TOX/2015/32

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

COT CONTRIBUTION TO SACN REVIEW OF COMPLEMENTARY AND YOUNG CHILD FEEDING; PROPOSED SCOPE OF WORK FOR 1-5 YEAR OLD CHILDREN

Background

1. The Scientific Advisory Committee on Nutrition (SACN) is undertaking a review of scientific evidence that bears on the Government's dietary recommendations for infants and young children. The review will identify new evidence that has emerged since the Government's current recommendations were formulated, and will appraise that evidence to determine whether the advice should be revised. The recommendations cover diet from birth to age five years, but is being considered in two stages, focussing first on infants aged 0 to 12 months, most of which has been completed, and now on advice for children aged 1 to 5 years. The COT overarching statement on infant feeding is included in Annex A[1]

2. SACN is examining the nutritional basis of the advice. The Committee on Toxicity in Food, Consumer Products and the Environment (COT) was asked to review the risks of toxicity from chemicals in the infant diet. This includes the impact of maternal and child nutrition on the development of atopic or autoimmune disease in children. Aspects of this have been considered by the COT at their June and September meetings with further parts to be considered in December with a view to publishing a separate statement in 2016.

3. In the reviews of the infant diet, the COT noted a lack of data on various chemicals in food in the UK. As a result the Food Standards Agency (FSA) has commissioned a number of surveys, which will help to improve the dietary exposure assessments. Consumption data from the Diet and Nutrition Survey for Infants and Young Children (DNSIYC) (DH, 2013) and recent data from the National Diet and Nutrition Survey Rolling Programme years 1-4 (NDNS) (Bates *et al.,* 2014) have been used for the estimation of exposure. The consumption data on metals and other elements are used in this scoping paper to provide an indication of exposure

[1] http://cot.food.gov.uk/sites/default/files/cot/cotstatementoverarch201203.pdf

from food (see Annex B), but total exposure has not been assessed at the current time. Annex C includes further detail on the health-based guidance values (HBGVs) used for comparison with the estimated exposures.

4. This paper proposes the scope of the COT evaluations for the 1 to 5 years age group, including information on data available for exposure assessment, and invites views on the format in which these should be published.

Possible topics for the COT review of the toxicity of chemicals in the diet of children aged 1-5 years

Substances considered but not evaluated in detail when the COT reviewed the risks of chemical toxicity in relation to the infant diet

Alcohol

5. The COT focussed on advice to breastfeeding women, in order to consider risks to the infant, concluding that current Government advice was supported by reports of minor behavioural effects in breastfed babies. Breastmilk may constitute a part of the diet for those over the age of one year, but declines with the transition to an adult diet. Data on consumption of breastmilk by children older than 1 year are available from DNSIYC. It is illegal to give alcohol to children under the age of 5 years old[2].

Caffeine

6. The COT focussed on exposure to the infant from breastmilk noting that the basis for the Government's current advice to breastfeeding mothers on caffeine consumption was extrapolated from that provided to pregnant women, and the available information did not provide a basis for refining it. There is no specific advice on caffeine consumption by children aged 1 to 5 years. Under UK law, drinks and foods to which caffeine is added have to be labelled "Not recommended for children or pregnant or breast-feeding women"[3].

7. The European Food Safety Authority (EFSA) recently published an opinion on the safety of caffeine, including the effects on young children (EFSA, 2015a). It concluded that the information available for this age group was insufficient to derive a safe level of caffeine intake, and therefore a safe intake level was scaled on a bodyweight basis from that identified for adults (3 mg/kg bw/day). The EFSA opinion included UK estimates of mean and 95th percentile caffeine intakes of 0.2 - 0.4 and

[2] https://www.gov.uk/alcohol-young-people-law
[3] https://www.food.gov.uk/science/additives/energydrinks

0.7 - 2.2 mg/kg bw/day, respectively by toddlers (aged 1-<3 years), and of 0.4 and 1.8 mg/kg bw/day, respectively, for other children (aged 3-<10 years). These could be refined to focus on the 1 to 5 year age group.

Bisphenol A

8. Bisphenol A (BPA) has been reviewed extensively by EFSA, most recently in 2015 (the COT responded to the consultation on the draft opinion). Whilst exposure of infants to BPA will be reduced by the precautionary ban on use in polycarbonate baby bottles in the EU which came into force in 2011, young children could be exposed to BPA from food contact materials.

9. EFSA (2015) established a temporary tolerable daily intake (tTDI) of 4 µg/kg bw/day based on a $BMDL_{10}$ of 8,960 µg/kg bw/day (human equivalent dose of 609 µg/kg bw/day) for kidney effects in mice and applying an uncertainty factor of 150 (inter- and intra-species differences and uncertainty in mammary gland, reproductive, neurobehavioural, immune and metabolic system effects). In comparing the exposures to the tTDI EFSA concluded that there were no health concerns from the dietary exposure for any age group (age groups started from 6 months old).

10. SACN have expressed a specific interest in comparing the potential risks of BPA exposure in 1 to 2 year old children to those 2 to 5 years old due to some complementary foods being sold in plastic packaging.

Phthalates

11. In 2011, the COT reviewed phthalates in the 2007 Total Diet Study (TDS)[4] and endorsed a number of tolerable daily intakes (TDIs). These were: diethylhexylphthalate (DEHP) 50 µg/kg bw (EFSA, 2005a), dibutylphthalate (DBP) 10 µg/kg bw (EFSA, 2005b), butylbenzylphthalate (BBP) 500 µg/kg bw (EFSA, 2005c), diethylphthalate (DEP) 500 µg/kg bw/day (WHO, 2003). TDIs have not been established for disobutylphthalate (DiBP) or dioctylphthalate (DOP). These TDIs were applied by COT in its review of the infant diet in 2012 (Annex A).

12. The COT concluded that dietary exposures, based on the 2007 TDS, were highest in toddlers in the >1.5 to 2.5 year old age group, but that all were below the relevant individual TDIs and were not of toxicological concern. COT also considered the sum of exposures. Whilst the sum of the dietary exposures was approximately double the most sensitive TDI, that of DBP, the Committee concluded this level did not indicate a concern for health due to most phthalates being less potent

[4] http://cot.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2011/cot201104

comparatively to DBP, the TDI for DBP is likely to be highly conservative and that DBP accounts for only approximately 5% of this cumulative exposure.

13. FSA does not hold any more recent data for phthalate levels in food.

Methylmercury

14. The COT, together with the SACN, considered risks and benefits of fish consumption in 2004 and this includes the risks associated with the presence of methylmercury in fish[5]. This provides the basis for the current Government advice that children should avoid eating shark, swordfish and marlin, the species with the highest levels of methylmercury.

15. In the overarching statement on infant feeding (Annex A) the Committee had noted that EFSA was reviewing methylmercury (MeHg) and would wait until the review was complete before deciding whether further review of MeHg was necessary. EFSA (2012a) revised the tolerable weekly intake (TWI) from 1.6 to 1.3 µg/kg bw, expressed as mercury. The COT subsequently reviewed the EFSA evaluation and concluded that the previous COT advice on methylmercury in the infant diet would not change since estimated intakes in infants were approximately three-fold lower than the EFSA TWI[6].

