TOX/2018/28

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

Review of potential risks from contaminants in the diet of infants aged 0 to 12 months and children aged 1 to 5 years

Introduction

1. The Committee on Toxicity (COT) was asked to review the risk of toxicity of chemicals in the diets of infants and 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. 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. A scoping paper (TOX/2015/32) "COT contribution to SACN review of complementary and young child feeding; proposed scope of work for 1 to 5 year old children" was reviewed by the COT in 2015. The following scoping paper (part I) is a follow up to the members request to have a more detailed look at a number of chemicals and provides an overview for tropane alkaloids (TAs), zinc, selenium and phthalates.

3. Annex I provides a brief summary on TAs, including a description of the previously establish Health Based Guidance Values (HBGVs) by the European Food Safety Authority (EFSA) in 2013. Following the approach taken by EFSA, an exposure assessment for (-)-hyoscyamine and (-)-scopolamine and well as the sum of (-)-hyoscyamine and (-)-scopolamine is provided using unpublished data collected for the Food Standards Agency (FSA).

4. Annex 2 provides a brief summary of zinc, including the (safe) upper levels and HBGVs established by other regulatory authorities. Concentrations of zinc have recently been measure in an FSA survey of metals and other elements in infant formula and foods (Infant Metal Survey, FSA 2016) and in the composite food samples of the 2014 Total Diet Study (TDS, FSA 2016); dietary exposures have been estimated and a risk characterisation has been included.

5. Annex 3 provides a short overview of selenium, including the upper intake level (UL) established by the Scientific Committee on Food (SCF). Selenium concentrations have recently been measure in an FSA survey of metals and other elements in infant formula and foods (Infant Metal Survey, FSA 2016) and in the composite food samples of the 2014 Total Diet Study (TDS, FSA 2016); dietary exposures have been estimated and a risk characterisation has been included.

6. Annex 4 provides a short overview of the phthalates, including the Tolerable Daily Intakes (TDIs) derived by EFSA and the World Health Organisation (WHO) for a limited number of these compounds. Phthalate concentrations have been measured in the composite food samples in a 2011 Study (FSA Report FD 10/05, FSA PROJECT C010482011); dietary exposures have been estimated and a risk characterisation has been included.

The Committee is asked to consider the chemicals and data presented in the scoping paper and to comment on the individual Annexes.

Secretariat

July 2018

Abbreviations

AI	Adequate Intake
ANS	Autonomic nervous system
AR	Average requirement
ARfD	Acute reference dose
bw	Body weight
CNS	Central nervous system
COMA	UK Committee on Medical Aspects of Food and Nutritional Policy
COT	Committee on Toxicology, Consumer Products and the Environment
DNSIYC	Diet and Nutrition Survey of Infants and Young Children
DRV	Dietary reference value
EC	European Commission
EFSA	European Food Safety Authority
EMA	European Medicine Agency
EVM	Expert Group on Vitamins and Minerals
FAO	Food and Agricultural Organisation of the United Nations
FSA	Food Standards Agency
GI tract	Gastrointestinal tract
HBGV	Health based guidance value
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LB	Lower bound
LOAEL	Lowest observed adverse effect level
LOD	Limit of detection
LOQ	Limit of quantification
MRL	Maximum residue limit
NDNS	National Diet and Nutrition Survey
NOAEL	No observed adverse effect level
PMTDI	Provisional maximum tolerable daily intake
PRI	Population reference intake
RNI	Reference nutrient intake
SCF	Scientific Committee on Food

SUL	Safe upper level
TAs	Tropane alkaloids
UB	Upper bound
UF	Uncertainty factor
UL	Upper limit
WHO	World Health Organisation
Zn	Zinc

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

Review of potential risks from contaminants in the diet of infants aged 0 to 12 months and children aged 1 to 5 years

Tropane alkaloids

7. Unless stated otherwise, general information was derived from the European Food Safety Authority's scientific opinion (EFSA, 2013).

Background

8. Tropane alkaloids (TAs) are secondary metabolites which naturally occur in several plant families, such as Brassicaceae, Solanaceae and Erythroxylaceae. TA are found in all parts of the plant and are responsible for the toxic effects of those plants.

9. The group of TAs composes of about 200 compounds, the best-known representatives are (-)-hyoscyamine, (-)-scopolamine and atropine, a racemic mix of (-)-hyoscyamine and (+)-hyoscyamine. Plant extracts containing TAs have been and are continued to be used in veterinary and human medicine, as are (-)-hyoscyamine, (-)-scopolamine and atropine. Uses include the treatment of wounds, gout, sleeplessness and pre-anaesthesia.

10. The genus Datura is known for its content of TAs and is widely distributed in temperate and tropical regions. Therefore, seeds have been found as impurities in linseed, soybean, millet, sunflower and buckwheat and products thereof.

11. TAs are readily absorbed from the gastrointestinal (GI) tract and distributed into tissues; excretion is predominantly via urine.

Toxicity

12. (-)-hyoscyamine and (-)-scopolamine are strong antimuscarinic agents; their toxicological effect is closely related to their pharmacological effect. Both compounds inhibit the muscarinic acetylcholine receptor in the central nervous system (CNS) and autonomic nervous system (ANS). However, they differ in the ability to affect the CNS, (-)-scopolamine having a more prominent effect on the CNS.

13. In humans, toxic effects of (-)-hyoscyamine and (-)-scopolamine include inhibition of saliva, bronchial and sweat gland secretion, dilation of pupils and paralysis of accommodation, change in heart rate, inhibition of urination, reduction in GI tone and inhibition of GI secretion. In extreme cases, toxic effects can include hallucination, delirium and coma.

14. Toxic effects of other TAs are largely unknown and only very limited data on occurrence in food and feed is available.

HBGVs

15. EFSA (2013) performed a risk assessment on (-)-hyoscyamine and (-)-scopolamine, the TAs for which both, occurrence and toxicity data were available.

16. Atropine is a racemic mixture of (-)-hyoscyamine and (+)-hyoscyamine; unlike (+)-hyoscyamine, (-)-hyoscyamine and (-)-scopolamine are naturally formed in plants. When atropine was reported in data on food and feed, EFSA used these data as (-)-hyoscyamine in their evaluation of TAs.

17. EFSA establish an acute reference dose (ARfD), as the pharmacological effects of (-)-hyoscyamine and (-)-scopolamine occur within a short time period after administration. The Panel assumed equivalent potency of (-)-hyoscyamine and (-)-scopolamine, due to their common mode of action and therefore set a group ARfD based on a human volunteer study. An uncertainty factor of 10 for interindividual differences (small study, healthy male volunteers) was applied to the no observed adverse effect level (NOAEL) of 0.16 µg/kg bw per day to derive an ARfD of 0.016 µg/kg bw per day.

18. The group ARfD is approximately two orders of magnitude lower than the lowest single therapeutic dose of (-)-hyoscyamine and (-)-scopolamine.

19. EFSA considered the ARfD to be protective against long term exposure due to the lack of bioaccumulation, genotoxicity and chronic toxicity of TAs.

20. The European Medicine Agency (EMA) and EFSA assessed the legal use of *Atropa belladonna* and atropine as authorised veterinary medicines in farm animals in 1997 and 2008. Since atropine is used infrequently and readily absorbed and eliminated, it was not considered necessary to establish a maximum residue limit (MRL) as animals are unlikely to be sent to slaughter immediately after treatment.

21. EMA and EFSA both concluded it was unlikely that residues of TAs in edible tissues (meat, milk, eggs) would be of risk to consumers.

22. Based on EFSAs conclusions that toddlers might significantly exceed the group ARfD through the diet and the fact that it is not always possible to distinguish between the enantiomers of hyoscyamine, a maximum level for atropine (reflecting the occurrence of (-)-hyoscyamine) and (-)-scopolamine of 1.0 µg/kg in cereal based food for infants and young children was derived by the European Commission (EC, 2016).

Exposure Assessment

Dietary exposure

23. The occurrence data for the exposure assessment are results from a survey from the unpublished final report on monitoring of tropane alkaloids in foods. Samples were taken from a wide variety of food groups and analysed for as many TAs for which reliable standards are available (FSA 102116, March 2017).

24. Consumption data (on a body weight basis) for the estimated dietary exposure are from the Diet and Nutrition Survey of Infants and Young Children

(DNSIYC) (DH, 2013) and from years 1-6 of the National Diet and Nutrition Survey (NDNS) (Bates et al., 2012 & 2014).

25. For the purposes of this scoping paper and following EFSAs approach, this assessment uses and reports atropine and (-)-scopolamine in food as (-)-hyoscyamine and (-)-scopolamine, respectively. The acute exposure assessments of infants and young children focused on (-)-hyoscyamine and (-)-scopolamine and the sum of (-)-hyoscyamine and (-)-scopolamine and the consumption of: (i) commercial infant and young children foods, (ii) breakfast cereals and (iii) teas (dry product). Consumption of these foods is assumed to be highest at the age groups of interest (children aged 4 to 18 months and 18 to 60 months) and therefore cover all other food groups.

26. Overall, the concentrations of TAs found in the survey were low, measured quantities of TAs were reported in only a limited number of samples.

27. (-)-Hyoscyamine was measured in 7 out of 47 samples (14.9%) of commercial infant and young children foods. The remainder of the samples (85.1%) were below the limit of quantification (LOQ) of 0.5 µg/kg but at or above the limit of detection (LOD) of 0.05 µg/kg. (-)-Scopolamine was measured in only 4 out of 47 samples (8.5%); the concentrations found in the remainder of the samples (91.5%) were below the LOQ of 0.5 µg/kg but at or above the LOD of 0.1 µg/kg.

28. (-)-Hyoscyamine was measured in 2 out of 29 samples (6.9%) of breakfast cereal. The concentrations in the remainder of the samples were below the LOQ of 0.5 µg/kg (93.1%), below the LOD of 0.05 µg/kg (17.2%), at the LOD (3.4%) or between the LOD and LOQ (72.4%). (-)-Scopolamine was measured in 1 out of 29 samples (3.4%); the remainder of the samples were below the LOQ (96.6%), below the LOD (58.6%), at the LOD (10.3%) or between the LOD and LOQ (27.6%).

29. (-)-Hyoscyamine was measured in 9 of the 29 samples (31%) of teas (dry product). The remainder of the samples were below the LOQ (69%) of which 65.5% were at the LOD. (-)-Scopolamine was measured in 5 of 29 samples (17.2%); the remainder of the samples was below the LOQ (82.8%), of which 69% were at the LOD.

30. Tea infusions were prepared from a selection of 20 tea samples and analysed for TAs. On average, it was found that 47% of the alkaloids transferred from the dry tea to the infusion (Stratton et al., 2017).

31. Average concentrations of (-)-hyoscyamine were estimated to be 0.18 ng/g lower bound (LB) and 0.43 ng/g upper bound (UB) (cereal-based infant foods), 0.02 ng/g LB and 0.15 ng/g UB (breakfast cereals) and 6.58 ng/g LB and 6.66 ng/g UB (teas, dry product) and used in the exposure assessment. Average levels of (-)-scopolamine were estimated to be 0.04 ng/g LB and 0.19 ng/g UB (cereal-based infant foods), 0.03 ng/g LB and 0.11 ng/g (breakfast cereals) and 2.45 ng/g LB and 2.55 ng/g UB (teas, dry product).

