the future analyses of these samples.

[1] Statement available at: https://cot.food.gov.uk/sites/default/files/cot/cotstatementoverarch201203.pdf

The BEED project

5. The Breastmilk, Environment, Early-life and Development (BEED) Study was originally commissioned to identify potential chemicals of concern in breast milk samples from UK women. These samples have been used to study individual level pollutant exposures around Municipal Waste Incinerators (MWI's) in the UK. Sampled across 3 sites in the UK, 1272 breast milk samples have been collected from 366 women taken from an area up to 20km away from MWI's. A large amount of socio-economic (SES), occupational and dietary data have been collected from these women and some chemical analyses have already been carried out, with funding already available to cover analysis of 42 metals from all samples. Participants may be considered representative of UK mothers given they come from both the north and south of Britain, and a range of SES and ethnic groups.

6. One publication looking at PBDE's and HBCDD's in breastmilk and food samples has been generated from this project from the first set of samples and this has been included as appendix B to this paper.

7. Further chemical analyses on a small number of samples are either planned or in progress (PCDD's, PDCF's, dioxin-like PCB's), as well as breast milk microbiota analysis. In addition, metabolomic profiling of ~3 breastmilk samples per mother provided over the first 3 months post-birth from 200 women (600 samples) has been funded to identify dynamic intra-individual versus inter-individual variations in BM metabolomic profiles. In the future, statistical analysis of the relationships between the environmental exposome (pollutant concentrations), BM metabolomic profiles, including longitudinal changes, and BM microbiota, are all planned.

Questions for the Committee:

8. The Committee have so far considered a number of chemicals and their prevalence in the infant diet. The conclusions that are available so far can be found in appendix A of this paper.

9. In 2004, the SUREmilk study was published. This was a pilot study to investigate how best to recruit, collect, store and manage an archive of breastmilk samples. This was not, therefore a rigorous survey of UK breastmilk samples, but has provided UK data for some of the chemicals of interest in Appendix A.

10. The COT published their opinion on the SUREmilk study in 2004[2], in which they raised concerns over the methodology of this study (given that it was a pilot study) and how representative the results were of UK breastmilk samples. This conclusion applies particularly to dioxins, and dioxin-like PCB's and the COT recommended continued monitoring of these contaminants in breastmilk.

[2] Available at: https://cot.food.gov.uk/sites/default/files/cot/cotsuremilk.pdf

11. With these points in mind the Committee are asked the following questions:

- Do members think that given the scarcity of UK breastmilk data and limitations of the existing UK data, there would be sufficient value in FSA becoming involved with this project?
- If so, do members wish to suggest chemicals from those considered so far, which should be prioritised for sampling?
- Members are invited to comment on the potential limitations of this study and whether these could be mitigated.

Secretariat
August 2017

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

Proposal for a breastmilk analysis study using pre-existing samples held by Imperial College London.

COT conclusions on the chemicals considered so far

12. Below are copied the breastmilk data, exposures and conclusions relating to breastmilk from the chemicals considered by the COT so far.

Acrylamide

13. Full statement available at:
https://cot.food.gov.uk/sites/default/files/finalacrylamidestatement.pdf

14. A literature search has not identified any data on acrylamide concentrations in breast milk in the UK. Of the available data on European women, those with the most relevant maternal exposure levels (equivalent to about 0.5 µg/kg bw/day), were from a study of 14 individuals and 4 pooled breastmilk samples from non-smoking Swedish mothers. The concentration of acrylamide was below the limit of quantitation (LOQ) of 0.5 µg/kg, except in one individual sample (0.51 µg/kg) (Fohgelberg *et al*., 2005). Therefore the COT concluded that the LOQ of 0.5 µg/kg could be used in an upper bound (UB) approach[3] to the exposure assessment.

15. The LOQ (0.5 µg/kg) from the study of Fohgelberg *et al*. (2005) has been used in an UB approach to estimate possible exposure from breast milk, based on the assumption of exclusive breastfeeding for 6 months and using data on breast milk consumption for infants aged 6 to 18 months. There were too few records of breast milk consumption for children older than 18 months in the NDNS to allow a reliable exposure assessment, and breast milk is expected to contribute minimally in this age group. This approach indicates that exposure from breast milk is likely to be less than 0.10 µg/kg bw/day (Table 1).

Table 1. Estimated UB acrylamide exposure from breastmilk based on LOQ of 0.5 µg/kg.

[3] The upper bound (UB) approach uses the value of the LOQ or LOD concentration for data that were < LOQ/LOD. The lower bound (LB) approach uses the value zero for data that were < LOQ/LOD

Consumers	Exposure (µg/kg bw/day) by age group (months)					
	0 to <4[a]	4 to <6[a]	6 to <9[b]	9 to <12[b]	12 to <15[b]	15 to <18[b]
Mean	0.068	0.051	0.033	0.019	0.015	0.013
High level	0.10	0.077	0.080	0.058	0.038	0.026

[a] *Mean and high level exposures were based on exclusive breastfeeding and consumption of 800 and 1200mL of milk for mean and high level, respectively.*
[b] *Consumption data from DNSYIC: high level is 97.5th percentile.*

16. *Conclusion:* Breastmilk is a minor source of acrylamide in the diet and levels would not be expected to be of concern.