16. EFSA (2012a) also established a TWI of 4 µg/kg bw for inorganic mercury, which was not considered by COT in its review of the infant diet. Estimates of dietary exposure for the 1 to 5 years age group do not indicate exceedance of this TWI (summarised in Table 2 in Annex B).

Persistent organic pollutants (POPS)

Dioxins and dioxin-like compounds

17. Dioxin and dioxin-like compounds include compounds such as polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and certain polychlorinated biphenyls that exhibit dioxin-like activity (DL-PCBs). These substances are lipophilic, bioaccumulate in fat, transfer into milk, and are excreted very slowly. As such these compounds are widely present in food, particularly in oily fish

18. The COT previously concluded that due to declining occurrence a full assessment was not required for infants.

[5] http://cot.food.gov.uk/sites/default/files/cot/fishreport200401.pdf
[6] http://cot.food.gov.uk/sites/default/files/Annual%20Report%202013%20for%20web_0.pdf

19. Concentrations of a range of dioxins and dioxin-like compound have been measured in the 2012 UK TDS and in UK fish. These data could be used to estimate exposures in 1 to 5 year old children.

Legacy pesticides

20. A number of biopersistent pesticides (aldrin, dieldrin, endrin, chlordane, heptachlor, hexachlorobenzene, mirex, toxaphene and DDT) that were banned in the 1980s and 1990s are still present in the environment and food chain, and are referred to as "legacy pesticides". The COT did not conduct a detailed review of these in the infant diet because levels in breast milk and food were generally declining and the available information did not indicate a concern for health.

Substances evaluated in detail when the COT reviewed the risks of chemical toxicity in relation to the infant diet

21. Following the infant feeding evaluations carried by COT, the FSA recently completed two surveys on the levels of metals and other elements in foods intended for infants and young children (Annex B). The exposure assessments for these surveys (Tables 2 for young children, and 6-10 for infant exposure estimates) could be used to update the evaluations of the metals and other elements that were considered in detail in relation to the infant diet.

Aluminium

22. In considering infant exposure to aluminium the COT[7] referred to the Joint Expert Committee on Food Additives (JECFA) provisional tolerable weekly intake (PTWI) of 2 mg/kg bw/week established in 2012 (FAO/WHO, 2012). Estimates of exposure from food for the 1 to 5 years age group do not indicate exceedance of this PTWI (Tables 2 in Annex B).

Lead

23. In considering infant exposure to lead, the COT[8] referred to the EFSA blood lead $BMDL_{01}$ (for the association of lead with intellectual function) of 12 µg/L which corresponded to a dietary intake value of 0.5 µg/kg bw/day (EFSA, 2010). Some high level estimates of exposure from food for the 1 to 5 years age group are in the region of this BMDL (Tables 2 in Annex B).

[7] http://cot.food.gov.uk/sites/default/files/cot/statealuminium.pdf
[8] http://cot.food.gov.uk/sites/default/files/cot/cotstatlead.pdf

Vitamin A

24. Excessive intakes of vitamin A can result in bulging fontanelles in infants, hepatotoxicity, changes in bone density, changes in lipid metabolism and teratogenicity. In considering vitamin A in the infant diet, the COT[9] set a tolerable upper level (TUL) of 200 µg retinol equivalents (RE)/kg bw/day specifically for infants and 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 per week

25. The Scientific Committee on Food (SCF, 2002a) set tolerable upper intake levels (TULs) of 800 and 1,200 µg RE/kg bw/day for children aged 1 to 3 years and 4 to 6 years, respectively. The SMCN has asked whether there are risks associated with increased consumption of foods rich in vitamin A by children aged 1 to 5 years.

Soya phytoestrogens

26. The COT was unable to set a health-based guidance value for soya phytoestrogens for infants due to limitations in the data and uncertainties in the inter-species extrapolations arising from differences in toxicokinetics. COT concluded that there was no need to change the current government advice that there is no substantive medical need for, nor health benefit gained from the use of soya-based formula and should only be used to ensure adequate nutrition[10].

27. There are no specific recommendations for children aged 1 to 5 years in relation to soya consumption. Whilst soya-based formula consumption would decrease, other sources of soya could increase in the diet, for example due to consumption of soya-based drinks.

28. SACN has expressed an interest in any potential risks from the consumption of soya-based drinks, as there is no current advice for the 1 to 5 year age group.

More recently classified POPs

Polybrominated diphenyl ethers

[9] http://cot.food.gov.uk/sites/default/files/cot/cotstavita.pdf
[10] http://cot.food.gov.uk/sites/default/files/cot/cotstaphytos.pdf

29. The COT[11] concluded that it was not possible to derive a health-based guidance value for polybrominated diphenyl ethers (PBDEs) and adopted a Margin of Exposure (MOE) approach for 4 specific congeners for which there were sufficient data to identify a toxicological reference point. COT identified 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.

30. EFSA had indicated previously possible concerns over dietary intakes of polybrominated diphenyl ethers in young children (EFSA, 2011a). Whilst the MOEs for BDE-47, -153 and -209 were not considered by EFSA to be likely to raise a health concern, the MOEs for BDE-99 for children between 1 and 3 years were 1.4 at mean exposures and 0.7 at high exposures could indicate a potential health concern.

31. Concentrations of PBDEs are available from the 2012 TDS, and could be used to estimate exposures in 1 to 5 year old children.

Perfluorooctane sulfonate

32. In considering infant exposures to perfluorooctane sulfonate (PFOS) via breast milk and infant formulae the COT[12] referred to its previous evaluation on PFOS (COT, 2006) and that of EFSA (EFSA, 2008), and the respective TDI values of 300 and 150 ng/kg bw/day, COT confirmed their TDI of 300 ng/kg bw/day. COT concluded that infant exposures were below both the COT and EFSA TDIs and did not indicate a need to develop dietary guidance for this age group.

33. EFSA (2012b) estimated mean PFOS exposure ranges of 0.58 ng/kg bw/day (lower bound (LB)) to 14 ng/kg bw/day (upper bound (UB)), for ‘toddlers’ (1-<3 years), and between 0.59 ng/kg bw/day (LB) to 10 ng/kg bw/day (UB) for ‘other children’ (3-<10 years). The 95th percentile exposure ranged from 2.1 ng/kg bw/day (LB) to 29 ng/kg bw/day (UB), for ‘toddlers’, and 2.3 ng/kg bw/day (LB) to 19 ng/kg bw/day (UB) for ‘other children’, which are all well below the TDI.

34. Data on PFOS in the 2012 TDS data could also be used to estimate exposures.

Polybrominated biphenyls

[11] http://cot.food.gov.uk/sites/default/files/PBDEstatementfinal.pdf
[12] http://cot.food.gov.uk/sites/default/files/cot/cotstatmpfos.pdf

35. In considering infant exposures to polybrominated biphenyls (PBBs), the COT determined that the most suitable approach should differ for planar and non-planar congeners. However, there were insufficient data for a meaningful risk assessment.[13]

36. Concentrations of PBBs have been measured in a UK TDS and in UK fish, and could be used to estimate exposures in 1 to 5 year old children.