32. The following tables provide the mean and 97.5th percentile estimated acute exposures (UB) to (-)-hyoscyamine, (-)-scopolamine and the sum of (-)-hyoscyamine and (-)-scopolamine from consumption of cereal-based infant foods (Table 1),

breakfast cereals (Table 2), teas (dry product; Table 3) and the combination of all 3 food categories (Table 4) for children aged 4 to 18 months and 18 to 60 months.

Table 1 Estimated TAs acute exposure for children aged 4 to 60 months from consumption of cereal-based infant foods, using data from the unpublished FSA report (retail survey; FSA 102116, 2017).

	Exposure LB-UB (ng/kg bw/day)					
	4 to 18 m-olds (n=2683)			**18 to 60 m-olds (n=1015)**		
	Number of consumers	**Mean**	**97.5th Percentile**	**Number of consumers**	**Mean**	**97.5th Percentile**
Hyoscyamine	1997	1.2-3.0	4.9-12	308	0.41-0.99	1.8-4.3
Scopolamine	1997	0.28-1.3	1.1-5.2	308	0.092-0.44	0.40-1.9
Total Exposure	**1997**	**1.5-4.3**	**6.0-17**	**308**	**0.50-1.4**	**2.2-6.1**

Table 2 Estimated TAs acute exposure for children aged 4 to 60 months from consumption of breakfast cereals, using data from the unpublished FSA report (retail survey; FSA 102116, 2017).

	Exposure LB-UB (ng/kg bw/day)					
	4 to 18 m-olds (n=2683)			**18 to 60 m-olds (n=1015)**		
	Number of consumers	**Mean**	**97.5th Percentile**	**Number of consumers**	**Mean**	**97.5th Percentile**
Hyoscyamine	1134	0.074-0.55	0.39-2.9	686	0.054-0.40	0.23-1.7
Scopolamine	1134	0.11-0.41	0.59-2.2	686	0.080-0.29	0.34-1.3
Total Exposure	**1134**	**0.18-0.96**	**0.98-5.1**	**686**	**0.13-0.70**	**0.57-3.0**

Table 3 Estimated TAs acute exposure for children aged 4 to 60 months from consumption of teas (dry product), using data from the unpublished FSA report (retail survey; FSA 102116, 2017).

	Exposure LB-UB (ng/kg bw/day)					
	4 to 18 m-olds (n=2683)			**18 to 60 m-olds (n=1015)**		
	Number of consumers	**Mean**	**97.5th Percentile**	**Number of consumers**	**Mean**	**97.5th Percentile**

Hyoscyamine	153	0.83-0.84	2.7	177	0.77-0.78	2.1-2.2
Scopolamine	153	0.31-0.32	1.0	177	0.29-0.30	0.79-0.82
Total Exposure	**153**	**1.1-1.2**	**3.7-3.8**	**177**	**1.1**	**2.9-3.0**

Table 4 Estimated TAs acute exposure for children aged 4 to 60 months from consumption of breakfast cereals, infant foods and teas (dry product), using data from the unpublished FSA report (retail survey; FSA 102116, 2017).

	Exposure LB-UB (ng/kg bw/day)					
	4 to 18 m-olds (n=2683)			**18 to 60 m-olds (n=1015)**		
	Number of consumers	**Mean**	**97.5th Percentile**	**Number of consumers**	**Mean**	**97.5th Percentile**
Hyoscyamine	2442	1.1-2.6	4.6-11*	836	0.33-0.76	1.8 -3.0*
Scopolamine	2442	0.28-1.2	1.1-4.9*	836	0.15-0.41	0.63-1.8*
Total Exposure	2442	**1.4-3.8**	**5.7-16**	**836**	**0.48-1.2**	**2.3-4.8**

* Determined from a distribution of consumption of any combination of categories rather than by summation of the respective individual 97.5th percentile consumption value for each of the three food categories

Human breast milk

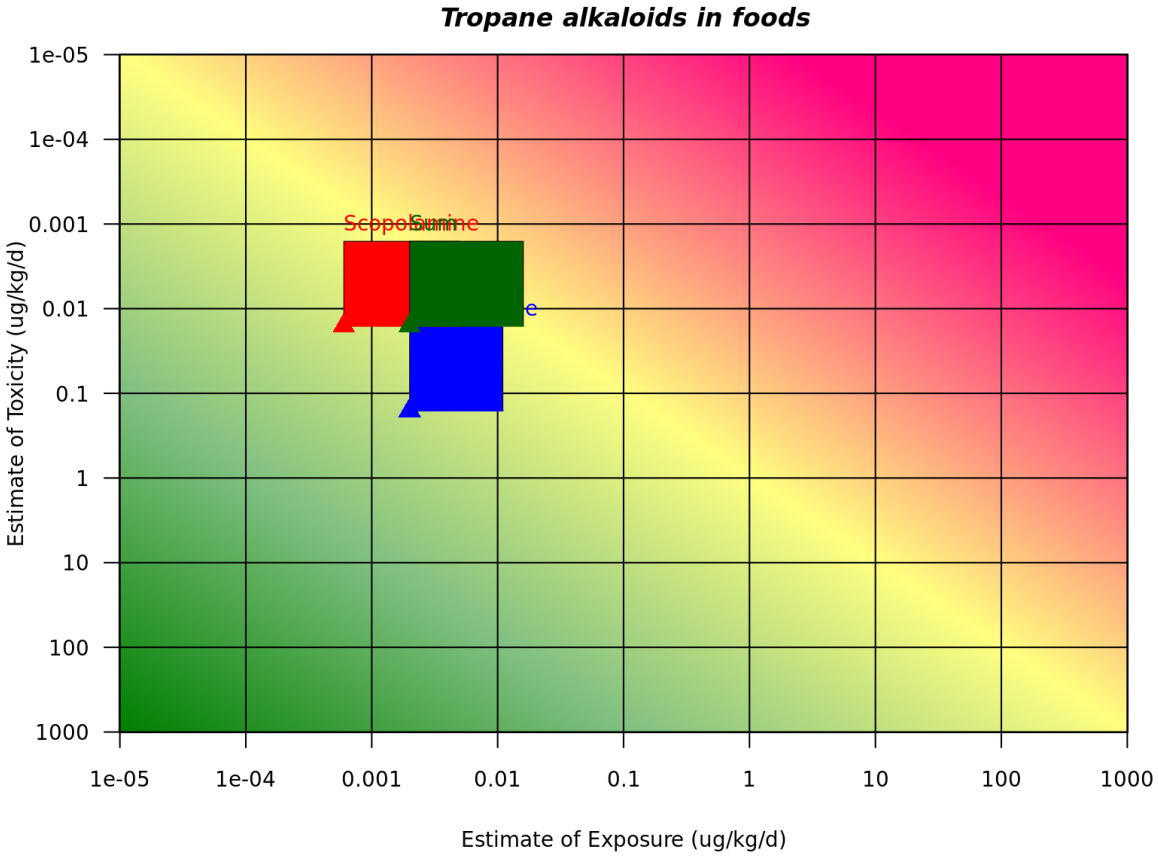
33. Little to no information is available of the transfer of TAs to breast milk; the limited information available reports that only limited amounts of tropane alkaloids, namely atropine, (-)-hyoscyamine and (-)-scopolamine are excreted into breast milk (EFSA, 2013). A literature search including the years since the last EFSA opinion on TAs has not resulted in any additional information.

Infant formula

34. No data is available on concentrations of TAs in infant formula.

Risk21

35. Figure 1 shows the 97.5th percentile estimated acute exposure for (-)-hyoscyamine, (-)-scopolamine and the sum of (-)-hyoscyamine and (-)-scopolamine for the consumption of breakfast cereals, infant foods and tea across all age groups.



Risk characterisation

36. EFSA established an ARfD of 0.016 µg/kg (16 ng/kg) bw per day based on the rapid onset of pharmacological effects; no HBGV was set for long term exposure as EFSA considered the ARfD to be effective in the absence of bioaccumulation, genotoxicity and chronic toxicity.

37. In infants and young children, the UB mean and 97.5th percentile estimated acute exposures to (-)-hyoscyamine and (-)-scopolamine and the sum of (-)-hyoscyamine and (-)-scopolamine for each individual food category and the sum of all three categories were below the ARfD. The only exceptions are the 97.5th percentile (UB) estimated exposures to the sum of (-)-hyoscyamine and (-)-scopolamine in cereal-based infant foods and all three food categories combined where exposures are at or close to the ARfD; however these are UB exposures, reflecting limited detection of (-)-hyoscyamine and (-)-scopolamine rather than being based on actual measured consentrations. The ARfD is based on a human (male) volunteer study and derived from a NOAEL with the application of an UF of 10 for interindividual differences. The exposures are unlikely to be of toxicological concern.

38. The limited information available on the transfer to and concentrations of TAs in breast milk does not indicate a toxicological concern.

39. No data on the concentration of TAs in infant formula is available; given the source of TAs and the assessment by the EMA and EFSA that it is unlikely for residues of TAs in milk to be of risk to the consumer, it is highly unlikely that TAs would be detected in infant formula or that levels reported would be of risk to infants.

Uncertainties in the risk characterisation

40. Although numerous TAs have been tested for and reported in the FSA unpublished report (2017), due to the lack of toxicity data, this risk assessment, only focused on (-)-hyoscyamine and (-)-scopolamine. Thus, the total dietary exposure of infants and young children to a combination of all TAs may be substantially underestimated. The estimated exposures are based on LB and UB concentrations, which reflect the uncertainties associated with concentrations being below the LOQ in the majority of the samples.

41. Insufficient data on the racemisation and degradation of TAs under conditions used for food preparation as well as the effects of *in vivo* racemisation or potential toxicity of degradation products further add to the overall uncertainty regarding the total dietary exposure.

Conclusions

42. EFSA established an ARfD of 16 ng/kg bw per day based on the rapid onset of pharmacological effects.

43. Overall, the levels of TAs detected in foods in the 2014 (unpublished) survey were low, with very few incidences of (-)-hyoscyamine and (-)-scopolamine at or above the LOQ. The average levels reported for (-)-hyoscyamine and (-)-scopolamine in cereal-based infant foods, breakfast cereals and teas (dry) were below the permitted maximum level of 1.0 µg/kg in cereal based food for infants and young children derived by the European Commission (EC, 2016). However, 4 out of 66 samples (3/46 from the EFSA survey, 1/20 from the FSA survey) were found to exceed the maximum level; the highest level found was 3.73 µg/kg (-)-hyoscyamine.

44. All estimated acute exposures of infant and young children to (-)-hyoscyamine and (-)-scopolamine or the sum of (-)-hyoscyamine and (-)-scopolamine are close to or below the ARfD of 16 ng/kg bw per day. The exposures are unlikely to be of toxicological concern.

45. Limited information is available on the transfer of TAs into breast milk; the limited information available prior to the EFSA opinion in 2013 does not indicate significant concentrations of TAs in breast milk. A recent literature search could not detect any new data or newer information on either the transfer to or concentration of TAs in breast milk since the 2013 EFSA opinion. The limited information available currently indicates no toxicological concern regarding TAs in breast milk.