Aluminium:

17. Full statements available at:
https://cot.food.gov.uk/sites/default/files/cot/statealuminium.pdf
https://cot.food.gov.uk/sites/default/files/finalaluminiumaddendum_0.pdf

18. Aluminium in breastmilk has been quantified in a number of studies from different countries.

19. The data from the UK come from a small study published in 1991, but their relevance is supported by more recent studies elsewhere. The women participating in these studies were from the general population of the country concerned.

Table 2: Concentrations of aluminium measured in human breast milk

Country	Number of samples	Mean (± SD) aluminium levels (ug/L)	Median aluminium levels (ug/L)	Range of aluminium levels (ug/L)
Australia[1]		30		
UK[2]	8	27	15	3-79
Spain[3]	45	23.9 (± 9.6)	25.0	7-42
Austria[4]	27		67	<10-380
Morocco[6]	396	17.3 (± 13.9)		1.3-62.2

[1]Weintraub *et al*., (1986), [2]Baxter *et al*., (1991), [3]Fernandez-Lorenzo *et al*., (1999), [4]Krachler *et al.*, (2000), [6]Zaida *et al.,* (2007)

20. *Conclusion:* From the limited data available on levels of aluminium in breastmilk of UK mothers, it appears that exposure to aluminium in inclusively breastfed infants is less than 10% of the PTWI.

Arsenic:

21. Full statement available at:

https://cot.food.gov.uk/sites/default/files/finalstatementonarsenic_0.pdf

22. There are limited data available on the concentration of arsenic in breast milk. Those data that are available often relate to women with high exposures to arsenic (e.g. due to the region they live in, or reliance on highly contaminated water) (EFSA, 2014), and rarely determine the species of arsenic present in samples.

23. A literature search did not identify any appropriate data for arsenic concentrations in breast milk in the UK. Therefore, a value of 0.33 µg/L, derived from a study by Björklund *et al*. (2012), has been used to estimate exposures to arsenic via breast milk in infants aged 0 to 18 months. This value was the median total arsenic concentration of 60 samples of breast milk collected in 2002-2009 from Swedish first-time mothers at 2-3 weeks postpartum. The limit of detection (LOD) was 0.007 µg/L, and the minimum and maximum reported concentrations were 0.041 and 4.6 µg/L respectively (Björklund *et al*., 2012).

24. Of the studies where arsenic speciation in breast milk has been determined, there is disparity between the proportion of arsenic reported to be present in the inorganic form, with some studies reporting that no inorganic arsenic was detected (Björklund *et al*., 2012), and others reporting that almost all of the arsenic detected was inorganic (Fängström *et al*., 2008). Due to the inconsistent data on the proportion of inorganic arsenic likely to be present in breast milk, the exposure assessments have been performed on the conservative assumption that 100% of the arsenic is inorganic.

25. No consumption data were available for exclusive breastfeeding in infants aged 0 to 6 months. Therefore, the default consumption values used by the COT in other evaluations of the infant diet of 800 and 1200 mL for average and high level consumption (EFSA, 2009) have been used to estimate exposures to inorganic arsenic from breast milk. These estimates were based on a median total arsenic concentration of 0.33 µg/L and the assumption that 100% of this is inorganic arsenic (paragraphs 18 and 19). The ranges of exposure to inorganic arsenic in exclusively breastfed 0 to 6 month olds were 0.034 to 0.045 and 0.051 to 0.067 µg/kg bw/day in average and high level consumers, respectively (Table 3).

Table 3. Estimated inorganic arsenic exposure from exclusive breastfeeding in 0 to 6 month old infants, with breast milk containing total arsenic at 0.33 µg/L.

Arsenic concentration (µg/L)	**Exposure (µg/kg bw/day)**			
	Average consumer (800 mL/day)		**High consumer (1200 mL/day)**	
	0 to <4 months	**4 to <6 months**	**0 to <4 months**	**4 to <6 months**
0.33	0.045	0.034	0.067	0.051

Values rounded to 2 significant figures (SF)

26. Data on breast milk consumption for infants aged 4 to 18 months were available from the DNSIYC and the NDNS, and have been used to estimate exposures at these ages (Table 4), based on a median inorganic arsenic concentration of 0.33 µg/L. There were too few records of breast milk consumption for children older than 18 months in the NDNS to allow a reliable exposure assessment, and breast milk is expected to contribute minimally in this age group.

27. Mean exposures to inorganic arsenic for 4 to 18 month olds were 0.0080 to 0.030 µg/kg bw/day, and 97.5th percentile exposures were 0.017 to 0.053 µg/kg bw/day (Table 4).

Table 4. Estimated inorganic arsenic exposure in 4 to 18 month old infants from breast milk, containing total arsenic at 0.33 µg/L.

Exposure (µg/kg bw/day)	**Age group (months)**				
	4 to <6	**6 to <9**	**9 to <12**	**12 to <15**	**15 to <18**
Mean	0.030	0.022	0.013	0.010	0.0080
97.5th percentile	0.051	0.053	0.038	0.025	0.017

Values rounded to 2 SF

28. *Conclusions:* Based on dietary exposures alone, the MOEs for 0 to 4 month olds that are either exclusively breastfed or exclusively fed ready-to-feed infant formula range from 40 to 100 at average and high level exposure. There are uncertainties in the assessment of risks to infants and young children from exposure to inorganic arsenic because, for some sources of exposure (e.g. breast milk and soil), it has been necessary to assume that all of the arsenic present in that source is inorganic. This was the case for sources where inorganic arsenic has not been measured, and consistent information about the proportion of inorganic arsenic likely to be present in that source of exposure has not necessarily been available. Such assumptions could potentially result in over-estimation of the exposures to inorganic arsenic.