Hexabromocyclododecanes

37. In considering infant exposures to hexabromocyclododecanes (HBCDDs) the COT applied the EFSA (2011b) reference point of 3 µg/kg bw/day in a MOE assessment. COT concluded that dietary exposures were not a cause for concern in infants, however exposures from the high levels observed in some domestic dust samples were.[14]

38. Concentrations of HBCDDs have been measured in the 2012 UK TDS, and could be used to estimate exposures in 1 to 5 year old children. An analysis of baby foods and infant formula reported the majority of values to be below the limit of quantification (reported as <0.01 - <0.02 µg/kg whole weight).

Hexachlorocyclohexanes

39. In relation to infant exposures to hexochlorocyclohexanes (HCHs) the COT confirmed that the RIVM TDI of 0.04 µg/kg bw was appropriate for assessment of γ-HCH. Exposure estimates was hindered by a lack of quantifiable data, and estimates based on possible exposures from infant formula and infant foods could be 5 or 10 times the TDI. However, the COT considered these levels to be unlikely in practice. Exposures from breast milk were also expected to be below the TDI, but could have a minor exceedance if the highest levels measured were used for the exposure estimate. COT did not consider this to constitute a risk to infant health as exposures have been shown to be declining.[15]

40. The data were insufficient to establish TDIs for α-HCH and β-HCH and COT applied a MOE approach. For α-HCH a reference point of 0.1 mg/kg bw/day for hepatotoxicity was identified, and the resulting MOEs were not considered to raise concerns with regards to infant health after taking into account the uncertainties in the data. A lowest observed adverse effect level (LOAEL) reference point of 0.18 mg/kg bw/day for centrilobular hypertrophy was identified for β-HCH. MOEs calculated from mean exposure estimates did not indicate a concern for health

[13] PBBs in the infant diet (second draft statement) - http://cot.food.gov.uk/sites/default/files/TOX%20-2015-06%20PBB%202nd%20Draft%20Statement.pdf
[14] http://cot.food.gov.uk/sites/default/files/HBCDDsstatementfinal.pdf
[15] http://cot.food.gov.uk/sites/default/files/cot/cotstatmhchs.pdf

(>450), however those based on the highest level measured in breast milk COT could not rule out a concern for health (MOEs between 16 and 22 depending on age group) although exposures this high were considered unlikely.

Endosulfan, pentachlorobenzene and chlordecone

41. In relation to exposures to infants from endosulfan, pentachlorobenzene and chlordecone the COT[16] concluded that the available data did not indicate a risk to health. Exposures to endosulfan and pentachlorobenzene were below their respective health-based guidance values; ADI of 6 µg endosulfan/kg bw derived from a no observed adverse effect level (NOAEL) of 600 µg/kg bw/day in rats and an uncertainty factor of 100, and TDI of 0.5 µg pentachlorobenzene/kg bw for hepatocellular hypertrophy and necrosis derived from a LOAEL of 5.2 mg/kg bw/day and an uncertainty factor of 10,000. Exposures to chlordecone were considered to be extremely low and continuing to decrease, such that even with its known toxicity and assuming it historical use adverse effects from dietary exposures were considered by COT to be unlikely.

42. The FSA have some survey data on levels of pentachlorobenzene in a range commercially available food products. These data could be used to estimate exposures in 1 to 5 year old children.

Possible additional substances

Arsenic

43. Arsenic in the infant diet was not reviewed since existing advice was that infants should not be given rice drinks (which can contain high levels of inorganic arsenic). Current advice is also that young children aged 1 to 5 years should not be given rice drinks[17], but there is no specific advice on other rice products.

44. Establishment of a health-based guidance value is not considered appropriate for inorganic arsenic due to its genotoxicity and carcinogenicity. EFSA (2009a) established a $BMDL_{01}$ of between 0.3 and 8 µg/kg bw/day for increased risk of lung, skin and bladder cancers and skin lesions. The EFSA concluded that this range of values should be used instead of a single reference point in the risk characterisation for inorganic arsenic (EFSA, 2009a). In 2011 JECFA identified a $BMDL_{0.5}$ of 3.0 µg/kg bw/day from epidemiology studies with a lung cancer endpoint.

[16] http://www.food.gov.uk/sites/default/files/cotstaonpops.pdf
[17] http://www.nhs.uk/conditions/pregnancy-and-baby/pages/drinks-and-cups-children.aspx#close

45. In 2014, EFSA identified 'toddlers' (1-<3 years) as the age class with the highest exposures. Mean and 95th percentile dietary exposures were estimated to range from 0.32 – 1.17 µg/kg bw/day (min LB - max UB) and 0.61 - 2.09 µg/kg bw/day (min LB - max UB). In children aged 3-<10 years mean and 95th percentile dietary exposures were estimated to range from 0.20 – 0.87 µg/kg bw/day (min LB - max UB) and 0.36 - 1.41 µg/kg bw/day (min LB - max UB), respectively. Important contributors in both groups were 'Grain-based processed products (non rice-based)', 'Milk and dairy products', drinking water and rice. In children aged 3-<10 years 'Wheat bread and rolls' were also considered an important contributor. (EFSA, 2014a).

46. The FSA commissioned a TDS and an infant metals study which measured inorganic arsenic concentrations. This data was used to estimate exposures and is included in Table 2 of Annex B. Comparison of these exposure estimates with the EFSA reference point of 0.3 - 8 µg/kg bw/day gives MOEs with a range of 0.2 - 31.

Cadmium

47. EFSA (2009b) established a TWI of 2.5 µg/kg bw for cadmium derived from modelling of a large human data set which required no application of uncertainty factors. EFSA (2012c) reported toddler (1-<3 years) mean and 95th percentile exposure estimates ranged between 3.84 – 6.77 µg/kg bw/week (min – max middle bound) and 5.32 – 10.01 µg/kg bw/week (min – max middle bound). Child (3-<10 years) mean and 95th percentile exposure estimates ranged between 3.13 – 5.03 µg/kg bw/week (min – max middle bound) and 4.58 – 10.2 µg/kg bw/week (min – max middle bound). (EFSA, 2012c).

48. Occurrence data are available from the recent TDS and a survey on metals in infant formulae and commercial foods. Estimated exposures indicate exceedance of the TWI (Table 2 in Annex B).

Chromium

49. Chromium (Cr) can exist in a variety of oxidation states; trivalent (Cr(III)) and hexavalent (Cr(VI)) predominate and are relatively stable. Cr(III) is a natural dietary constituent present in a variety of foods and was previously thought to be an essential element. Cr(VI) most commonly occurs in industrial processes and may be present in drinking water. EFSA (2014b) established a TDI for Cr(III) of 300 µg/kg bw. Cr(VI) is genotoxic and carcinogenic and as such EFSA used an MOE approach, based on a $BMDL_{10}$ of 1.0 mg Cr(VI)/kg bw/day from a 2-year carcinogenicity study.

50. EFSA estimated toddlers' dietary exposure of Cr(III) for mean consumers to be 2.3 to 5.9 µg/kg bw/day (min LB - max UB) and for 95th percentile consumers to be between 3.4 and 9.0 µg/kg bw/day. Young children (3-<10 years) had estimated

dietary Cr(III) mean and 95th percentile exposures of 1.6 - 4.9 µg/kg bw/day (min LB-max UB) and 2.9 - 7.9 µg/kg bw/day, respectively. The exposure to both age groups is well below the TDI. EFSA (2014b).