Questions to be asked to the Committee

i) Do the Committee agree with the ARfD established by EFSA in 2013?

ii) Do the Committee agree with EFSAs conclusions that an ARfD would also protect against long term exposure?

iii) Do the Committee consider it sufficient to include a brief summary of the important points (HBGVs, exposure, conclusions) in the overarching statement?

iv) Do the members have any other comments?

Secretariat

July 2018

References

Bates B, Lennox A, Prentice A, Bates C, Page P, Nicholson S, Swan G (2014). National Diet and Nutrition Survey Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/2009 – 2011/2012) https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/594360/NDNS_Y1_to_4_UK_report_executive_summary_revised_February_2017.pdf

Bates B, Cox L, Nicholson S, Page P, Prentice A, Steer T Swan G (2016). National Diet and Nutrition Survey Results from Years 5 and 6 (combined) of the Rolling Programme (2012/2013 – 2013/2014) https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/551352/NDNS_Y5_6_UK_Main_Text.pdf

Commission Regulation (EU) 2016/239. Amending Regulation (EC) No 1881/2006 as regards maximumlevels of tropane alkaloids in certain vereal-based foods for infants and young children. Offical Journal of the European Union L 45/3. http://eur-lex.europa.eu/legal-lontent/EN/TXT/PDF/?uri=CELEX:32016R0239&from=EN

DH (Department of Health) (2013). Diet and Nutrition Survey of Infants and Young Children (DNSIYC), 2011. http://transparency.dh.gov.uk/2013/03/13/dnsiyc-2011/

EFSA (2013). Scientific Opinion on Tropane alkaloids in food and feed. EFSA Journal, 11(10):3386. http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2013.3386/epdf

Lennox A, Sommerville J, Ong K, Henderson H, Allen R (2013). Diet and Nutrition Survey of Infants and Young Children. https://www.gov.uk/government/publications/diet-and-nutrition-survey-of-infants-and-young-children-2011

Stratton J, Clough J, Leon I, Sehlanova M and MacDonald S. (2017). FINAL REPORT: Monitoring of tropane alkaloids in foods. (Unpublished); Fera Science Ltd.

Appendix 1

Literature search terms

The focus of this scoping paper was a first comparison of estimated exposures in UK children aged 1-5 years to the current HBGVs set by EFSA in 2013.

To update our knowledge since the EFSA opinion in 2013, we carried out a literature search using PubMed with emphasis on breast milk data.

No specific time period was covered by the search.

Search terms

Tropane alkaloids and breast milk
Tropane alkaloids and breastfeeding
Scopolamine and breast milk
Scopolamine and breastfeeding
Hyoscyamine and breast milk
Hyoscyamine and breastfeeding
Atropine and breast milk
Atropine and breastfeeding
Tropane alkaloids and infant formula
Tropane alkaloids and formula
Tropane alkaloids and milk
Tropane alkaloids and infant milk
Scopolamine and infant formula
Hyoscyamine and infant formula

No papers for TAs concentrations in breast milk and infant formula were identified.

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

Review of potential risks from contaminants in the diet of infants aged 0 to 12 months and children aged 1 to 5 years

Zinc

46. Unless indicated otherwise, the sources of information for this summary were previous assessments by the European Food Safety Authority (EFSA, 2014), the Scientific Committee on Food (SCF, 2003), the Expert Group on Vitamins and Minerals (EMV, 2003) and the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT, 2018).

Background

47. The Food Standards Agency (FSA) has completed a survey of 15 elements in the 2014 survey of metals and other elements in infant formula, commercial infant foods and other foods (FSIS, 2014). The results of the survey included information on concentrations of zinc (Zn) and estimated dietary exposures were calculated for the COT statement on metals and other elements (2018)[1]. The previous COT statement (2008)[2] covered infants and children age 4 to 18 months, the following scoping paper covers infants aged 0 to 12 months and children 1 to 5 years.

48. Zinc is an essential trace element found in all plant and animal tissue. It plays a role in a wide range of biochemical and physiological functions; it's key biochemical role is in the regulation of gene expression, including transcriptional and translational control/modulation. Zinc furthermore has catalytic/structural roles in enzymes and a regulatory role in signal transduction.

49. Red meat, legumes, eggs, fish, grains and grain based products, unrefined and fortified cereal and raisins are dietary sources of zinc. In the UK, zinc supplements provide an intake of up to 50 mg per day.

50. The initial absorption of zinc occurs in the stomach, the majority however is absorbed in the upper small intestine. The absorption of zinc salts depends on solubility and is regulated in response to the quantity of bioavailable zinc. When ingested, zinc will be firmly bound; virtually no zinc will circulate unbound. Zinc is secreted in and excreted from the intestinal tract and movement across the intestinal wall will depend on the concentration of zinc in the body.

Toxicity

51. Zinc is not stored in the body; excess intakes of zinc lead to a reduced absorption and increased excretion. However, acute and chronic zinc poisonings have been documented in humans, often as a result of food/drink storage in galvanised containers.

---

[1] https://cot.food.gov.uk/sites/default/files/2014infantmetalssurveystatement.pdf
[2] https://cot.food.gov.uk/sites/default/files/cot/cotstatementtds200808.pdf

52. Gastrointestinal distress, including abdominal pains, diarrhoea and gastric pain, vomiting and nausea are common symptoms of acute oral exposure to zinc. Excessive or chronic high zinc intakes lead to biochemical and physiological changes, such as interference with the absorption of copper from the gastrointestinal tract. This can result in severe neurological diseases, anaemia and bone abnormalities, attributed to secondary copper deficiency.

HBGVs and UL

53. The drinking water quality standards for European countries, including the UK, provide a regulatory maximum limit for zinc of 5 mg/L. The World Health Organisation (WHO) recommends that the concentration of zinc in drinking water should not exceed 3 mg/L.

54. Zinc is present in licensed medicine products for the treatment and prevention of deficiencies. Products available from a pharmacist have a maximum daily dose of 150 mg, products available for general sale have concentrations of 5 mg.

55. Composition for follow-on formulae is regulated by Directive 2006/141/EC, composition of nutritionally complete foods for special medical purposes intended for use by infants are regulated by Directive 1999/21/EC. Processed cereal-based foods for infants and young children are regulated by Directive 2006/125/EC; other foodstuffs intended for infants and young children should provide at least 15% of the reference values for nutrition labelling for foods intended for infants and young children as laid down in Directive 2006/141/EC.

56. The EVM (2003) derived a safe upper level (SUL) for supplemental zinc of 25 mg per day (equivalent to 0.4 mg/kg bw per day, 60 kg in addition to dietary zinc) based on a lowest observed adverse effect level (LOAEL) of 50 mg per day for potential secondary copper deficiency in epidemiological studies. An uncertainty factor (UF) of 2 was applied for extrapolation from a LOAEL to a no observed adverse effect level (NOAEL).

57. The Joint FAO/WHO Expert Committee on Food Additives (JECFA, 1982) established a provisional maximum tolerable daily intake (PMTDI) of 0.3 – 1.0 mg/kg bw per day (for adults) based on clinical studies administrating zinc sulphate (equivalent to 200 mg elemental zinc) over several months without adverse effects.

58. The SCF (2003; 2006; 2017) derived a tolerable upper intake level (UL) of 25 mg per day for adults (equivalent to 0.4 mg/kg bw per day, 60 kg bw) based on a NOAEL of 50 mg per day for a wide range of indicators for copper status in epidemiological studies and the application of an UF of 2 for the small number of subjects and relative short time period. In the absence of adequate data for children, the SCF chose to extrapolate from adults to children on a body weight basis, resulting in an UL of 7 mg per day (equivalent to 0.5 mg/kg bw per day[3]) for children age 1-3 years and 10 mg per day (equivalent to 0.3 mg/kg bw per day[3]) for children age 4-6 years.

[3] Calculated for this scoping paper using the body weight from the 1-6 National Diet and Nutrition Survey (NDNS) (Bates et al., 2012 & 2014).

59. EFSA (2014) assessed the dietary reference values (DRVs)[4] for zinc and derived population reference intakes (PRIs)[5] for infants and children based on the PRIs for adults by assuming a coefficient for variation of 10%. The resulting PRIs for infants and children aged 7 to 11 months, 1 to 3 years and 4 to 6 years are 2.9, 4.3 and 5.5 mg per day, respectively.

Exposure Assessment

Dietary exposure

60. Consumption data (on a body weight basis) for the estimated dietary exposure are from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) (DH, 2013) and from years 1-6 of the National Diet and Nutrition Survey (NDNS) (Bates et al., 2012 & 2014)

61. Concentrations of zinc have recently been measure in an FSA survey of metals and other elements in infant formula and foods (Infant Metal Survey, FSA 2916a) and in the composite food samples of the 2014 Total Diet Study (TDS, FSA 2016b). Table 1 provides the mean and 97.5th percentile estimated dietary exposures to zinc for children aged 4 to < 12 months and 1 to < 5 years.

Table 1 Estimated mean and 97.5th percentile exposure to zinc (mg per day) in children aged 4 to < 12 months and 1 to < 5 years.

Age	Exposure (mg per day)	
	Mean	97.5th percentile
4 months to < 12 months*	4.3	7.0
1 to < 1.5 years**	3.7	7.1
1.5 to < 2 years**	4.5	8.0
2 to < 3 years**	4.5	7.2
3 to < 4 years**	4.7	7.7
4 to < 5 years**	5.1	8.1

* Exposure assessments for this age group were calculated from concentration data from the Infant Metals Survey, (FSA 2016a) using consumption data from DNSIYC.

** Exposure assessments for this age group were calculated from concentration data from the TDS (FSA, 2016b) using consumption data from NDNS

Human breast milk

62. A zinc concentration of 0.3 mg per 100 mL was reported for mature breast milk in McCance and Widdowson (2015). The value was obtained using pooled samples of breast milk donated from 96 mothers from different parts of Great Britain. 53% of the mothers reported taking vitamins and/or iron supplements during breastfeeding but the zinc content of the supplements, if any, was not reported. The value reported in McCance and Widdowson, although originally from 1975, falls within the range of zinc concentrations reported in more recent UK and European data.

[4] Complete set of nutrient recommendations and reference values, such as population reference intakes, average requirements, adequate intake levels and lover threshold intake.

[5] Level of a (nutrient) intake that is adequate for virtually all people in a population

63. Based on the concentrations reported in McCance and Widdowson (2015), zinc exposures were estimated for exclusively breastfed infants consuming average (800 mL) and high-level (1200 mL) volumes of breast milk (Table 3).