29. Overall, the inorganic arsenic exposures for exclusively breastfed or formula-fed UK infants aged 0 to 4 months generated MOEs that were generally greater than 10 and would therefore be considered of low concern.

Endosulfan isomers, pentachlorobenzene and chlordecone:

30. Full statements available at:
https://cot.food.gov.uk/sites/default/files/cotstaonpops.pdf

31. No data available on endosulfans in UK breastmilk. A UK monitoring study on pesticides in a wide range of foods determined that alpha- and beta-

endosulfans were not detected in any of the samples at levels above the reporting limit of 10 micrograms/kg. Data from Finland and Denmark suggest that median levels of alpha-endosulfan in breastmilk samples (65 from each country) were approximately 0.27 and 0.21 microgram/L from Finland and Denmark respectively. Beta-endosulfan was not detected, but LOD was not reported). In Spain, 23 breast milk samples were analysed and alpha-endosulfan was found at median levels of 0.87 (max 1.00) and beta-endosulfan was found at 7.29 (max 26.89) microgram/L breastmilk. Infant exposure is below the ADI of 6 microg/kg bw/day set by JMPR.

32. No data are available for pentachlorobenzene in UK breast milk samples. Data from Finland and Denmark suggest that breastmilk contained approximately 0.01 microgram/L pentachlorobenzene. Exposure is likely to be well below the TDI set by Health Canada of 0.5 microgram/kg bw/day.

33. No data are available for chlordecone in UK breastmilk samples and no monitoring has been carried out in other foods. The COT concluded that UK exposures are likely to be extremely low and decreasing and adverse effects attributable to chlordecone are unlikely.

HBCDD's:

34. Full statements available at:
https://cot.food.gov.uk/sites/default/files/HBCDDsstatementfinal.pdf
https://cot.food.gov.uk/sites/default/files/finaladdendumonhbcdds.pdf

35. A UK study based in Birmingham found HBCDD's in 34 samples of breastmilk. Mean total concentration of alpha-, beta- and gamma-HBCDD's was 208 pg/kg whole weight (5.95 ng/kg lipid weight assuming 3.5% fat). These were in broad agreement with a study in Ireland that found a mean summed concentration of HBCDD enantiomers of 3.52 ng/kg lipid weight.

Table 5 HBCDD in 34 samples of breastmilk from the UK

Reference	Isomer	HBCDD concentrations in breastmilk (ng/kg whole weight[a])			
		Arithmetic mean	Minimum	Median	Maximum
Abdallah & Harrad (2011)	Alpha-	0.17	0.026	0.11	0.69
	Beta-	0.011	0.0028	0.011	0.26
	Gamma-	0.026	0.0046	0.020	0.080
	Sum	0.21	0.036	0.13	0.78

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

36. *Conclusion:* Intakes from food unlikely to be a concern, but exposure from dust may be. No recommendation for levels in breastmilk.

Alpha-, beta- and gamma hexachlorocyclohexanes

37. Full statement available at:
https://cot.food.gov.uk/sites/default/files/cot/cotstatmhchs.pdf

γ-HCH

38. Table 6 shows the concentrations of γ-HCH in breast milk from studies in UK populations published since 1982. Concentrations in breast milk sampled since the use of lindane was phased out in 2000 are clearly lower than in earlier samples.

Table 6. Concentrations of γ-HCH in breast milk sampled in the UK from reports published since 1982.

N	μg/kg milk fat					Mean μg/kg whole milk	% samples with detectable residues	Years of sample collection	Reference
	A. mean	G. mean	Med.	Min.	Max.				
102	30	N.R.	10	<10	270	1	55	1979-1980	Collins et al., 1982
-	-	-	-	-	-	<1	0	1984	MAFF, 1998
193	<20	N.R.	<20	<20	160	<1	18	1989-1991	Dwarka et al., 1995
156	35[a]	N.R.	25	<8	200	<1	2	1997-1998	Harris et al., 1999
48	<10	<10	<10	<10	<10	<0.35[b]	0	2001-2002	Woolridge et al., 2004
54	N.R.	0.8	0.6	N.D.	7.7	0.028[b]	91[c]	2001-2003	Kalantzi et al., 2004b

A. mean. Arithmetic mean, G. mean. Geometric mean, Med. Median, Min. Minimum, Max. Maximum, N.R. Not reported.
[a] Confirmed as arithmetic mean by C Harris (personal communication)
[b] Estimated assuming 3.5% fat in whole milk
[c] Limits of detection appear to have been much lower in this study than in earlier investigations (<0.001 mg/kg fat *cf.* 0.008-0.02 mg/kg fat)

39. As part of the 3rd WHO human milk field study, γ-HCH was analysed in 16 samples of pooled human milk from 10 European countries (Bulgaria, Czech Republic, Germany, Ireland, Italy, Luxembourg, Norway, Russia, Spain and Ukraine) and 11 pools from 6 non-European countries (Brazil, Egypt, Fiji, Hong Kong, Philippines and USA) (Malisch et al., 2004). In the samples from European countries the concentrations of γ-HCH ranged from < 1 to 13 μg/kg fat.