51. Occurrence data are available from the recent TDS and a survey on metals in infant formulae and commercial foods. Estimated exposures do not indicate exceedance of the TWI (Table 2 in Annex B).

Copper

52. Copper is an essential element and the highest levels in foods are in offal, seafood, nuts and seeds, but it is also found in whole bran and whole bran products. Exposure to copper can also occur from the environment either from industrial processes or via copper water pipes.

53. The Scientific Committee on Food (SCF) established adult tolerable upper intake levels (UL) based on a NOAEL of 10 mg/day for the absence of any adverse effect on liver function in a human study. The SCF used an uncertainty factor of 2 to derive the adult UL of 5 mg/day. The SCF extrapolated these values to establish UL values for copper of 1 and 2 mg/day for children of 1 to 3 and 4 to 6 years (80 and 105 µg/kg bw/day), respectively (SCF, 2003a).

54. Estimated exposures for children aged 1 to 5 years do not indicate exceedance of, but are close to, the UL (Table 2 in Annex B).

Iodine

55. Iodine is an essential nutrient for mammals, which is required to produce thyroid hormones. Iodine can accumulate in some marine organisms. Milk is also a key source as cows are fed a high iodine diet in the winter to increase the level of iodine in the milk (EFSA, 2014c).

56. In 2000, the COT[18] considered iodine in cow's milk, and specifically intakes in young children who are the highest consumers of milk. In their conclusions, the COT stated that whilst some children exceed the JECFA PMTDI from 1989, intakes were unlikely to pose a risk to health (COT, 2000). The SCF has established a UL of 200 µg/day for 1-3 year olds (SCF, 2002b), and nutrition requirements for 1-3 year olds (EFSA, 2014c).

57. More recently, the SACN noted that there is a lack of knowledge on the UK iodine status with some sectors of the population likely to be deficient such as girls of

[18] http://cot.food.gov.uk/sites/default/files/cot/iodin2.pdf

reproductive age, pregnant and lactating females and dairy and fish avoiders (SACN, 2014).

58. Occurrence data are available from the recent TDS and a survey on metals in infant formulae and commercial foods. Estimated exposures indicate an exceedance of the HBGV (Table 2 in Annex B).

Nickel

59. Nickel occurs is found in foods especially cocoa, soya beans, oatmeal, hazelnuts, almonds, legumes and drinking water, due to both natural and anthropogenic sources.

60. In 2015 EFSA derived a TDI of 2.8 µg/kg bw for nickel, noting that it may not be sufficiently protective of individuals sensitized to nickel. EFSA selected a $BMDL_{10}$ of 1.1 µg/kg bw as an acute reference point and concluded that an MOE of 10 or higher would be indicative of a low health concern for nickel-sensitive individuals. EFSA concluded that current chronic dietary exposures are of concern for the general population. (EFSA, 2015c).

61. UK chronic dietary exposure estimates have previously been calculated by Rose *et al.,* (2010), using the 2006 UK TDS. These estimates for toddlers and children exceed the EFSA TDI. In toddlers (1.5 – 4.5 years) and young people (4 – 18 years) the mean exposure estimates were 4.17 – 4.87 and 2.62 – 3.05 µg/kg bw/day (LB – UB), respectively, and 97.5^{th} percentile estimates were 7.54 – 8.32 and 5.27 – 5.82 µg/kg bw/day (LB – UB), respectively.

62. For acute exposures, EFSA derived MOEs using European mean and high-level exposure estimates and found that all were considerably below 10 for all age classes.

63. Recent (2015) occurrence data are available from the recent TDS and a survey on metals in infant formulae and commercial foods. Estimated exposures indicate an exceedance of the TDI (Table 2 in Annex B).

Manganese

64. Manganese is an essential dietary mineral for mammals; it is a component of metalloenzymes such as superoxide dismutase, arginase and pyruvate carboxylase, and is involved in amino acid, lipid and carbohydrate metabolism (EFSA, 2013a).

65. The SCF (2000) concluded that it was inappropriate to establish a TUL due to a considerable degree of uncertainty in the available data. The WHO (2011) established a TDI of 0.06 mg/kg of body weight by dividing the NOAEL of 11 mg/day

(the upper range of normal manganese intake) by an uncertainty factor of 3 (to allow for the possible increased bioavailability of manganese from water) assuming an adult body weight of 60 kg.

66. Rose *et al.,* (2010) calculated manganese exposure estimates from TDS data for UK toddlers as 168 and 305 µg/kg bw/day for mean and 97.5th percentile consumers, respectively, and for children aged 4 to 18 years as 106 and 201 µg/kg bw/day for mean and 97.5th percentile consumers, respectively.

67. Recent occurrence data are available from the TDS (2015) and a survey on metals in infant formulae and commercial foods (Table 2 in Annex B). However there is no robust HBGV for manganese.

Zinc

68. Zinc is an essential trace element that plays a key role in a number of cellular processes. In the body, zinc interacts with a number of other essential nutrients. Zinc competes with iron for absorption and interferes with the gastrointestinal uptake of copper. Excess zinc may decrease the uptake of magnesium and calcium (EVM, 2003).

69. The SCF concluded that the NOAEL for zinc is about 50 mg/day and recommended a tolerable upper intake level (UL) of zinc (from dietary and supplemental sources) of 25 mg/day and extrapolated to a UL of 7 mg/day for children aged 1 to 3 years (SCF, 2003b).

70. Estimated exposures for children aged 1 to 5 years indicate exceedance of the UL (Table 2 in Annex B).

Mycotoxins

71. There are a wide range of mycotoxins that can affect key crops such as wheat, oats, rice, corn, and maize, and also nuts, spices, dried fruits and fruit juices such as apple. Further exposures can occur due to contamination of feed for livestock potentially resulting in presence of mycotoxins in carcass meat, offal and milk.

72. EFSA (2014d) assessed the dietary exposures of a number of mycotoxins (Fusarium toxins zearalenone, nivalenol, T-2 and HT-2 toxins and fumonisins). Nivalenol and T-2 and HT-2 were not considered to be of concern for any age group as the exposures were generally lower than the TDI. Using the LB approach for zearalenone even high consumers (from all populations) would not exceed the TDI of 0.25 µg/kg bw. Using the upper bound approach the 95th percentile consumers in the toddler group could exceed the zearalenone TDI by up to 2.7-fold. EFSA

considered a number of studies of fumonisins and estimated that 0.2 - 14% (LB) and 43 - 66% (UB) toddlers (1-<3 years) and 0 - 38% (LB) and 11 - 59% (UB) other children (3-<10 years) could exceed the PMTDI of 2 µg/kg bw/day. At 95th percentile LB exposure other children exceeded the PMTDI by up to 2.5-fold (LB) and 3-fold (UB). (EFSA, 2014d).

73. In December 2015 the FSA will receive data on levels of mycotoxins in foods from a TDS, which could be used to estimate potential exposures to 1 to 5 year old children.

Tropane Alkaloids

74. Tropane alkaloids are found in plants of several families including *Brassicaceae, Solanaceae*, and can be found as contaminants, often in cereals. EFSA (2013) established a group acute reference dose (ARfD) of 0.016 µg/kg bw expressed as the sum of (-)-hyoscyamine and (-)-scopolamine and estimated that acute dietary exposures for toddler consumers could be up to seven times the group ARfD, based on data on tropane alkaloids in cereal-based food for infants and young children. There were insufficient data on other types of food to allow exposure estimation for other age groups.(EFSA, 2013b).