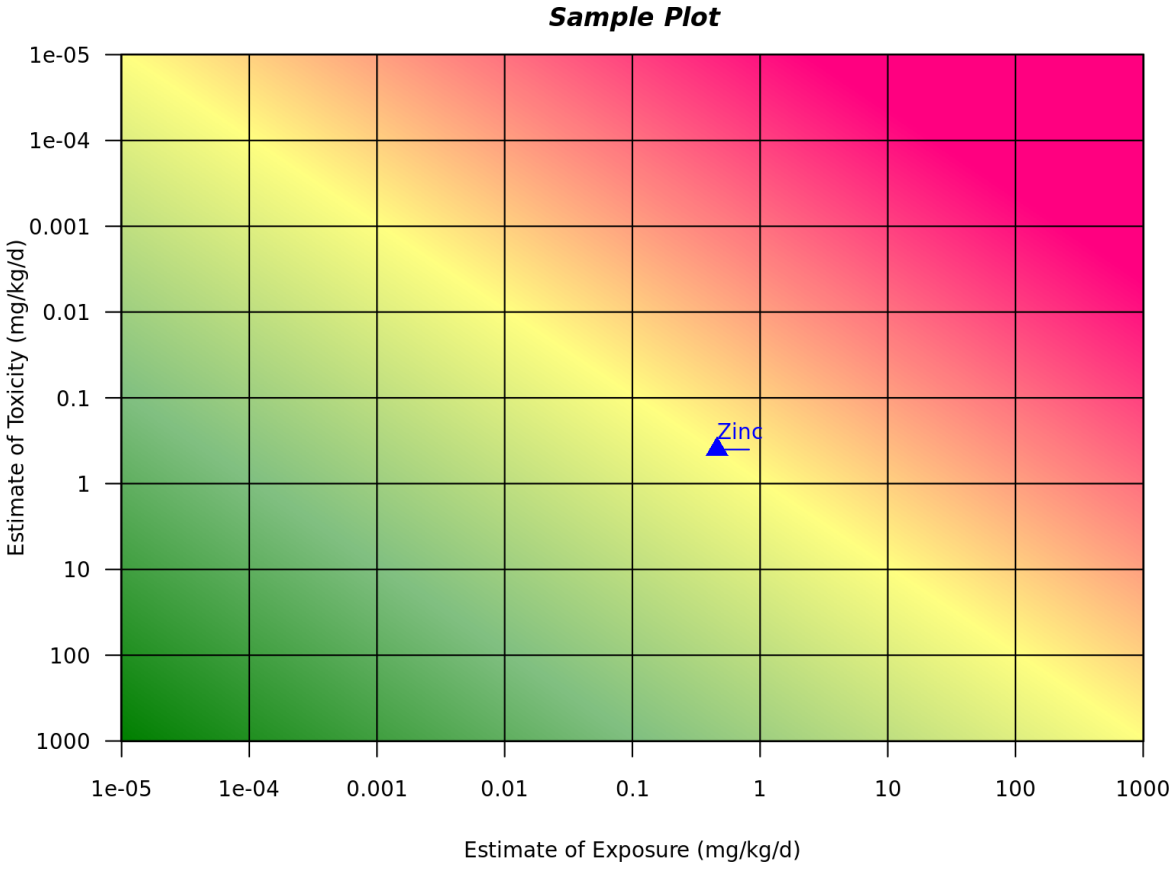
Table 3 Zinc exposure (mg per day) from exclusive breastfeeding estimated for average and high-level consumption of breast milk.

Zinc concentration (mg/L)	Exposure (mg per 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
3	2.4	2.4	3.6	3.6

Infant exposure is based on consumption of 800 mL or 1200 mL per day, and expressed on a bodyweight (5.9 kg for infants aged 0-4 months and 7.8 kg for infants aged 4 to < 6 months) basis. Values rounded to 2 significant figures (SF)

Risk 21

64. Figure 1 shows the 97.5th percentile estimated dietary exposure for zinc across all age groups.



Risk characterisation

65. The ULs derived by SCF for children start at the age of 12 months and would therefore not be applicable to infants aged 4 to < 12 months. Using the same approach as SCF the extrapolated UL for infants aged 4 to < 12 months would be 3.6 mg per day (equivalent to 0.4 µg/kg bw per day, based on a bodyweight of 9 kg for infants from DNSIYC).

66. For infants aged 4 to < 12 months the mean and 97.5th percentile estimated exposures exceed the UL of 3.6 mg per day 1 and 2-fold, respectively. The mean estimated exposures for children aged 1 to < 4 years are below the UL of 7 mg per day set by SCF; the 97.5th percentile estimated exposures are at or marginally above the UL. Estimated mean and 97.5th percentile exposure for children aged 4 to < 5 years are below the UL of 10 mg per day set by SCF.

67. Assuming a zinc concentration of 3 mg/L in breast milk, estimated exposures for exclusively breastfed infants (0 to 6 months) are within or at the UL of 3.6 mg per day for infants.

68. Current estimated dietary exposure did not indicate excessive zinc intake and are therefore unlikely to be of toxicological concern.

69. All HBGVs and UL for infants and children are derived from extrapolation from adults, based on epidemiological/clinical studies in adults. It is therefore difficult to identify a HBGV or UL which is applicable for all infants and children.

70. EFSA derived an average requirement (AR) for dietary zinc for infants > 7 months and children based on an extrapolation from estimates of adult losses plus zinc requirements for growth. The AR range from 2.4 mg per day (infants 7 to 11 months of age) to 11.8 mg per day (adolescent boys).

71. The UK Committee on Medical Aspects of Food and Nutritional Policy (COMA) derived reference nutrient intakes (RNIs) for infants, toddlers and other children of 4, 5 and 6.5 mg/day, respectively (DH, 1991).

72. The mean estimated exposures in infants exceed the AR set by EFSA and are at the RNI set by COMA; mean estimated exposures for all other age groups are within or at the RNIs set by COMA. The 97.5th percentile estimated exposures exceed the RNIs in all age groups.

73. As stated previously for HBGVs and UL, these average requirements were an extrapolation from adults due to the absence of knowledge about variations and it has been noted by EFSA, that children have a larger loss of zinc than adults.

Conclusions

74. Estimated dietary exposures for children aged 4 to < 12 months and 1 to < 5 years do not indicate excessive zinc intake, either from breastmilk or other foods and are therefore unlikely to be of toxicological concern.

75. The levels however do exceed the AR/RNIs set by other regulatory bodies but as with the HBGVs and ULs, these are derived by extrapolation from adults and it is difficult to identify how applicable they are to infants, toddlers and young children.

Questions to be asked to the Committee

i) Do the Committee agree that the exposure from dietary zinc is not of toxicological concern?

ii) Do the Committee consider it sufficient to include a brief summary of the important points (HBGVs, exposure, conclusions) in the overarching statement?

iii) Do the members have any other comments?

Secretariat

July 2018

References

Bates B, Lennox A, Prentice A, Bates C, Page P, Nicholson S, Swan G (2014). National Diet and Nutrition Survey Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/2009 – 2011/2012) https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/594360/NDNS_Y1_to_4_UK_report_executive_summary_revised_February_2017.pdf

Bates B, Cox L, Nicholson S, Page P, Prentice A, Steer T Swan G (2016). National Diet and Nutrition Survey Results from Years 5 and 6 (combined) of the Rolling Programme (2012/2013 – 2013/2014) https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/551352/NDNS_Y5_6_UK_Main_Text.pdf

Bates CJ and Tsuchiya H (1990). Zinc in breast milk during prolonged lactation: comparison between the UK and the Gambia. Eur J Cli Nutr 44(1):61-69

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (2018). Statement on the results of the 2014 survey of metals and other elements in infant food. https://cot.food.gov.uk/cotstatements/cotstatementsyrs/cot-statements-2018/statement-on-the-results-of-the-2014-survey-of-metals-and-other-elements-in-infant-foods

Department of Health (1991). Dietary Reference Values for Food Energy and Nutrients for the United Kingdom. Report of the Panel on Dietary Reference Values, Committee on Medical Aspects of Food and Nutrition Policy. HMSO, London.

Department of Health (2013). Diet and Nutrition Survey of Infants and Young Children (DNSIYC), 2011. http://transparency.dh.gov.uk/2013/03/13/dnsiyc-2011/

Domelloef M, Loennerdal B, Dewey KG, Cohen RJ, Hernell O (2004). Iron, zinc and copper concentrations in breast milk in independent maternal mineral status. Am J Vlin Nutr 79(1): 11-115.

European Food Safety Authority (2014). Scientific Opinion on Dietary Reference Values for zinc. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). EFSA Journal 12(10): 3844. https://www.efsa.europa.eu/sites/default/files/consultation/140514%2C0.pdf

Expert Group on Vitamins and Minerals (2003). Safe Upper Levels for Vitamins and Minerals. https://cot.food.gov.uk/sites/default/files/vitmin2003.pdf

FSA (2016a). Survey of metals and other elements in infant foods (to be published).

FSA (2016b). Study of metals and other elements in the 2014 Total Diet Study (to be published).

Fransson GB, Gebre-Medhin M, Hanbraeus L (1984). The human milk contents of iron, copper, zinc, calcium and magnesium in a population with havitually high intake of iron. Acta Paediatr Scand 73($): 471-476.

Joint FAO/WHO Expert Committee on Food Additives (1982). Evaluation of certain food additives and contaminants. Twenty-sixth Report. WHO Technical Report Series 683. http://apps.who.int/iris/bitstream/handle/10665/41546/WHO_TRS_683.pdf;jsessionid=AA31C89A6E5CC1E119FADF28E6896153?sequence=1

Kantol M and Vartiainen T (2001). Changes in selenium, zinc, copper and cadmium contents in human milk during the time when selenium has been supplemented to fertilizers in Finland. J Trace Elem Med Biol 15(1): 11-17.

Ortega RM, Andres P, Martinez RM, Lopez-Sobaler AM, Quintas ME (1997). Zinc levels in maternal milk: the influence of nutritional status with respect to zinc during the third trimester of pregnancy. Eur J Cli Nutr 51(4): 253-258.

Rydzewska A and Krol I (1996). Contents of zinc, copper and cadmium in milk of women living in Poznan. Ginekol Pol 67(£): 125-128.

Scientific Committee on Food (2003). Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Zinc. European Commission, Health & Consumer Protection Directorate-General. https://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scf_out177_en.pdf

Scientific Committee on Food (2006). Opinion of the Scientific Panel on Dietetic Product, Nutrition and Allergies on Tolerable Upper Intake Levels for Vitamins and Minerals. http://www.efsa.europa.eu/sites/default/files/efsa_rep/blobserver_assets/ndatolerableuil.pdf

Scientific Committee on Consumer Safety (2017). Opinion on water-soluble zinc salts used in oral hygiene products. European Union. https://ec.europa.eu/health/sites/health/files/scientific_committees/consumer_safety/docs/sccs_o_207.pdf

Stawarz R, Formicki G, Massanyi P (2007). Daily fluctuation and distribution of xenobioticx, nutritional and biogenic elements in human milk from Southern Poland. J Enironm Sci Health A Tox Hazard Subst Environ Eng 42(*): 1169-1175.

Wasowicz W, Gromadzinska J, Szram K, Rydzynski K, Cieslak J, Pietrazak Z (2001). Selenium, zinc and copper concentrations in the blood and milk of lactating women. Biol Trace Elem Res 79(3): 221-233.

Appendix 1

Literature search terms

The focus of this scoping paper was a first comparison of estimated exposures in UK children aged 1-5 years to the current HBGVs and (S)UL.

To update our knowledge, we carried out a literature search using PubMed with emphasis on breast milk data.

No specific time period was covered by the search.

Search terms (Number of papers retrieved)

Zinc	and	Breast milk Breastfeeding		
		Breast milk	and	United Kingdom (2), England, Britain Wales, Scotland, Ireland Netherlands, Belgium, France Germany, Austria, Switzerland Spain, Italy, Greece, Portugal Norway, Finland (1), Sweden (2) Poland (3), Hungary, Russia, Ukraine, Serbia Estonia, Romania, Bulgaria, Moldova

A total of eight papers with European breast milk data were identified; however, none of the retrieved papers were subsequently used for the exposure assessment.