40. Levels of HCH isomers in breast milk in studies on populations in other European countries published since 1995 are summarised in Table 7. As in the UK, levels have decreased since use of lindane was phased out.

Table 7. Concentrations of γ-HCH in breast milk sampled in other European countries from reports published since 1995.

Country (City/Region)	µg/kg milk fat		Years of sample collection	Reference
Sweden	Mean 75 in 1978		1975-1990	Vaz, 1995
	Mean 27 in 1990			
Spain (Huelva / Andalucia)	Mean 80; maximum 200 (after 1 month breastfeeding)		1989-1990	Martinez Montero et al., 1993
	Mean 71; maximum 130 (after 3 months breastfeeding)			
Germany (Saxony)	Median 5; 95th centile 3,240		1992-1993	Raum et al., 1998
Germany (Saxony)	Median 12		1992-1993	Schlaud et al., 1995
German (Saxony – Rural areas)	Median 16		1992-1993	Schlaud et al., 1995
Greece (South West)	Mean 58 (µg/L in whole milk)		1995-1997	Schinas et al., 2000
Norway (Oslo)	Mean 0.7		2000-2001	Polder et al., 2008
Norway (Tromsø)	Mean 0.3		2000-2001	Polder et al., 2008
Germany (North Rhine-Westphalia)	Mean 20		1984	P Fürst, personal communication to EFSA, 2005.
	Mean < 1		2001	
Spain (Almeria, agricultural area and Granada, urban area / Andalucia)	(1-7 days)	Mean 0.31 in Almeria	Not reported	Campoy et al., 2001
		Mean 1.60 in Granada		
	(6-12 days)	Mean 0.28 in Almeria		
		Mean 1.90 in Granada		
	(13-35 days)	Mean 0.32 in Almeria		
		Mean 0.82 in Granada		

41. Estimates of exposures from breast milk were based on the geometric mean concentration (0.8 µg/kg fat, 0.028 µg/kg whole milk) of γ-HCH in breast milk from the most recent UK study presented in Table 6 (Kalantzi et al., 2004b) as an indicator of central tendency, and also on the maximum level (7.7 µg/kg fat, 0.27 µg/kg whole milk). It was assumed that the fat content of breast milk was 3.5 % (see Table 8). Given the trends observed since monitoring began in the 1970s, concentrations of γ-HCH in breast milk are expected to have decreased since 2001-2003 when the survey by Kalantzi et al. (2004b) was conducted. Thus, the values assumed are likely to overestimate current exposures.

Table 8. Exposure of infants to γ-HCH (µg/kg bw/day) from exclusive breastfeeding estimated for average and high consumption of milk.

Estimated γ-HCH concentration in whole breast milk (µg/kg)	Age in months (milk consumption per day)			
	0-4.0 (800 mL)	0-4.0 (1200 mL)	>4.0-6.0 (800 mL)	>4.0-6.0 (1200 mL)
Geometric mean - 0.028	0.0038	0.0057	0.0028	0.0043
Maximum - 0.27	0.037	0.055	0.028	0.042

α-HCH

42. In a study that collected 92 samples of breast milk from 48 donors in the UK during 2001-2002, α-HCH was not found at a limit of detection of 0.01 mg/kg fat (Woolridge et al., 2004).

43. In the context of the 3rd WHO human milk field study (2000-2001), α-HCH was analysed in 16 samples of pooled human milk from 10 European countries (Bulgaria, Czech Republic, Germany, Ireland, Italy, Luxembourg, Norway, Russia, Spain and Ukraine) and 11 pools from 6 non-European countries (Brazil, Egypt, Fiji, Hong Kong, Philippines and USA) (Malisch et al., 2004). The α-HCH concentrations in the pools from Bulgaria, Russia and Ukraine ranged from 0.002 to 0.006 mg/kg fat, the highest value coming from the Ukraine. These samples may have been affected by local sources of contamination, making them unrepresentative of the UK. α-HCH was not detected in other European samples at an LOD of 0.001 mg/kg fat.

44. Since there are no quantified measurements of α-HCH relevant to breast milk in the UK, a worst case estimation was based on the LOD (1 µg/kg fat), which was not exceeded in those European countries contributing to the 3rd WHO human milk field study which were considered to be most relevant to the UK. These worst case exposures are presented in Table 8, and are calculated with the assumption that the fat content of breast milk is 3.5 %, and therefore the LOD of 1 µg/kg fat is equivalent to 0.035 µg/kg whole breast milk.

Table 9. Theoretical maximum exposure of infants to α-HCH (µg/kg bw/day) from exclusive breastfeeding estimated for average and high consumption of breast milk.

α-HCH concentration	Age in months (consumption volume per day)			
	0-4.0 (800 mL)	0-4.0 (1200 mL)	>4.0-6.0 (800 mL)	>4.0-6.0 (1200 mL)
< LOD of 0.035 µg/kg in whole breast milk	< 0.0047	< 0.0071	< 0.0036	< 0.0054

β-HCH

45. A temporal decline in the levels of β-HCH in breast milk is apparent from the scientific literature. Table 10 shows the concentrations of β-HCH in breast milk from studies in UK populations published since 1965.