75. The FSA and EFSA are cofunding a study to investigate the potential tropane alkaloid contamination in a range of processed and unprocessed cereals and grains, products processed derived from these, and certain vegetables suggests to contain tropane alkaloids. It is due to be completed in October 2016.

Perchlorate

76. Perchlorate is an environmental chemical contaminant, from both natural and anthropogenic sources. Perchlorate can be found in a wide range of foods, but the highest mean levels have been report as being in vegetables, fruits, vegetable and fruit juice and infant formulae.

77. EFSA (2014e) established a TDI of 0.3 µg/kg bw/day based on inhibition of thyroid iodine uptake which may lead to adverse effects on the thyroid and concluded that an acute reference dose (ARfD) was not warranted. EFSA estimated exposures for ‘toddlers’ (1-<3 years of age) and ‘other children’ (3-<10 years of age). Mean chronic dietary exposure ranged from 0.07 - 0.37 µg/kg bw/day and 0.18 - 0.50 µg/kg b/day (min LB - max UB), and 95th percentile chronic dietary exposure ranged from 0.19 - 0.72 µg/kg bw/day and 0.34 - 0.97 µg/kg bw/day (min LB - max UB), for ‘other children’ and ’toddlers’ respectively. (EFSA, 2014e).

78. The FSA is undertaking a perchlorate monitoring study in UK produce. Data from this study should be available by the end of 2016, and could be used to estimate exposures in 1 to 5 year old children.

Chlorate

79. Chlorate was formerly used as a herbicide and has been banned since 2008. Chlorine based disinfection agents for drinking water, for water used in food preparation and food contact surfaces produce chlorate as a by-product.

80. EFSA (2015d) set an ARfD of 36 µg/kg bw and a TDI of 3 µg/kg bw/day. The estimated UB mean and 95th percentile acute exposures were reported as 5.5 – 10.6 µg/kg bw/day and 10.9 – 18.0 µg/kg bw/day (min - max), respectively for toddlers (aged 1-<3 years), and 2.5 – 7.0 µg/kg bw/day and 4.9 – 16.9 µg/kg bw/day (min - max), respectively for children (aged 3-<10 years) The estimated mean and 95th percentile chronic UK exposures were 2.3 - 2.9 and 4.0 - 4.8 µg/kg bw/day (LB - UB), respectively for toddlers aged 1-<3 years old. For children aged 3-<10 years old they were 2.6 - 3.2 and 4.3 - 5.2 µg/kg bw/day. The occurrence data were considered insufficient for exposure assessment from yogurt and infant/follow-on formula, although there were indications of high levels in these sources. (EFSA, 2015d).

81. The FSA is undertaking a chlorate monitoring study in fruit and vegetables. Data from which should be available by the end of 2015, and could be used to estimate exposures in 1 to 5 year old children.

Acrylamide

82. EFSA concluded that acrylamide is genotoxic and carcinogenic, and that other toxic effects include neurotoxicity and reproductive toxicity. Major sources of acrylamide are potato and cereal-based baked, fried, roasted or grilled items. EFSA estimated dietary exposure using UK consumption data for different age groups, and the highest was in the toddler (1-<3 years) and other children (3-<10 years) age groups. The MOEs were in the region of 100 and 60 respectively, for average and high level toddler consumers. (EFSA, 2015e).

Furan

83. Furan forms in heat treated foods. It is a liver carcinogen in rodents. In 2011, JECFA calculated a $BMDL_{10}$ of 0.96 mg/kg bw/d as the reference point for an MOE calculation. Using estimated mean and high-level exposures (inclusive of children) of 0.001 and 0.002 mg/kg bw/day, MOEs of 960 and 480 were calculated. JECFA considered these MOEs to indicate a concern for human health. FAO/WHO. (2012).

84. EFSA reported the levels of furan in a range of food groups. Mean estimated exposures (LB - UB) in children aged 3-<10 years were 0.04 - 0.22 µg/kg bw/day, and for toddlers aged 1-3 years 0.05 - 0.31 µg/kg bw/day. High-level (95^{th} percentile) estimated exposures (LB-UB) in children aged 3-<10 years was 0.09 - 0.46 µg/kg bw/day, and for toddlers aged 1-<3 years 0.2 - 1.4 µg/kg bw/day. The main contributors to the exposures in these age groups were fruit juices, milk-based products and cereal-based products, and additionally in 1-<3 year olds jarred baby foods. (EFSA, 2011c).

85. The FSA has undertaken a furan in foods survey, which could be used to estimate exposures in 1 to 5 year old children.

Polycyclic aromatic hydrocarbons

86. Polycyclic aromatic hydrocarbons (PAHs) are a broad range of compounds, some of which are genotoxic and carcinogenic. They can be found in vegetables from atmospheric deposition, fish and shellfish from contaminated waters or from deliberate manufacturing processes that produce smoked foods. EFSA (2008b) concluded that the sum of benzo(a)pyrene (BaP), benzo[a]anthracene, benzo[b]fluoranthane and chrysene (PAH4) should be used as a marker of exposure to PAHs in food. An MOE approach was adopted using the $BMDL_{10}$ of 0.07 and 0.34 mg/kg bw/day, for BaP and the sum of the PAH4 respectively, as reference points. EFSA estimated UK exposures to PAH4 to be on average 936 ng/day, with the 97.5^{th} estimation to be 1,661 ng/day (based on a 60 kg body weight). High-level consumers were found to have MOEs close to or less than the value of 10,000, which as proposed by EFSA indicates a concern for health. No MOE estimates were calculated for young children. (EFSA, 2008b).

87. UK FSA 2012 TDS data are available and could be used to estimate exposures.

Perfluorooctanoic acid

88. Perfluorooctanoic acid (PFOA) has been widely used in industrial and consumer applications including stain- and water-resistant coatings for fabrics and carpets, oil-resistant coatings for paper products approved for food contact, fire-fighting foams, mining and oil well surfactants, floor polishes, and insecticide formulations. A number of different perfluorinated organic compounds have been widely found in the environment. (EFSA, 2008a).

89. EFSA (2008a) established a TDI for PFOA of 1.5 µg/kg bw/day by applying an overall uncertainty factor (UF) of 200 to the $BMDL_{10}$ of 0.3 mg/kg bw. An UF of 100 was used for inter- and intra-species differences and an additional UF of 2 to

compensate for uncertainties relating to the internal dose kinetics. This TDI was endorsed by COT in 2009[19].

90. EFSA (2008a) estimated UK toddler (1.5-4.5 years) dietary exposures to PFOA of 4 - 200 and 10 - 300 ng/kg bw/day for average and high level consumers, respectively. EFSA (2012) reported new occurrence data and estimated mean PFOA exposure ranges of 0.20 - 17 ng/kg bw/day (LB-UB), for toddlers (1-<3 years), and between 0.10 - 13 ng/kg bw/day (LB-UB) for 'other children' (3-<10 years). The 95th percentile exposure ranged from 0.44 - 32 ng/kg bw/day (LB-UB), for toddlers, and 0.20 - 30 ng/kg bw/day (LB-UB) for children aged 3-<10 years.