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

Scoping paper of potential risks from contaminants in the diet of children aged 1 to 5 years

Selenium

Background

76. Selenium is a group VI metal with both metallic and non-metallic properties (EVM, 2003). It exists in four oxidation states (-2, 1, +2, +6) and forms compounds analogous to those formed by sulphur.

77. In food, selenium is mainly present in organic compounds, as L-selenomethionine and L-selenocysteine, with lower amounts in inorganic compounds, as selenate and selenite and is an essential micronutrient to human health. It is present in a number of foodstuffs, notably nuts, offal, eggs and poultry and mushrooms and in lower quantities in fruits and vegetables with the exception of members of *Brassica* genus (cabbage, cauliflower etc) which contain relatively high amounts of selenium (SCF, 2000; Kieniszek and Stanislaw, 2016).

78. Selenium compounds are readily absorbed in the small intestine. Selenium is an essential element to human health and is widely distributed throughout the body and can be detected in breast milk. It has also been reported to cross the placenta in animals. Selenium compounds are incorporated in selenoproteins, which have a variety of biological functions including antioxidant effects, T-cell immunity, thyroid hormone metabolism, selenium homeostasis and transport, and skeletal and cardiac muscle metabolism.

79. Upon absorption, selenium compounds can also bind to selenium binding proteins or, as a way of regulating selenium metabolism, form methylated metabolites in the liver. These compounds are excreted predominantly in the urine. Excretion of selenium can also occur at a smaller extend in the faeces or, for some volatile compounds in the breath (EFSA, 2014; EVM, 2003).

Toxicity

80. Selenium deficiency interferes with the expression and function of selenoproteins. Although the clinical manifestations are poorly defined symptoms reported from epidemiological studies in populations with low selenium intake and patients receiving selenium-free total parenteral nutrition include skeletal myopathy, cardiomyopathy and muscle weakness. Selenium deficiency is also linked to the manifestation of the degenerative Keshan and Kashin-Beck disease (SCF, 2000; EFSA, 2014).

81. High exposure to selenium can lead to acute toxicity. This is characterised by hypersalivation, emesis and garlic aroma on the breath. Other symptoms include severe vomiting and diarrhoea, hair loss, neurological disturbance and fatigue (EVM,2003).

82. Chronic toxicity, or selenosis, leads to hair and nail changes, skin lesions and clinical neurological effects such as peripheral hypoaesthesia, acroparasthaesiae, pain and hyperreflexia; numbness, convulsions and paralysis may then develop (EVM, 2003).

83. Carcinogenicity of selenium has been assessed in a number of studies. These are generally inconclusive mainly due to issues with the study design and interpretation. Except for some selenium compounds not used in food, i.e. selenium sulphide, selenium diethyldithiocarbamate, bis-amino-phenyl selenium dihydroxide, experimental data do not indicate that inorganic selenium salts or organic selenium compounds relevant in food and nutrition are carcinogenic. A number of *in vivo* and *in vitro* studies have also been used to evaluate the genotoxic potential of selenium compounds. The SCF considered that the effects seen *in vitro* systems and also *in vivo* at toxic doses, were related to the generation of reactive oxygen radicals, were dose dependent and showed a threshold *in vivo* and not occurring at nutritionally adequate intakes (SCF, 2000).The SCF also found that there was no evidence for teratogenicity in epidemiological studies in populations with very high selenium consumption and in a reproductive study in macaques fed selenomethionine at 25,150, and 300 µg/kg/bw/d. The no observed adverse effect level (NOAEL) in the study was 25 µg/kg bw/d due to maternal toxicity occurring in the mid and high dose groups, characterised by emesis and loss of appetite (SCF,2000). The Expert Group on Vitamins and Minerals (EVM) noted that adverse effects have been reported on the reproductive system of various animals, though not primates.

HBGV

Upper Intake Level (UL)

84. The Scientific Committee on Food (SCF) established in 2000 anUL for selenium at 300 µg/day for adults, including pregnant and lactating women. This was based on a NOAEL of 850 µg/day for clinical selenosis (Yang *et al.,* 1989*)* and applying an uncertainty factor of 3. The NOAEL was derived based on the absence of clinical signs in individuals with selenium levels below 1000 µg/L. In the absence of data to derive specific ULs for children, the SCF extrapolated the UL from adults to children based on reference body weights. The proposed UL values for children and adolescents were 60, 90, 130, 200 and 250 µg/day for children aged 1-3, 4-6, 7-10, 11-14 and 15-17 years respectively.

85. In their evaluation, the EVM used the same data set as the SCF to derive an UL of 450 µg/day. They considered that there were discrepancies in NOAELs in the series of studies conducted by Yang *et al.* and therefore used the Lowest Adverse Effect Level (LOAEL) of 900 µg/day and applied an uncertainty factor of 2 to

extrapolate to a NOAEL. An uncertainty factor for inter-individual variation was not deemed necessary as they considered that the value was based on a population study.

Dietary Reference Values (DRVs)

86. In 2014, the EFSA Panel on Dietetic Products, Nutrition and Allergies (EFSA,2014) derived DRVs for selenium. The criterium for establishing the DVR in adults was the levelling off of plasma selenoprotein P which would indicate adequate supply of selenium to all tissues. For infants aged 7–11 months, an Adequate Intake (AI) of 15 µg/day was derived by extrapolating upwards from the estimated selenium intake with breast milk of younger exclusively breast-fed infants, taking into account differences in reference body weights.

87. The AIs for children were extrapolated from the adult AI (70µg/day) by isometric scaling and the application of a growth factor. These resulted in AIs of 15 µg/day for children aged 1 to 3 years and 20 µg/day for children aged 4-6 years.

Exposure Assessment

Dietary exposure

88. Consumption data (on a body weight basis) for the estimated dietary exposure are from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) (DH, 2013) and from years 1-6 of the National Diet and Nutrition Survey (NDNS) (Bates et al., 2012 & 2014)

89. Concentrations of selenium have recently been measured in an FSA survey of metals and other elements in infant formulae and foods (referred to as the Infant Metals Survey, FSA 2016a), and in the composite food samples of the 2014 Total Diet Study (TDS, FSA 2016b). The exposure data derived from the Infant Metals Survey allow estimation of selenium exposure in infant formula, commercial infant foods and the most commonly consumed adult foods ('other foods') as sold, whereas the results from the TDS are based on analysis of food that is prepared as for consumption. In addition, the Infant Metals Survey included analysis of infant formulae and commercial infant foods which are not included in the TDS. Table 1 provides the mean and 97.5th percentile dietary exposures to selenium for children aged 4 months to 5 years. The mean exposures to selenium range from 7 µg/day (lowest lower-bound (LB)) to 46 µg/day (highest upper-bound (UB)). The corresponding 97.5th percentile exposures range from 20 to 76 µg/day.

Table 1 Estimated mean and 97.5th percentile exposure to selenium (µg/ per day) in infants aged 4 months to 5 years.

Age	Exposure (µg/ day) LB-UB range	
	Mean	97.5th percentile
4m to 1 year*	7-15	20-25
1 to <1.5 yrs*	13-15	25-27
1.5 to <2 yrs+	18-39	35-62
2 to <3 yrs+	18-40	33-61
3 to <4 yrs+	20-43	36-72

4 to<5 yrs+	22-46	43-76

Values are rounded to 2 significant figures (SF).. The LB was calculated by treating concentration data < LOD as 0, while the UB was determined by treating values <LOD as equal to the LOD.

* Exposure assessments for this age group were calculated from concentration data from the Infant Metals Survey, (FSA 2016a) using consumption data from DNSIYC.

+ Exposure assessments for this age group were calculated from concentration data from the TDS (FSA, 2016b) using consumption data from NDNS

Human breast milk

90. Based on a number on European studies, the EFSA Panel on Dietetic Products, Nutrition and Allergies in 2014 (EFSA, 2014) considered an average concentration in mature breast milk in the EU of 15 µg/L. An older review by J. Dorea (2002) reports mean/median concentrations of selenium in human breast milk that range from 8.3µg/L in the 1-12 months stage of lactation (Radzanowski *et al.*1997) to 20.6 µg/L in mature milk (Foster *et al.* 1996).

91. Taking a conservative approach, the highest concentration of the UK specific data reported in Foster *et al.* (1996) was used to estimate exposures for exclusively breastfed infants consuming average (800 mL) and high-level (1200 mL) volumes of breast milk (Table 3).

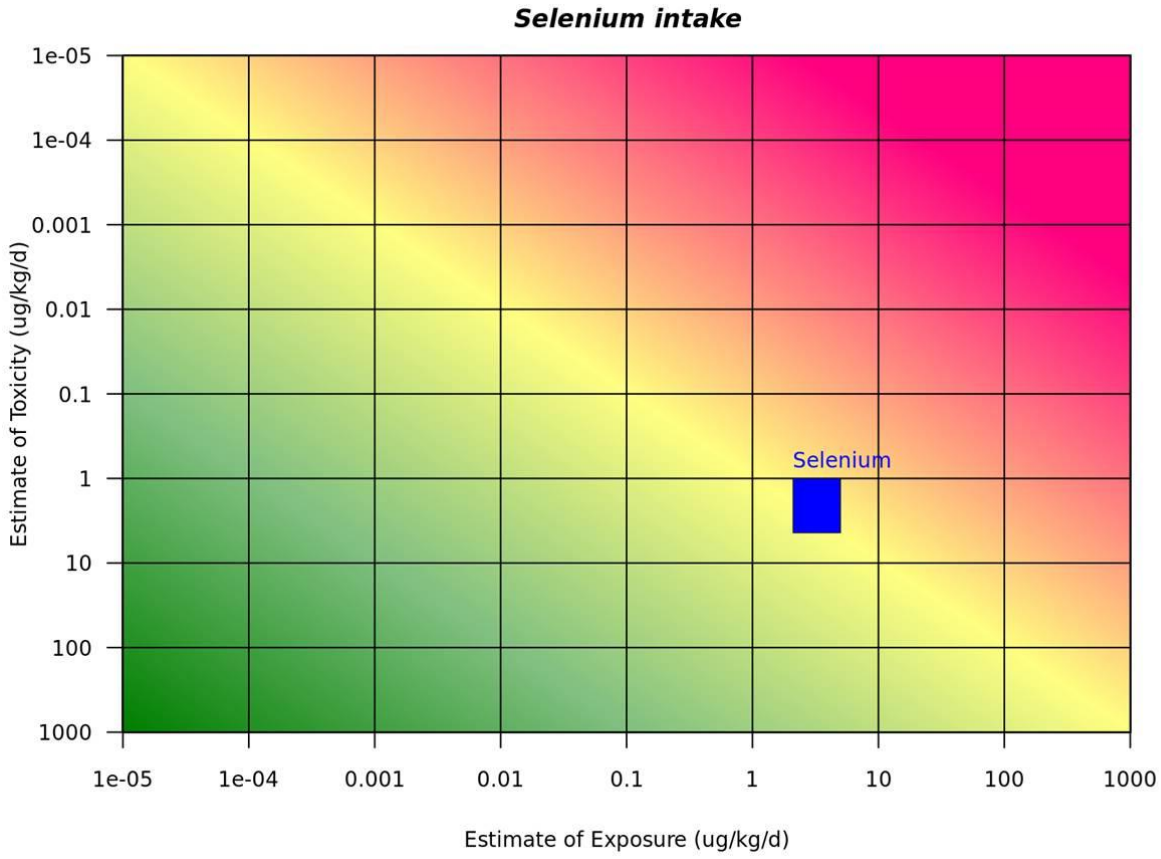
Table 3 Selenium exposure (µg/ per day) from exclusive breastfeeding estimated for average and high-level consumption of breast milk.