Table 10. Reported concentrations of β-HCH in breast milk in the UK from studies published since 1965.

N	µg/kg milk fat					Mean µg/kg whole milk	% samples with detectable residues	Years of sample collection	Reference
	A. mean	G. mean	Med.	Min.	Max.				
19	N.D.	N.R.	N.D.	7	33	13 (A or G not specified)	100	1963-1964	Egan et al., 1965
102	220	N.R.	150	10	4400	7	80	1979-1980	Collins et al., 1982
-	-	-	-	-	-	5 (A or G not specified)	95	1984	MAFF, 1998
193	80	N.R.	60	<20	990	2	82	1989-1991	Dwarka et al., 1995
156	68[a]	N.R.	50	<8	750	1	36	1997-1998	Harris et al., 1999
92	<100	<100	<100	<100	<100	<3.5[b]	0	2001-2002	Woolridge et al., 2004
54	40	15	17	1.2	1500	1.4[b]	100[c]	2001-2003	Kalantzi et al., 2004b

A. mean. Arithmetic mean, G. mean. Geometric mean, Med. Median, Min. Minimum, Max. Maximum., N.R. Not reported.
[a] Confirmed as arithmetic mean by C Harris (personal communication)
[b] Estimated from arithmetic mean assuming 3.5% fat in whole milk
[c] Limits of detection appear to have been much lower in this study than in those conducted earlier (<0.001 mg/kg fat *vs.* 0.01 mg/kg fat)

46. As part of the 3rd WHO human milk field study (2000-2001), β-HCH was analysed in 16 samples of pooled human milk from 10 European countries (Bulgaria, Czech Republic, Germany, Ireland, Italy, Luxembourg, Norway, Russia, Spain and Ukraine) and 11 samples of pooled human milk from 6 non-European countries (Brazil, Egypt, Fiji, Hong Kong, Philippines and USA) (Malisch et al., 2004). The β-HCH concentrations in the samples from European countries ranged from 11 to 279 µg/kg fat.

47. Levels of β-HCH in breast milk in populations from other European countries and the United States that have been published since 1994 are shown in Table 11.

Table 11. Concentrations of β-HCH in breast milk samples from other European countries and the United States, published since 1994

Country (City/Region)	µg/kg milk fat	Years samples collected	Reference
Italy (average of Rome, Milan, Florence and Pavia)	Mean 130	1987	Larsen et al., 1994
Germany (North)	Median 200	1986-1997	Schade and Heinzow, 1998
	Median 50		
Spain	Mean or median? 240	1991	Hernandez et al. in Wong et al., 2002
Germany (Saxony)	Median 40; 95th centile, 7,970	1992-1993	Raum et al., 1998
Germany (Saxony)	Median 59	1992-1993	Schlaud et al., 1995
German (Saxony – Rural areas)	Median 45	1992-1993	Schlaud et al., 1995
Russia (Murmansk)	Mean 853	1993	Polder et al., 1998
Russia (Monchegorsk)	Mean 740	1993	Polder et al., 1998
Ukraine	Median 731**;** 90thcentile, 1,305	1993-1994	Gladen et al., 1999
Norway (Oslo)	Mean 14 mean	2000-2001	Polder et al., 2008
Norway (Tromsø)	Mean 10	2000-2001	Polder et al., 2008
Germany (North Rhine-Westphalia)	Mean 130	1984	P Fürst, personal communication to EFSA, 2005.
	Mean 20	2001	
North Germany	Median 11.6	2006	Zietz et al., 2008
USA (California)	Urban median 0.22; 75th centile, 0.24	2002-2007	Weldon et al., 2011
	Rural median 0.44; 75th centile, 0.52		

48. In a study of a German cohort, the median levels of β-HCH in breast milk were positively correlated with maternal age and negatively associated with parity and the total duration of breast-feeding. Post-pregnancy body mass index was a significant positive predictor of having higher concentrations of β-HCH in breast milk. Women who had followed a low-fat diet for at least 3 years had lower β-HCH levels in their breast milk than women whose diet included large quantities of meat (Schade, 1998).

49. Table 12 shows estimates of exposure to β-HCH based on the arithmetic mean value from the most recent UK study presented in Table 9 (i.e. 40 µg/kg milk fat, equivalent to 1.4 µg/kg whole milk assuming that the fat content of breast milk was 3.5 %), and also the maximum level (1500 µg/kg fat, equivalent to 52.5 µg/kg whole milk) of β-HCH in breast milk (Kalantzi et al., 2004b). The arithmetic mean was selected since it reflects the higher values reported by Kalantzi et al. (2004b), and is more conservative than the geometric mean. The arithmetic mean is considered to be a more plausible

estimate of exposures than the maximum value since the distribution of the data and comparison with other studies indicated that the maximum value might not be reliable. The second highest reported level was 40 µg/kg milk fat, i.e. the same as the arithmetic mean. Furthermore, levels are expected to have decreased since 2001-2003, when samples were collected by Kalantzi et al. (2004b).