91. UK FSA TDS 2012 data for PFOA are available and could also be used to estimate exposures.

Tetrabromobisphenol A

92. Tetrabromobisphenol A (TBBPA) is a brominated flame retardant. In 2004 COT[20] had recommended a TDI of 1 mg/kg bw/day based on a 90 day two generation reproductive study, and applying an uncertainty factor of 1000 to account for inter- and intra-species differences and for the lack of chronic toxicity studies. EFSA (2011d) determined a $BMDL_{10}$ of 16 mg/kg bw/day for effects on thyroid hormones from a 28 day study. Due to the uncertainties in the database EFSA did not consider it appropriate to generate a HBGV for TBBPA and adopted a MOE approach. The exposure assessment was a hypothetical worst case assessment as all levels reported were <LOQ. MOEs ranged between 6×10^6 and 3×10^5. EFSA did not consider such exposures to likely to be of concern to human health. Further analyses of exposures via breast milk for infants and for combined food and dust exposures in children similarly were not deem likely to raise a health concern.

93. In considering exposure to infants from the diet in 2014, COT was presented a discussion paper on TBBPA exposures (TOX/2014/09)[21]. COT concluded that it was not possible to perform a meaningful risk assessment due to a lack of an appropriate reference point, as they did not consider the EFSA or previous COT reference points appropriate anymore, and limited quantitative exposure data. A statement was not produced, but the COT agreed that it would be appropriate to revisit TBBPA and its derivatives later, after it had considered other groups of BFRs as part of its work on infant diet.

94. Data from the 2012 TDS indicated levels across all TDS food groups were below the limit of quantification (reported as between <0.01 - <0.02 µg/kg fat weight,

[19] http://cot.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2009/cot200902
[20] http://cot.food.gov.uk/sites/default/files/cot/cotstatements04tbbpa.pdf
[21] http://cot.food.gov.uk/sites/default/files/cot/tox20149.pdf

equivalent to <0.03 - <4.76 µg/kg whole weight), with the exception of 'fats and oils' which reported levels of 0.02 µg/kg fat weight (0.03 µg/kg whole weight) and 'potatoes' which had indicative levels of 0.01 µg/kg fat weight (0.19 µg/kg whole weight). An FSA survey of baby foods and infant foods (2015) did not report any levels above the limit of quantification (<0.01 - <0.06 µg/kg whole weight).

Substances subject to regulatory approval

Veterinary Medicines & Pesticides

95. The risk assessments for the setting of Maximum Residue Levels (MRLs) for pesticides take into account exposures for multiple age groups including young children. However it should be noted that these MRLs are not solely safety-based – they are based on the residue levels found in field trials of the proposed use of the specific pesticide, but are only set if a risk assessments using the results of the same field trials (using average residue levels for chronic exposure and a high residue level for acute) indicate no concerns for chronic or acute exposures. Thus the MRLs should ensure that residues are no higher than needed but are also safe.

96. The MRLs for veterinary medicines are largely derived from the ADI, or a proportion of it to allow for other uses of the compound. However, the process involves assuming a body weight for a human of 60 kg and that they eat a particular model diet (300 g muscle meat, 100 g liver, 50 g kidney, 50 g fat, 1.5 litres milk, 100 g egg, 20 g honey) per day. Whilst the MRLs are largely considered adequate for young children, there can be exceptions.

Food Additives

97. As for pesticides and veterinary medicines, the approval process for food additives and colours takes into account potential exposure of different age groups.

98. Current government advice is for individuals to reduce their sugar intake, which could lead to increased intake of sweeteners. The SMCN has therefore expressed an interest in assessing potential risks from sweeteners

Overall approach

99. Substances that were considered by the COT in the infant diet could be addressed by addenda to the already-published statements or as short statements focussing on the exposure assessments for the 1-5 years age group, cross-referring to the toxicological information in the statements on the infant diet with updates where necessary. Additional topics will require more comprehensive evaluations.

Questions asked of the Committee

i. Members are invited to consider each of the chemicals discussed in this paper, and advise on whether they should be included in reviews of risks of chemicals in the diet of young children (aged 1 to 5 years).

ii. Do Members have additional suggestions for inclusion in the review?

iii. Do Members consider that the COT statements on the infant diet should be revised in light of the new data to allow improved exposure assessments?

iv. Do Members have recommendations for the format of the outputs of the Committees reviews?

Secretariat
October 2015

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

COT CONTRIBUTION TO SACN REVIEW OF COMPLEMENTARY AND YOUNG CHILD FEEDING; PROPOSED SCOPE OF WORK

Overarching statement on risks of chemical toxicity and allergic disease in relation to infant diet

Available at
http://cot.food.gov.uk/sites/default/files/cot/cotstatementoverarch201203.pdf

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

COT CONTRIBUTION TO SACN REVIEW OF COMPLEMENTARY AND YOUNG CHILD FEEDING; PROPOSED SCOPE OF WORK

Estimates of exposure to metals and other elements

Secretariat
October 2015

FSA Surveys of metals and other elements in foods intended for infants and young children

Two surveys were conducted during 2014 to measure the concentrations of elements in food consumed by infants and young children. The first survey was a total diet study (TDS) which focused on sampling foods eaten by young children (18 months and older, including adult foods) and the other was a survey on types of foods eaten by infants younger than 18 months (referred to as the Infant Survey).

TDS consist of: (i) selecting foods based on food consumption data, to represent as best as possible a typical diet; (ii) their preparation to food as consumed and (iii) the subsequent pooling of related foods before analysing the composite samples for elements.

The Infant Survey on the other hand measured the concentrations of metals and other elements in food 'as sold', in the following categories: commercial infant foods, infant formula and 'non infant specific complementary foods' – i.e. foods that are or may be consumed by infants but are not specifically manufactured or intended for infants, such as bread and bananas, were also analyzed.

TDS

The concentrations of 26 elements, including metals were measured in the 2014 UK TDS. Composite samples for 27 TDS food groups (Table 1) were collected from 24 UK towns and analysed for their levels of: aluminium, antimony, arsenic, barium, bismuth, cadmium, chromium, copper, germanium, indium, inorganic arsenic, iodine, lead, manganese, mercury, molybdenum, nickel, palladium, platinum, rhodium, ruthenium, selenium, strontium, thallium, tin and zinc. Where appropriate, tap water was used in the preparation and cooking of food samples. The results from this survey were used together with food consumption data from the Diet and Nutrition Survey for Infants and Young Children (DNSIYC) (DH, 2013) for ages 12 to 18 months and the National Diet and Nutrition Survey Rolling Programme years 1-4 (NDNS) (Bates *et al.,* 2014) for age 18 months to 5 years, to estimate dietary exposures of the general UK population to these elements.