Selenium concentration (mg/L)	Exposure (µg per day)	
	Average consumer (800 mL/day)	High consumer (1200 mL/day)
	0 to < 6 months	0 to < 6 months
20.6	16	25

Values rounded to 2 SF

Risk 21

92. Figure 1 shows the 97.5th percentile estimated dietary exposure for selenium.



Risk characterisation

Dietary exposure

93. Data in Table 1 indicate that UB mean and 97.5th percentile exposures are within or close to their respective ULs for children aged 1-3 and 4-6 years. For the age group of 3 to <4 years, the UL is likely between the ULs set for 1-3 years and 4-6 years and therefore exposures are not of concern.

94. As the UL extrapolated by SCF starts at the age of 1 years old, it would not apply to infants aged between 4-12 months. In their evaluation the SCF extrapolated from the UL set for adults on a body weight basis, to derive a UL for children. Using the same approach and assuming that the body weight for adults used by SCF is 68 kg (SCF,1993), the extrapolated UL for infants aged 4 to 12 months would be 40 µg/day (rounded to 2SF, based on a bodyweight of 9.12 kg for infants from DNSIYC). Based on Table 1, the UB exposures at the mean and 97.5th percentile for infants is below the UL.

Human breast milk

95. The extrapolated UL would be 26 µg/day for infants 0 to <4 months (assuming a bodyweight of 5.9 kg) and 34 µg/day for >4 to <6 months old infants (assuming a

bw of 7.8 kg). For the age groups of 0 to<4 and >4 to <6 months, the average and high level exposure via breast milk are below the ULs calculated.

Conclusions

96. Based on the data presented above, the estimated dietary exposures in infants and young children are not of toxicological concern.

Questions to be asked to the Committee

i) Do the Committee agree that the exposure from dietary selenium is not of toxicological concern?
ii) Do the members have any other comments?

Secretariat

June 2018

References

- Bates B, Cox L, Nicholson S, Page P, Prentice A, Steer T Swan G (2016). National Diet and Nutrition Survey Results from Years 5 and 6 (combined) of the Rolling Programme (2012/2013 – 2013/2014) https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/551352/NDNS_Y5_6_UK_Main_Text.pdf
- Bates B, Lennox A, Prentice A, Bates C, Page P, Nicholson S, Swan G (2014). National Diet and Nutrition Survey Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/2009 – 2011/2012) https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/594360/NDNS_Y1_to_4_UK_report_executive_summary_revised_February_2017.pdf
- Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (2018). Statement on the results of the 2014 survey of metals and other elements in infant food. https://cot.food.gov.uk/cotstatements/cotstatementsyrs/cot-statements-2018/statement-on-the-results-of-the-2014-survey-of-metals-and-other-elements-in-infant-foods
- Dorea J.G (2002). Review article: Selenium and breast-feeding. British Journal of Nutrition (2002), 88, 443–461.
- European Food Safety Authority (2014). Scientific Opinion on Dietary Reference Values for selenium. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). EFSA Journal 2014;12(10):3846. https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2014.3846
- Expert Group on Vitamins and Minerals (2003). Safe Upper Levels for Vitamins and Minerals. https://cot.food.gov.uk/sites/default/files/vitmin2003.pdf
- Foster LH, Kondza B & Surner S (1996) Selenium content of breast milk and infant formulae: an estimation of intakes in the UK. Metal Ions in Biology and Medicine 4, 505–507.
- Kieliszek M, Błazejak S (2016). Current Knowledge on the Importance of Selenium in Food for Living Organisms: A Review. Molecules 2016, 21, 609; doi:10.3390/molecules21050609
- Radzanowski GM, Jackson K, Pramuk K & Kaup SM (1997) Comparison of trace elements and macronutrients in breast milk of women from eight different geographical locations. In Trace Elements in Man and Animals, TEMA-10. Evian, France: NRC Research Press.
- Scientific Committee for Food (1993). Commission of the European Communities. Reports of the Scientific Committee for Food of the European Community. Thirty-first series. Nutrient and energy intakes for the European Community. Commission of the European Communities, Luxembourg.
- Scientific Committee on Food (2000). Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Selenium. https://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scf_out80g_en.pdf
- FSA (2016a). Survey of metals and other elements in infant foods (to be published)
- FSA (2016b). Study of metals and other elements in the 2014 Total Diet Study. (to be published)

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

Scoping Paper on the potential risks from phthalates in the diet of infants aged 0 to 12 months and children aged 1 to 5 years

Introduction

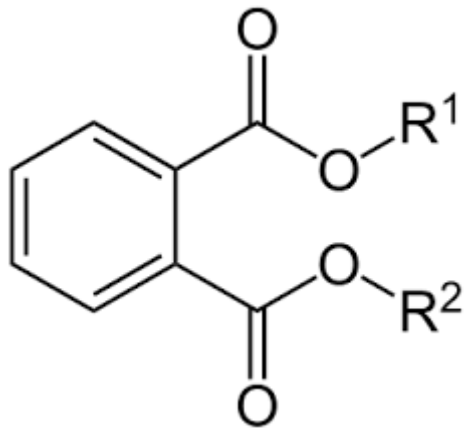
97. The Scientific Advisory Committee on Nutrition (SACN) is undertaking a review of scientific evidence that will inform the Government's dietary recommendations for infants and young children. The SACN is examining the nutritional basis of the advice. The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) was asked to review the risks of toxicity from chemicals in the diet of infants, most of which has been completed, 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.

98. This discussion paper estimates phthalate exposures for infants and young children in the UK aged 0 to 12 months and 1 to 5 years, respectively.

Background

99. Phthalates are esters of the aromatic dicarboxylic acid phthalic acid (Fig 1) that have a long history of use as additives to plastics to improve their flexibility but also have wide applicability across industry, for example in pharmaceutical coatings, paints, cosmetics and food contact materials.

Figure 1. Structure of phthalate esters. R1 and R2 are hydrocarbon groups. (EFSA 2005)



100. Phthalates do not form covalent bonds with the material into which they are incorporated. The extensive and historic use of phthalates has led to their being widely distributed in the environment and the food chain. The general population is

exposed to phthalates via food and drinking water, but also through inhalation and dermal exposure, as well as *in utero*. (Heudorf *et al* 2007).

101. In 2005, EFSA performed risk assessments on a small range of the most widely used phthalates and derived tolerable daily intake values (TDIs) for them, as shown in Table 1. Table 1 also includes the TDI for diethyl phthalate (DEP) that was derived by the World Health Organization in 2003.

Table 1. TDI values derived for six phthalates by EFSA and WHO.

Phthalate	TDI (mg/kg bw)	Basis
Dibutyl phthalate (DBP)	0.01*	Male rat reproductive development
Di-(2-ethylhexyl) phthalate (DEHP)	0.05*	Testicular and developmental toxicity
Benzylbutyl phthalate (BBP)	0.5*	Testicular toxicity and reduced ano-genital distance
Di-isononly phthalate (DiNP)	0.15*	Increased liver and kidney weights in rats
Di-isodecyl phthalate (DiDP)	0.15*	Dog liver swelling and hepatocyte vacuolisation
Diethyl phthalate (DEP)	5.0†	Developmental toxicity in mice

*Values from EFSA (2005 a – e)
†Value from WHO (2003)

102. Fromme *et al* (2013) presented data on total phthalate intake and dietary intake in 25 children aged 15 – 21 months. Intakes of DEP, DBP, Di-isobutyl phthalate (DiBP) and BBP were all markedly greater in total than in the diet, whereas the majority of DEHP intake was from the diet. The maximum daily intake from all sources were below their respective TDI value except for DiBP, for which the authors estimated the TDI to be the same as that for its straight chain isomer DBP, 0.01 mg/kg bw/ day. However, they stated that a higher TDI for DiBP (0.1 mg/kg bw/day) had also been derived:

https://www.cpsc.gov/s3fs-public/ToxicityReviewOfDiBP.pdf

103. In May 2011, COT produced a statement on dietary exposure to phthalates with data from the Total Diet Study (TDS), concentrating on the six compounds in Table 1 and concluded that the levels of phthalates that were found in samples from the 2007 TDS did not indicate a risk to human health from dietary exposure alone, either when the compounds were assessed alone or in combination

https://cot.food.gov.uk/sites/default/files/cot/cotstatementphthalates201104.pdf

Phthalates in breast milk

104. The concentration values of Del Bubba *et al* (2018) are the most recent and comprehensive European data set found in the literature and so these will be used to

assess the exposure and intake of the phthalates measured in breast milk in the absence of UK values.

Table 2 The concentration of 5 phthalates in breast milk (from Del Bubba, 2018)

Phthalate	**Number of samples**	**Minimum concentration (µg/L)**	**Mean concentration (µg/L)**	**Maximum concentration (µg/L)**
DBP	9	<3.5	7.1	19
DEHP	9	13	34	94
BBP	9	<2.0	1.7	3.2
DiNP	9	6.3	20	51
DiBP	9	11	37	77

Infant Formula

105. Del Bubba *et al* (2018) analysed 4 commercially available ready to use infant formulae, taking 5 samples per formula. The mean values found for the phthalates assayed were as follows in Table 3

Table 3 Concentration of phthalates in infant formula (from Del Bubba *et al* (2018))

Phthalate	Infant formula, Mean phthalate concentration (µg/kg)
DBP	6.2 - 11.0
DEHP	18 - 75
BBP	3.0 - 5.9
DiNP	2.1 - 2.9
DiBP	18 - 25

Drinking water

106. Potable tap water may be used in making up infant formula. The water companies in England & Wales, Scotland and Northern Ireland do not routinely survey UK drinking water for phthalates. Data from Spain and Portugal were available in the literature for phthalates in tap water. In Spain, across 7 locations, Dominguez- Morueco *et al* (2014) found that DBP was the most prevalent phthalate in tap water, at the highest concentration of 0.91 µg/l (range 0.33 – 0.91, mean 0.63 µg/l). In Portugal, Santana *et al* (2014) found DiBP at 0.17 µg/l DEHP at 0.13 – 0.17 µg/l in 2 of 4 locations.

Exposure

Exposure of infants to phthalates in breast milk

107. Using the minimum, average and maximum concentration data for phthalates in breast milk from Del Bubba *et a*l (2018) and estimated body weights for infants aged 0 - <4 months (5.9 kg, DH 1994) and 4 - <6 months (7.8 kg, DH 2013), the exposure of infants with either average (800 ml/day) or high (1200 ml/day) intake was calculated. See Table 4 below.

Table 4 Exposure of infants to phthalates in breast milk in age groups 0 - <4 months and 4 - < 6 months consuming breast milk at 800 ml and 1200 ml per day.