Table 12. Exposures of infants to β-HCH (µg/kg bw/day) from exclusive breastfeeding estimated for average and high consumption of milk**.**

β-HCH concentration estimated in whole breast milk (µg/kg)	Age in months (consumption volume per day)			
	0-4.0 (800 mL)	0-4.0 (1200 mL)	>4.0-6.0 (800 mL)	>4.0-6.0 (1200 mL)
Arithmetic mean - 1.4	0.19	0.29	0.14	0.22
Maximum - 52.5	7.12	10.68	5.39	8.08

50. *Conclusion:* Estimated exposures to γ-HCH from breast milk are expected to be below the TDI of 0.04 µg/kg bw, except if there were high consumption of breast milk containing the compound at the maximum reported concentration in UK breast milk in 2001-3, which would give a minor exceedance. Given that levels in breast milk have been decreasing over time, the COT does not consider that this represents a concern for the health of breastfed infants.

Iodine

51. Full statement has not yet been published.

52. An iodine concentration of 70 µg/kg is reported for mature breast milk in McCance and Widdowson (2015). This value was obtained using the pooled samples of breast milk donated by 96 mothers from different parts of Great Britain. Up to 15% of the mothers in this study took vitamin and/or iron supplements during lactation but the iodine content of the supplements, if any, was not reported. No data specifically focussing on the influence of regular use of iodine supplements on levels of iodine in breast milk of UK mothers were identified.

53. No consumption data were available for exclusive breastfeeding in infants aged 0 to 6 months. Therefore, the default consumption values used by the COT in other evaluations of the infant diet, of 800 and 1200 mL for average and high level consumption, have been used to estimate exposures to iodine from breast milk. The ranges of mean and high-level exposure to iodine in exclusively breast-fed 0 to 6 month old infants were 7.2 - 9.5 µg/kg bw/day and 11 - 14 µg/kg bw/day respectively (Table 2).

54. Data on breast milk consumption for infants and young children aged 4 to 18 months were available from the DNSIYC and the NDNS, and have been

used to estimate exposures at these ages (Table 2), based on a mean iodine concentration of 70 µg/kg (paragraph 17). There were too few records of breast milk consumption for children older than 18 months in the NDNS to allow a reliable exposure assessment, and breast milk is expected to contribute minimally in this age group.

55. Mean exposures to iodine from breast milk for 4 to 18 month olds were 1.8 to 6.4 µg/kg bw/day, and 97.5th percentile exposures were 3.6 to 11 µg/kg bw/day (Table 13).

Table 13. Estimated iodine exposure in 0 to 18 month old infants and young children from breast milk, containing iodine at 70 µg/kg.

Exposure (µg/kg bw/day)	**Age group (months)**					
	0 to <4	**4 to <6**	**6 to <9**	**9 to <12**	**12 to <15**	**15 to <18**
Average	9.5[a]	7.2[a] 6.4[b]	4.7[b]	2.7[b]	2.1[b]	1.8[b]
High-level	14[a]	11[a] 11[b]	11[b]	8.1[b]	5.3[b]	3.6[b]

[a] Based on default consumption values of 800 and 1200 mL for average and high level exclusive consumption of breast milk.
[b] Based on mean and 97.5th percentile consumption of breast milk from DNSIYC (DH,2013)
Values rounded to 2 significant figures (SF)

56. *Conclusion:* No data specifically focussing on the influence of regular use of iodine supplements on levels of iodine in breast milk of UK mothers were identified. A more accurate estimate of iodine exposure in breast-fed infants, which takes account of more recent data on levels in breast milk and the influence of iodine supplement use in lactating UK mothers would be of value.

Lead:

57. Full statements available at:
https://cot.food.gov.uk/sites/default/files/cot/cotstatlead.pdf
https://cot.food.gov.uk/sites/default/files/finaladdendumonlead.pdf

58. Lactation requires significant remodelling of bone calcium which also releases lead which is a significant storage site for lead in the body. It is estimated that up to 5% of bone mass is mobilised during lactation. It has been suggested that women with higher bone lead levels may mobilise more lead into the blood stream during pregnancy and lactation than those with lower lead burdens (Tellez-Rojo et al, 2002).

59. Infant blood lead levels were found to significantly correlate with breastmilk lead levels (Ettinger et al, 2004b). As part of the SUREmilk study (2004) levels of lead were measured in breastmilk from UK women, the highest concentration in an individual sample being 2.6 microgram/kg. The COT noted that the SUREmilk samples were collected primarily to explore the viability of breastmilk collection methods, and not part of a rigorous survey.

60. A marginally low MOE (0.9) was calculated for high consumers of breastmilk at ages 0-3 months when the highest UK lead concentration from the SUREmilk study was used. This indicated that a low risk of effects attributable to lead cannot be ruled out. This is, however, based on an unusually high concentration of lead in breastmilk, and is for exposure to a cumulative toxicant over a relatively short period. The calculated MOE for high breastmilk consumers at older ages was <1.

Addendum 2016:

61. Since no new data were available for breast milk, the estimated exposures of exclusively breastfed infants, aged 0 to 6 months were calculated using default values for mean (800 mL) and high level (1,200 mL) consumption, in line with previous COT evaluations (Table 3).

62. Data on breast milk consumption have now become available from DNSIYC and these were used in estimating exposure from breast milk in the 6-18 months age groups based on the maximum lead level of 2.6 µg/L (Table 14). 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 to lead exposure in this age group.

Table 14. Lead exposure (µg/kg bw/day) from breastfeeding estimated for consumption of breast milk containing lead at 2.6 µg/L.