Table1. Food groups used for analysis of 26 elements in the 2014 TDS

TDS Food Groups*	
Bread	Fresh Fruit
Miscellaneous Cereals	Fruit Products
Carcase Meat	Non Alcoholic Beverages
Offal	Milk
Meat Products	Dairy Products
Poultry	Nuts
Fish	Alcoholic Drinks
Fats and Oils	Meat Substitutes
Eggs	Snacks
Sugars	Desserts
Green Vegetables	Condiments
Potatoes	Tap Water
Other Vegetables	Bottled Water
Canned Vegetables	

*Food samples representative of the UK diet are purchased throughout the year in 24 towns covering the UK and 137 categories of foods are combined into 27 groups of similar foods for analysis

Exposure Assessment

Table 2 summarises lower and upper bound (UB) total dietary exposures to 26 elements, estimated using either DNSIYC (for infants younger than 18 months) or NDNS (for children between 18 months and 5 years of age) consumption data and the concentration of each element that was identified in the food groups.

Table 2. Estimated 97.5th percentile exposure of children age 1 to 5 years to 26 elements in food together with health-based guidance values (HBGVs) where available (µg/kg bw/day)

Elements	12-14.99 Months (n=670)[b]	15-18 Months (n=605)[b]	1.5-4.99 Years (n=429)[b]	HBGV/BMDL[c]
Al	176-179[a]	187-189	175-177	286
Total As	8.71-9.21	8.94-9.20	6.84-7.12	N/A
Ba	34.2	34.5	30.9	20
Bi	0.78-0.82	0.54-0.63	0.30-0.39	N/A
Cd	0.61-0.93	0.60-0.89	0.52-0.80	0.36
Cr	3.37-5.19	3.22-5.27	2.91-4.70	300
Cu	59.8-60.6	63.4-64.1	57.0-58.0	68.5
Ge	0.00-0.18	0.00-0.18	0.00-0.16	N/A
Hg	0.21-0.27	0.22-0.28	0.17-0.22	0.57
I	24.2-24.3	21.5-21.6	17.0	13.7
iAs	0.32-1.24	0.33-1.16	0.26-1.02	BMDL 0.3-8.0
In	0.01-0.09	0.01-0.09	0.00-0.08	N/A
Mn	280	288	268	N/A
Mo	8.58-8.85	8.60-8.64	6.71-6.92	6.9
Ni	7.69-8.68	7.80-8.77	7.06-8.00	2.8
Pb	0.29-0.46	0.29-0.49	0.25-0.44	BMDL 0.5
Pd	0.04-0.18	0.04-0.19	0.04-0.17	N/A
Pt	0.00-0.18	0.00-0.18	0.00-0.16	N/A
Rh	0.00-0.09	0.00-0.09	0.00-0.08	N/A
Ru	0.00-0.18	0.00-0.18	0.00-0.16	N/A
Sb	0.06-0.12	0.06-0.12	0.06-0.11	6
Se	3.16-5.14	3.18-5.14	2.36-4.48	4.1
Sn	302-303	256-258	260-261	2000
Sr	104	101	93.7	130
Ti	0.05-0.37	0.06-0.39	0.08-0.35	N/A
Zn	726	703	500-502	480

a Ranges are lower bound (< LOD as 0) to upper bound (<LOD as the LOD), respectively. If there is only one figure all data were > LOD
b Number of children in the survey
c Values are HBGVs unless BMDL is stated

Infant Survey

The concentrations of 16 elements, including metals were measured in three categories of foods intended for infants and young children in a recent FSA survey: Infant Formula (Table 3), Commercial Infant Foods (Table 4), and groups of food comprising of the top 50 most commonly consumed varieties of complementary foods (Table 5).

Table 3. Infant formula

Dry Powder	Made Up Formula
First and Hungrier Milk	First Milk and Hungrier Milk
Follow On Milk	Follow On milk
Growing Up Milk	Growing up Milk
Soy Milk	
Goat Milk	
Organic Milk	
Comfort Milk	

Table 4. Commercial infant foods

Commercial Infant Foods
Cereal Based Foods and Dishes
Dairy Based Foods and Dishes
Fruit Based Foods and Dishes
Meat and Fish Based Foods and Dishes
Snacks (Sweet and Savoury)
Other Savoury Based Foods and Dishes (excluding Meat)
Drinks

Table 5. Groups of complementary foods comprising the top 50 most commonly eaten varieties.

Infant Survey Food Groups	
Beverages	Fruit Products
Bread	Green Vegetables
Canned Vegetables	Meat Products
Cereals	Milk
Dairy Products	Other Vegetables
Eggs	Potatoes
Fish	Poultry/Chicken
Fresh Fruit	

Exposure Assessments

Tables 6, 7 and 8, 9 and 10 summarise lower- and upper-bound total dietary exposures to 16 elements, estimated using concentration data from varieties of infant formulae (Table 3), commercial infant foods (Table 4) and complementary foods (Table 5) using DNSIYC (DH, 2013) consumption data. The data for each food category is reported separately so that the contribution to exposure from each class could be assessed more transparently for the most relevant infant age group. However, it is possible to report combined exposures from all categories for each age group if this is needed.

Exposures to elements from complementary foods (Table 10) were generally higher than from other categories of food eaten by older infants. The exposures to all elements estimated in the TDS for the 12-14.99 month and 15-18 month age groups (Table 2) were higher than those determined from the infant survey for the corresponding age groups. This is due to the larger number of foods informing the exposure estimate in the TDS compared to those included in the food categories in the infant survey.

Table 6. Infant Formula - First and Follow on Milk (97.5th percentile in µg/kg bw/d)

Elements	4-5.99 Months (n=116)[b]	6-8.99 Months (n=606)[b]	9-11.99 Months (n=686)[b]	HBGV/BMDL[c]
Al	2.53-4.78[a]	2.00-3.82	1.59-2.86	286
Total As	0.00-0.03	0.00-0.04	0.00-0.04	N/A
Cd	0.00-0.02	0.00-0.02	0.00-0.02	0.36
Cr	0.02-0.42	0.00-0.34	0.00-0.27	300
Cu	52.8	40.7	30.3	68.5
Fe	850	852	770	N/A
Hg	0.00-0.02	0.00-0.02	0.00-0.02	0.57
I	16.3-20.1	14.7-15.3	10.8-12.7	13.7
iAs	0.00-0.03	0.00-0.03	0.00-0.03	BMDL 0.3-8.0
Mn	8.85-9.97	7.55-7.82	5.79-6.42	N/A
Ni	0.02-1.26	0.00-0.96	0.00-0.66	2.8
Pb	0.00-0.04	0.00-0.05	0.00-0.04	BMDL 0.5
Sb	0.00-0.14	0.00-0.11	0.00-0.08	6
Se	0.12-2.57	0.04-1.97	0.10-1.51	4.1
Sn	0.00-0.42	0.00-0.33	0.00-0.27	2000
Zn	788-839	638-650	512-542	480

a Ranges are lower bound (< LOD as 0) to upper bound (<LOD as the LOD), respectively. If there is only one figure all data were > LOD
b Number of children in the survey
c Values are HBGVs unless BMDL is stated

Table 7. Infant Formula - Growing Up Milk (12 Months Plus) (Maximum LB-UB Range) (µg/kg bw/day)

Elements	12-14.99 Months (n=670)[b]	15-18 Months (n=605)[b]	HBGV/BMDL[c]
Al	0.88-1.69[a]	0.65-1.26	286
Total As	0.02-0.04	0.01-0.03	N/A
Cd	0.00-0.02	0.00-0.01	0.36
Cr	0.00-0.17	0.00-0.13	300
Cu	19.5	15.0	68.5
Fe	577	445	N/A
Hg	0.00-0.01	0.00-0.01	0.57
I	7.9	6.09	13.7
iAs	0.01-0.03	0.01-0.02	BMDL 0.3-8.0
Mn	3.67	2.83	N/A
Ni	0.00-0.50	0.00-0.38	2.8
Pb	0.00-0.03	0.00-0.02	BMDL 0.5
Sb	0.00-0.05	0.00-0.03	6
Se	0.00-0.80	0.00-0.61	4.1
Sn	0.00-0.17	0.00-0.13	2000
Zn	430	331	480

a Treating occurrence data < LOD as 0 and as the LOD, respectively. If there is only one figure all data were > LOD
b Number of children in the survey
c Values are HBGVs unless BMDL is stated
Maximum values given as 97.5 percentile could not be derived due to limited number of individuals who consumed the formula.