Phthalate	Level	Exposure (μg/kg bw/day)			
		0 – <4 months		4 – <6 months	
		800 ml/day	1200 ml/day	800 ml/day	1200 ml/day
DBP	Min	0.47	0.71	0.36	0.54
	Mean	0.96	1.4	0.71	1.1
	Max	2.6	3.9	2.0	2.9
DEHP	Min	1.8	2.6	1.3	2.0
	Mean	4.1	6.9	3.5	5.2
	Max	13	19	9.6	14
BBP	Min	<0.27	<0.41	<0.21	<0.31
	Mean	0.23	0.35	0.17	0.26
	Max	0.43	0.65	0.33	0.49
DINP	Min	0.85	1.3	0.64	0.97
	Mean	<2.7	<4.1	<2.1	<3.1
	Max	6.91	10	5.2	7.9
DiBP	Min	1.5	2.2	1.1	1.7
	Mean	5.1	7.6	3.8	5.7
	Max	10	16	7.9	11

Infant Formula

108. Since the maximum levels of phthalates measured above in infant formulae are in the same order of magnitude as those in breast milk, exposures would also be expected to fall within the same range as those arising from consumption of breast milk. The phthalates found in tap water would make only a minor impact on the levels in infant formula.

Exposure of infants and young children to phthalates in different foodstuffs

109. In August 2011, a survey of contaminants in food was undertaken by the FSA (Bradley 2011). Fifteen phthalates were surveyed. These data were used in this assessment. To estimate the total exposure of infants and young children to phthalates in food, exposure calculations were performed on di-(2ethylhexyl) phthalate (DEHP), the phthalate found in the highest concentration, and in dibutyl phthalate (DBP), the phthalate with the lowest TDI as determined by EFSA. To cover the rest of the phthalates, the total exposure to all compounds was also estimated.

110. The exposures of infants aged 4 – <18 months and 18 - <60 months to DEHP, DBP and total phthalates in the diet are shown in Tables 5 and 6. The values for all phthalates have no lower or upper bounds.

Table 5. Exposure to phthalates in food for infants aged 4 - <18 months

		Exposure (μg/kg bw/day)					
		DEHP		DBP		All phthalates	
		Mean	97.5%	Mean	97.5%	Mean	97.5%
Total	LB	3.5	14	0.14	0.39	8.28	20
	UB	4.3	14	0.46	1.0		

Table 6. Exposure to phthalates in food for infants aged 18 - <60 months

		Exposure (μg/kg bw/day)					
		DEHP		DBP		All phthalates	
		Mean	97.5%	Mean	97.5%	Mean	97.5%
Total	LB	3.3	7.3	0.23	0.42	10	18
	UB	4.6	8.5	0.56	0.93		

111. A breakdown of the exposure to the phthalates in each dietary component is presented in Annex A.

Risk characterisation

112. Where the compounds were found in dietary matrices (breast milk, infant formulae, food) they were compared with their respective EU TDIs for risk assessment purposes. Where other phthalates without derived TDIs are found, they were compared with the lowest listed TDI, that of DBP in order to give the most conservative risk assessment.

Table 7. Intake of phthalates as a percentage of their TDI in infants in age groups 0 - <4 months and 4 - < 6 months consuming breast milk at 800 ml and 1200 ml per day.

Phthalate	Level	Intake of phthalates as %TDI			
		0 – <4 months		4 – <6 months	
		800 ml/day	1200 ml/day	800 ml/day	1200 ml/day
DBP	Min	4.7	7.1	3.6	5.4
	Mean	9.6	14.	7.1	11
	Max	26	29	20	29
DEHP	Min	3.5	5.3	2.7	4.00
	Mean	9.2	14	7.0	10
	Max	26	38	19	29
BBP	Min	<0.054	<0.082	<0.042	<0.062
	Mean	0.046	0.07	0.034	0.052
	Max	0.086	0.13	0.066	0.098
DINP	Min	0.57	0.85	0.43	0.65
	Mean	<1.3	<2.7	<1.4	<2.1
	Max	4.6	6.9	3.5	5.2
DiBP*	Min	15	23	11	17

	Mean	50	76	38	57
	Max	100	160	79	120

*Using the TDI for DBP, 0.01 mg/kg bw/day

113. Table 7 shows that the intakes of the measured phthalates in breast milk are all well below their respective TDIs except for DiBP, where the highest level of intake at the maximum measured concentration exceeds the TDI by up to 60%. However, considering that the TDI for this compound could be ten times higher than used above, this is probably an overestimate.

Intake of phthalates through consumption of food.

114. Table 8, below, shows the intake of DEHP, DBP and all 15 measured phthalates in foodstuffs in the 4 - < 18-month age-group. DEHP and DBP are compared with their relevant TDI values and all phthalates with the lowest established TDI, 0.01 mg/kg.bw/day.

Table 8. Intake of phthalates in food as a percentage of the TDI 4 - <18 months

		Intake of phthalates as % of TDI					
		DEHP		DBP		All phthalates	
		Mean	97.5%	Mean	97.5%	Mean	97.5%
Total	LB	6.9	28	1.5	3.9	83	200
	UB	8.7	29	4.2	10		

LB = lower bound, UB = upper bound

115. In the 4 – <18-month age group, neither the most prevalent (DEHP) nor the most potent (DBP) phthalate exceeds that compound's TDI l at the mean nor the 97.5th percentile consumption level. However, when all the phthalates in the study were taken together and compared with the lowest established TDI, that of 0.01 mg/kg bw/day of DBP, the overall intake of all phthalates from all sources is up to approximately 200% of the TDI in the 97.5th percentile consumption group. However, all the other TDI values established by EFSA, and the value for DEP established by the WHO are at least 5-fold that of DBP and had the intake values been compared with the most prevalent phthalate, DEHP, rather than the most potent, then the total 97.5th percentile level for all phthalates would be only around 40% of the TDI.

116. Table 9, below, shows the intake of DEHP, DBP and all 15 measured phthalates in foodstuffs in the 18 - <60-month age group. DEHP and DBP are compared with their relevant TDI values and all phthalates with the lowest established TDI, 0.01 mg/kg.bw/day.

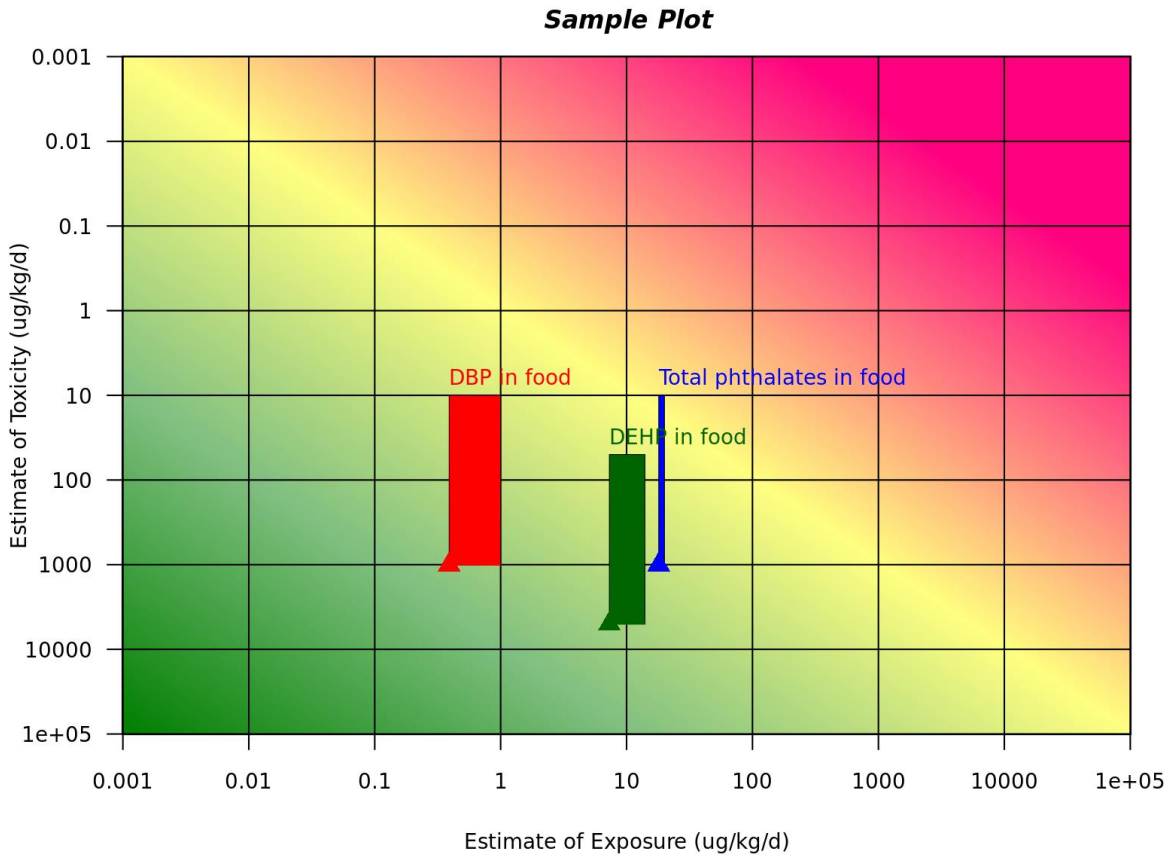
Table 9. Intake of phthalates in food as a percentage of the TDI 18 – <60 months

		Intake of phthalates as % of TDI					
		DEHP		DBP		All phthalates	
		Mean	97.5%	Mean	97.5%	Mean	97.5%
Total	LB	6.7	15	2.3	4.	100	180
	UB	9.1	17	5.3	9.32		