	Age group (months)					
	0 to 4[a]	**>4 to 6[a]**	**>6 to 9[b]**	**>9 to 12[b]**	**12 to 15[b]**	**15 to 18[b]**
Number of consumers	N/A	N/A	140	124	66	32
Mean	0.35	0.27	0.17	0.099	0.076	0.066
High level	0.53	0.40	0.41	0.30	0.19	0.13

[a] Mean and high level lead exposures were based on exclusive breastfeeding and consumption of 800 and 1,200mL, respectively (COT, 2013).
[b] Consumption data from DNSIYC; high level is 97.5th percentile.
Values rounded to 2 significant figures (SF).

63. *Conclusion:* For infants aged 0-6 months old fed breastmilk, ready to feed drinks and powdered formula made with water containing typical lead

concentrations, any risk would be small. This assessment does not indicate a need for specific advice on lead relating to the diet of infants and young children.

Polybrominated Biphenyls (PBB's)

64. Full statement available at:
https://cot.food.gov.uk/sites/default/files/pbbstatementfinal.pdf

65. In the EFSA (2010) opinion, the only European data on PBBs in breast milk were from Germany (published in 1988), and from Denmark and Finland (published in 2008). Since then, one study by Bramwell *et al.* (2014) has reported PBB levels in breast milk in the UK. The only congener that was analysed in all four of these studies was PBB-153. Mean levels of PBB-153 were 0.2 ng/g fat (range 0.04 - 1.5 ng/g fat)[4], and 0.134 ng/g fat (range 0.03 - 1.21 ng/g fat), in the Danish (n = 65) and Finnish (n = 65) samples respectively. In the German study (n = 25), PBB-153 occurred at a mean concentration of 1.03 ng/g fat (range 0.29 - 2.8 ng/g fat, median 0.75 ng/g fat). In the UK, a median concentration of 0.08 ng/g fat (range 0.06 – 0.79 ng/g fat) was reported in six individuals.

66. Comparison of the levels of PBBs in these studies is complicated by differences in the PBB congeners measured, and even for PBB-153 the published findings have been summarised in different ways (either by means or by medians) (Table 15).

Table 15: PBB-153 levels in breast milk (ng/g fat).

Country	Number of samples	Mean	Median	Range	Year study published
Germany	25	1.03	0.75	0.29 - 2.8	1988
Finland	65	0.13	-	0.03 - 1.20	2008
Denmark	65	0.2	-	0.04 - 1.5	2008
UK	6	-	0.08	0.06 - 0.79	2014

67. *Conclusions:* The Committee considers that it would be useful to obtain more data on levels of PBBs in foods in the UK. However, further research on the toxicity of PBBs is not a high priority since their use is now restricted, and exposures are likely to decrease further over time.

Polybrominated diphenyl ethers (PBDE's):

68. Full statement available at:
https://cot.food.gov.uk/sites/default/files/PBDEstatementfinal.pdf

69. Table 14 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 16 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)

70. Table 17 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 17. 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

71. *Conclusions:* 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.

72. 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.

73. 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.

PFOS:

74. Full statement available at:
https://cot.food.gov.uk/sites/default/files/cot/cotstatmpfos.pdf

75. No UK data are available but data are available from studies in 4 European countries (Table 18).

Table 18: Concentrations of PFOS in breast milk in recent EU studies.

Region, Country	Year of sampling	No. of samples	Mean (SEM) (ng/L)	Median (ng/L)	Range (ng/L)	Reference
Barcelona, Spain	2009	20	116 (42)	84	<LOQ-865	Llorca et al, 2010
France	2010	30	78	74	24-171	Kadar et al, 2011
Belgium	2009-2010	40 (P & M)	130	NR	NR	Croes et al, 2012
Bologna,	2010	21 (P)	57 (13)	NR	<15-	Barbarossa

Italy					288	et al, 2013
		16 (M)	36 (7)	NR	<15-116	

P-primiparous, M-multiparous, SEM standard error of the mean, NR-not reported.

76. Data suggest that intakes will be well below the TDI of 300ng/kg bw/day set by the COT and below the TDI of 150 ng/kg bw/day set by EFSA.

Soya phytoestrogens:

77. Full statement available at: https://cot.food.gov.uk/sites/default/files/cot/cotstaphytos.pdf

78. The 2003 COT report noted that isoflavones are excreted in human milk at low concentrations reflecting maternal diet, with the highest concentrations in the breast milk of mothers following vegetarian or vegan diets. In one study, means (and ranges in brackets) of total isoflavone concentrations in breast milk samples (sum of genistein and daidzein expressed as mg aglycone/kg) were as follows: mothers consuming omnivorous diet (n=14): 0.001 (0 – 0.002); mothers with vegetarian diet (n=14): 0.004 (0.001 – 0.010) and mothers with vegan diet (n=11): 0.011 (0.002 – 0.032) (MAFF, 1998a).

79. Other research had found total isoflavones in breast milk at concentrations of 0.0016-0.0136 mg aglycone/L in women consuming an omnivorous diet (Setchell et al., 1997; Setchell et al., 1998). Consumption of foods such as roasted soya beans has been shown to give levels of isoflavones in the breast milk of vegans of up to 0.032 mg/L (Franke and Custer, 1996; MAFF, 1998b).