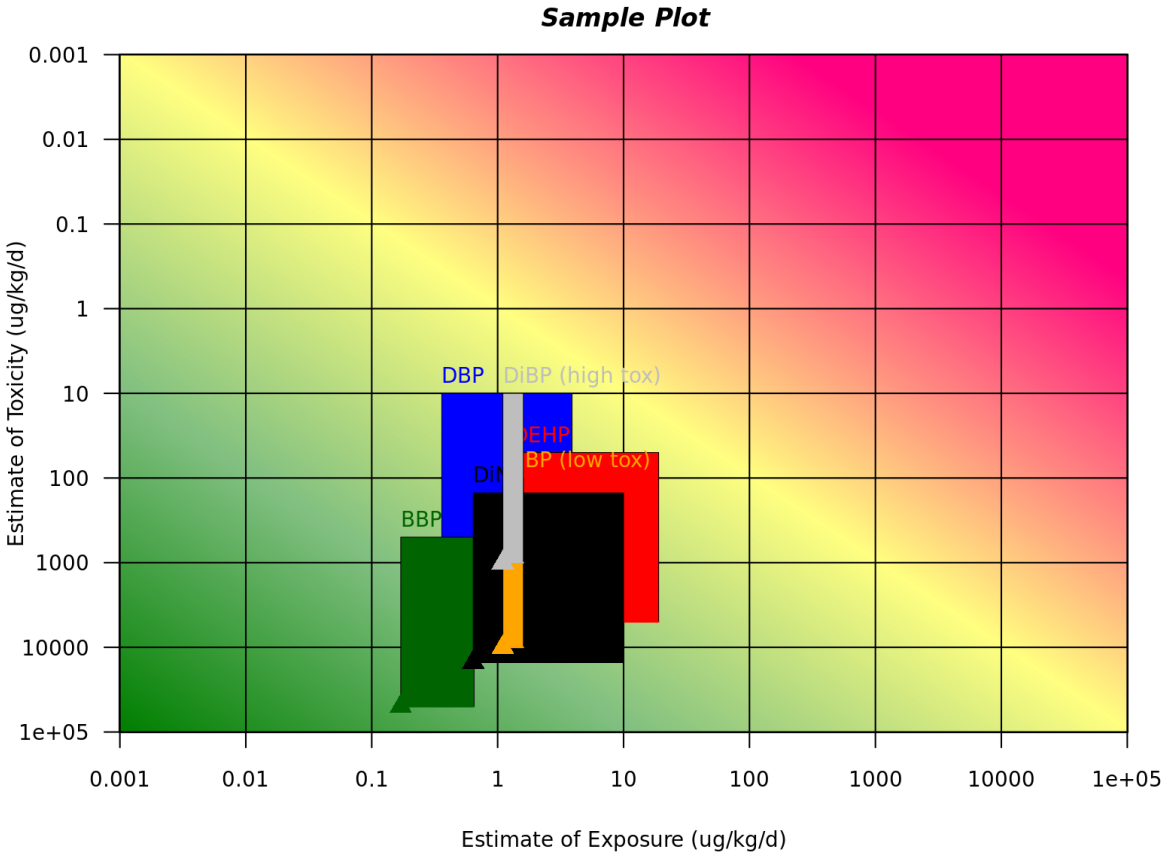
117. In the 18 - <60-month age group, once again neither the most prevalent (DEHP) nor the most potent (DBP) phthalate exceeds that compound's TDI l at the mean nor the 97.5th percentile consumption level. However, when all the phthalates in the study were taken together and compared with the lowest established TDI, that of 0.01 mg/kg bw/day of DBP, the overall intake of all phthalates from all sources is up to approximately 180% of the TDI in the 97.5th percentile consumption group. However, as noted above, had the intake values been compared with the most prevalent phthalate, DEHP, rather than the most potent, then the total 97.5th percentile level for all phthalates would be only around 36% of the TDI.

Risk21

118. Figure 1 shows the 97.5th percentile estimated dietary exposure for phthalates.



119. Figure 2 shows the 97.5th percentile estimated exposure for phthalates in breast milk.



Conclusions

120. Of all the phthalates found in breast milk, the only one that exceeded the TDI was DiBP in the high-level consumers, at up to 60% exceedance for the 0 - <4-month age group. Although undesirable, this is not a great exceedance and decreases as the infants grow. Moreover, this value assumed that the TDI of this compound was the same as that for its straight-chain isomer, DBP, which may be an underestimate of the true TDI value. All of the phthalates may therefore be lower than their TDI in all consumers.

121. Levels of phthalates in infant formula are in the same order of magnitude to those in breast milk so the exposure and risk from these is also likely to be similar.

122. None of the commodities in the diet individually exceed the TDI for the most prevalent nor the most potent phthalate although when all 15 measured phthalates were taken together and compared with the TDI of the most potent, exposure exceeded the TDI by 100% and 80% in the 4 - <18 month and the 18 - <60month age group respectively. This risk assessment is probably very conservative since the TDI of DBP is at least 5-fold lower than the next-most potent compound.

Questions for the Committee

1. Does the Committee agree with the approach of applying the lowest known TDI to perform the risk characterisation for all the phthalates combined?

2. In the light of the levels found in breast milk and food, does the Committee think that a full paper with risk assessments on other routes of exposure, ie, dust, soil and air should be performed and presented?

3. Do members have any further comments to make?

References

Bradley EL 2011 Report FD 10/05 FSA PROJECT C01048 Determination of phthalates in foods and establishing methodology to distinguish their source.

Del Bubba M, Ancillotti C, Checchini , L, Fibbi D, Rossini D, Ciofi L, Rivoira L, Profeti C, Orlandini S, Furlanetto S. Determination of phthalate diesters and monoesters in human milk and infant formula fy fat extraction ,size-exclusion chromatography clean-up and gas chromatography-mass spectrometry detection. Journal of Pharmaceutical and Biomedical analysis 2018 **148**:6 – 16.

EFSA 2005a Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and material in Contact with Food (AFC) on a request from the Commission related to Butylbenzylphthalate (BBP) for use in food contact materials. The EFSA Journal 2005. **241**: 1 – 14.

EFSA 2005b Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and material in Contact with Food (AFC) on a request from the Commission related to Di-Butylphthalate (DBP) for use in food contact materials. The EFSA Journal 2005. **242**: 1 – 17.

EFSA 2005c Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and material in Contact with Food (AFC) on a request from the Commission related to Bis(2-ethylhexyl) phthalate (DEHP) for use in food contact materials. The EFSA Journal 2005. **243**: 1 – 20.

EFSA 2005d Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and material in Contact with Food (AFC) on a request from the Commission related to Di-isononylphthalate (DiNP) for use in food contact materials. The EFSA Journal 2005. **244**: 1 – 18.

EFSA 2005e Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and material in Contact with Food (AFC) on a request from the Commission related to Di-isodecylphthalate (DiDP) for use in food contact materials. The EFSA Journal 2005. **245**: 1 – 14.

DH (1994) 'The COMA report on Weaning and the Weaning Diet.' Report on Health and Social Subjects 45. The Stationary Office, London

DH (2013). Diet and Nutrition Survey of Infants and Young Children (DNSIYC), 2011. Available at: http://transparency.dh.gov.uk/2013/03/13/dnsiyc-2011/

Dominguez-Morueco N, González-Alonso S, Valcárcel Y. Phthalate occurrence in rivers and tap water from central Spain. Science of the Total Environment 2014. **500-501**:139 - 146

Fromme H, Gruber L, Schuster R, Schlummer M, Kiranoglu M, Bolte G, Völkel W. Phthalate and di-(2ethylhexyl) adipate (DEHA) intake by German infants based on the results of a duplicate diet study and biomonitoring data (INES 2). Food and Chemical Toxicology 2013 **53**: 272 – 280

Heudorf U, Mersch-Sundermann V, Angerer J. Phthalates: toxicology and exposure. International Journal of Hygiene and Environmental Health 2007 210:623 – 634.
Santana J, Giraudi C, Marengo E, Robotti E, Pires S, Nunes I, Gaspar EM. 2014 Preliminary toxicological assessment of phthalate esters from drinking water in Portugal. Environmental Science and Pollution Research 2014 **21**: 1380 – 1390.

The World Health Organization (WHO) Diethyl Phthalate. Concise International Chemical Assessment Document 52 2003

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

Scoping Paper on the potential risks from phthalates in the diet of infants aged 0 to 12 months and children aged 1 to 5 years

Annex A Phthalates on dietary commodities

Table 1. Exposure to phthalates in food 4 - 18 months

Commodity	Exposure (μg/kg bw/day)					
	DEHP		DBP		All phthalates	
	Mean	97.5%	Mean	97.5%	Mean	97.5%
Bread	0.1819	0.7361	0.0237	0.0957	0.273	1.1047
Misc cereals	0.4011	1.4735	0.053	0.1946	1.3052	4.7943
Carcase meat	0.0755	0.4516	0.0053	0.0317	0.0976	0.584
Offals	0.0008	0	0-0.0001	0	0.0011	0
Meat products	0.2124	1.46	0.0099	0.0683	0.1052	0.7231
Poultry	0.2562	1.3307	0-0.0052	0-0.0269	0.1408	0.7312
Fish	0.5065	2.9969	0.006	0.0353	0.1322	0.7824
Fats and oils	0-0.003	0-0.0237	0.0015	0.0117	0.0083	0.0658
Eggs	0-0.0201	0-0.1325	0-0.0023	0-0.0152	0.048	0.3164
Sugars	0.0334	0.2056	0.0019	0.0119	0.0194	0.1192
Green veg	0-0.0147	0-0.0769	0-0.0164	0-0.086	0.2179	1.1424
Potatoes	0-0.0863	0-0.3459	0-0.0249	0-0.1	0.4236	1.698
Other veg	0.0922	0.3291	0-0.0196	0-0.07	0.5458	1.9483
Canned veg	0-0.0207	0-0.1419	0-0.0045	0-0.0307	0.1834	1.2558
Fresh fruit	0-0.0781	0-0.2987	0-0.0701	0-0.2681	0.4237	1.6195
Fruit products	0-0.0307	0-0.2514	0-0.0128	0-0.1049	0.3826	3.1299
Non alc beverages	0-0.1956	0-0.707	0.0451	0.1632	0.9966	3.6032
Milk	0-0.436	0-1.9205	0-0.0671	0-0.2955	1.0791	4.7531
Dairy products	1.694	12.9367	0-0.0903	0-0.6896	1.8902	14.4354

Nuts	0.0018	0.0232	0.0004	0.0059	0.0076	0.0992
Total	3.455-4.341	13.9887-14.407	0.1468-0.4602	0.3892-1.0251	8.2814	19.5404

Table 2. Exposure to phthalates in food 18 – 60 months

Commodity	Exposure (μg/kg bw/day)					
	DEHP		DBP		All phthalates	
	Mean	97.5%	Mean	97.5%	Mean	97.5%
Bread	0.3163	0.8325	0.0411	0.1082	0.4746	1.2494
Misc cereals	0.534	1.4438	0.0705	0.1907	1.7376	4.6974
Carcase meat	0.0753	0.3719	0.0053	0.0261	0.0973	0.4809
Offals	0.0008	0	0-0.0001	0	0.0011	0
Meat products	0.4952	1.8096	0.0232	0.0847	0.2453	0.8963
Poultry	0.368	1.3279	0-0.0074	0-0.0268	0.2022	0.7297
Fish	0.6998	2.7569	0.0082	0.0325	0.1827	0.7197
Fats and oils	0-0.0042	0-0.0259	0.0021	0.0128	0.0118	0.0719
Eggs	0-0.0224	0-0.1274	0-0.0026	0-0.0146	0.0536	0.3043
Sugars	0.1012	0.3869	0.0059	0.0224	0.0586	0.2243
Green veg	0-0.0098	0-0.0433	0-0.011	0-0.0484	0.1455	0.6429
Potatoes	0-0.0864	0-0.2608	0-0.025	0-0.0754	0.4243	1.2803
Other veg	0.0704	0.2151	0-0.015	0-0.0457	0.4167	1.2731
Canned veg	0-0.0283	0-0.133	0-0.0061	0-0.0288	0.2504	1.1764
Fresh fruit	0-0.1047	0-0.2877	0-0.094	0-0.2582	0.5676	1.5599
Fruit products	0-0.1196	0-0.634	0-0.0499	0-0.2645	1.4887	7.8921
Non alc beverages	0-0.3131	0-0.7647	0.0723	0.1765	1.5958	3.897
Milk	0-0.5315	0-1.6232	0-0.0818	0-0.2497	1.3155	4.0172
Dairy products	0.6728	3.1068	0-0.0359	0-0.1656	0.7507	3.4667
Nuts	0.0059	0.0726	0.0015	0.0184	0.0253	0.3112
Total	3.3397-4.5599	7.287-8.4589	0.2301-0.5587	0.4217-0.932	10.0456	18.1726