80. In a study conducted in the US, milk samples were collected from breastfeeding mothers before and after consumption of a soya protein beverage (25 g soya protein/36.5 g of beverage, containing 55 mg isoflavones; daidzein:genistein:glycitein = 1:1:0.1). The mean (SEM) levels of isoflavones in breast milk increased from 5.1 (2.2) nmol/L to 70.7 (19.2) nmol/L after 2-4 days of daily consumption. The daidzein to genistein ratio in breast milk was on average 0.6. Therefore it can be estimated that when expressed as µg/L, levels of genistein increased from 0.00055 to 0.00764, and of daidzein from 0.00078 to 0.01078 (Franke et al., 2006). In Canada, samples of breast milk were collected after delivery from women aged at least 35 years (details of their diets were not reported). The mean concentrations of isoflavones in breast milk samples were 0.00087 µg/L (genistein) and 0.00036 µg/L (daidzein) for women with male infants and 0.00036 µg/L (genistein) and 0.00016 µg/L (daidzein) for women with female infants (Jarrell et al., 2012).

81. COT concluded that exposures to isoflavones from breastmilk (even where mother are consuming a vegetarian or vegan diet) are highly unlikely to cause adverse effects.

Vitamin A:

82. Full statement available at:
https://cot.food.gov.uk/sites/default/files/cot/cotstavita.pdf

83. Limited data available on vitamin A in breastmilk. Levels of vitamin A in breastmilk from well-nourished women in Europe are reported to be between 40-70 micrograms RE/100mL (Ross and Harvey, 2003). Limited information is available about the impact of supplementation on levels of vitamin A in breastmilk. In a single dose study in healthy women from Brazil given 200 000 IU retinyl palmitate immediately postpartum, breast milk samples were taken 24h and 30days after dosing. Concentrations at 24h and 30 days post-partum were 165 and 51 microgram RE/100mL compared to 93 and 37 micrograms RE/100mL in supplemented and control women respectively.

84. Exposures for exclusively breastfed or exclusively infant formula fed infants have been calculated assuming values of 800 mL and 1200 mL, for average and high-level daily consumption respectively. Bodyweight data for infants aged 4 to <6 months are from DNSIYC (DH, 2013), with an average of 7.8 kg. Since DNSIYC did not include infants younger than 4 months, a value of 5.9 kg for infants aged 0-3 months, from an older survey (DH, 1994), is applied to infants aged 0-<4 months.

85. Mean and high-level intake of vitamin A in exclusively breastfed infants, based on the upper end of the reported range of vitamin A concentrations in breast milk of 70 µg RE/100 mL are in the region of 72 to 95 µg RE/kg bw/day and 110 to 140 µg RE/kg bw/day, respectively (Table 1). Vitamin A supplement intake by lactating mothers in the UK would be expected to potentially increase levels of vitamin A in breast milk by less than two-fold. Thus, the estimated vitamin A intake of an infant breastfed by a mother taking vitamin A dietary supplements would be less than twice the highest value of 140 µg RE/kg bw/day in Table 19 i.e. less than 280 µg RE/kg bw/day.

Table 19 Vitamin A exposure (µg RE/kg bw/day) from exclusive feeding on breast milk or infant formula.

	Age in months (consumption volume)[a]			
	0-<4 (800 mL)	**0-<4 (1200 mL)**	**4-<6 (800 mL)**	**4-<6 (1200 mL)**
Breast milk (70 µg RE/100 mL)	95	140	72	110
Formula milk[b] (77 µg RE/100 mL)	100	160	79	120
Formula milk (82 µg RE/100 mL)[c]	110	170	84	130

[a] *Exposures were calculated using an average bodyweight of 5.9 kg for 0 to <4 month olds and 7.8 kg for 4 to <6 month olds*.

[b] *Based on the recent EU regulatory limit of* 77 µg RE/100 mL
[c] *Based on the upper-end of the range for major brands of UK infant formula, as reported previously(COT 2013) .*
Data reported to 2 significant figures.

86. Where mothers are not taking vitamin A supplements, the estimated exposure of exclusively breastfed infants is below the TUL and not a health concern. Maternal use of dietary supplements could increase the exposure. Whilst available data do not allow precise prediction of effects on breast milk in mothers taking supplements on the UK market, the increase in vitamin A concentrations is likely to be less than twofold. Thus, any resultant exceedance of TUL would only be minor. Moreover, it would be only for a short period of time.

87. Overall the COT, concluded that there is potential for some infants to exceed the TUL under the following circumstances:

- If exclusively breastfed by mothers taking dietary supplements containing high levels of vitamin A,
- If fed with infant formula at the upper limit of the retinol content allowed by regulation,
- If given high dose vitamin A supplements
- If consuming liver more than once a week

88. The possibility of adverse effects from such exceedances cannot be excluded, but if they do occur, it is likely to be only a very small proportion of infants.

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

Proposal for a breastmilk analysis study using pre-existing samples held by Imperial College London.

Tao F, Abou-Elwaf Abdallaha M, Ashworth DC, Douglas P, Toledano MB, Harrad S (2017) Emerging and legacy flame retardants in UK human milk and food suggest slow response to restrictions on use of PBDEs and HBCDD Environment International 105. 95-104

This publication is available in a peer-reviewed journal in the public domain and will not therefore be attached to the web-version of this paper.