Table 8**.** Infant Formula – Other types of Infant Formula* (LB-UB Range) (µg/kg bw/day).

Elements	4-5.99 Months (n=116)[b]	6-8.99 Months (n=606)[b]	9-11.99 Months (n=686)[b,d]	12-14.99 Months (n=670)[b,c]	15-18 Months (n=605)	HBGV/BMDL[e]
	Max[c]	P97.5[d]	P97.5[d]	Max[c]	Max[c]	
Al	27	26.4	30.8	24.32	17.6	286
As	0.07	0.1	0.08	0.07	0.05	N/A
Cd	0.12	0.11	0.13	0.1	0.08	0.36
Cr	0.37-0.58	0.42-0.82	0.46-0.91	0.33-0.52	0.24-0.38	300
Cu	30.8	80.0	36.8	27.7	20.1	68.5
Fe	691	1256	787	622	450	N/A
Hg	0.00-0.01	0.00-0.02	0.00-0.01	0.00-0.01	0.00-0.01	0.57
I	9.05	18.6	10.32	8.15	5.9	13.7
iAs	0.05	0.12	0.06	0.04	0.03	BMDL 0.3-8.0
Mn	29.5	28.9	33.6	26.6	19.2	N/A
Ni	2.12	2.07	2.41	1.91	1.38	2.8
Pb	0.00-0.05	0.14	0.00-0.06	0.00-0.05	0.00-0.03	BMDL 0.5
Sb	0.00-0.06	0.00-0.10	0.00-0.07	0.00-0.06	0.00-0.04	6
Se	1.56	2.27	2.15	1.4	1.01	4.1
Sn	0.00-0.24	0.00-0.58	0.00-0.30	0.00-0.22	0.00-0.16	2000
Zn	487	889	555	439	318	480

*Other formula include: Soy, Goat and Organic varieties.
a Ranges are lower bound (< LOD as 0) to upper bound (<LOD as the LOD), respectively. If there is only one figure all data were > LOD
b Number of children in the survey
c Maximum values given as 97.5th percentile could not be derived due to limited numbers of individuals who consumed the formula
d 97.5th percentile
e Values are HBGVs unless BMDL is stated

Table 9. Commercial Foods (97.5th percentile in µg/kg bw/day)

Elements	Lower to upper bound[a] dietary exposure to various elements		HBGV/BMDL[c]
	12-14.99 Months (n=670)[b]	15-18 Months (n=605)[b]	
Al	46.0	27.8	286
As	0.44	0.29	N/A
Cd	0.21-0.22	0.14	0.36
Cr	1.14-1.51	0.68-0.90	300
Cu	20.9	12.6	68.5
Fe	282	175	N/A
Hg	0.00-0.03	0.00-0.02	0.57
I	1.08-1.19	0.55-0.65	13.7
iAs	0.20-0.34	0.11-0.22	BMDL 0.3-8.0
Mn	64.9	41.5	N/A
Ni	2.00-2.77	1.21-1.72	2.8
Pb	0.10-0.15	0.07-0.08	BMDL 0.5
Sb	0.00-0.09	0.00-0.06	6
Se	0.44-0.47	0.28-0.29	4.1
Sn	1.46-1.63	0.89-0.99	2000
Zn	185	112	480

a Treating occurrence data < LOD as 0 and as the LOD, respectively. If there is only one figure all data were > LOD
b Number of children in the survey
c Values are HBGVs unless BMDL is stated

Table 10. Commonly consumed complementary foods (97.5th percentile µg/kg bw/day)

Elements	Lower to upper bound[a] dietary exposure to various elements		HBGV/BMDL[c]
	12-14.99 Months (n=670)[b]	15-18 Months (n=605)[b]	
Al	51.7-52.6	51.5-52.9	286
As	4.39-4.40	4.36-4.37	N/A
Cd	0.54-0.55	0.53	0.36
Cr	0.83-1.30	0.85-1.27	300
Cu	39.0	39.6	68.5
Fe	454-457	466-472	N/A
Hg	0.14-0.16	0.13-0.15	0.57
I	22.7	19.0	13.7
iAs	0.37-0.39	0.39-0.41	BMDL 0.3-8.0
Mn	174	175	N/A
Ni	2.63-3.84	2.47-3.48	2.8
Pb	0.12-0.17	0.10-0.15	BMDL 0.5
Sb	0.00-0.14	0.00-0.13	6
Se	2.22	2.36	4.1
Sn	311	226	2000
Zn	410	379	480

a Treating occurrence data < LOD as 0 and as the LOD, respectively. If there is only one figure all data were > LOD

b Number of children in the survey

c Values are HBGVs unless BMDL is stated

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

COT CONTRIBUTION TO SACN REVIEW OF COMPLEMENTARY AND YOUNG CHILD FEEDING; PROPOSED SCOPE OF WORK

Annex C contains the various health-based guidance values that are currently available for the elements included in the Total Diet Study and the Infant Metals Survey.

Secretariat
October 2015

Table 1. Health-based guidance values (HBGVs) for the elements included in the Total Diet Study and the Infant Metals Survey. The HBGVs have been presented in two formats: as they have been reported in the literature, and converted to standard units (µg/kg bw/day) for ease of comparison with exposure values.

Element	HBGV as reported	HBGV (µg/kg bw/day)
Aluminium	JECFA PTWI 2 mg/kg bw	285.7
Antimony	WHO TDI 6 µg/kg bw	6
Arsenic	N/A	N/A
Inorganic arsenic	EFSA $BMDL_{01}$ 0.3-8 µg/kg bw/day	0.3-8
Barium	WHO TDI 20 µg/kg bw	20
Bismuth	N/A	N/A
Cadmium	EFSA TWI 2.5 µg/kg bw	0.36
Chromium*	EFSA TDI 0.3 mg/kg bw	300
Copper*	SCF UL 1 mg/day (1-3 year olds) or JECFA PMTDI 50-500 µg/kg bw/day	68.5** (SCF) or 50-500 (JECFA)
Germanium	N/A	N/A
Indium	N/A	N/A
Iodine	SCF UL 200 µg/day (for 1-3 year olds)	13.7** (SCF)
Iron	N/A	N/A
Lead	EFSA $BMDL_{01}$ 12µg/L of blood (see note)	0.5***
Manganese*	(WHO TDI 60 µg/kg bw – see note)	(60)
Mercury	EFSA TWI 4 µg/kg bw	0.57
Methylmercury	EFSA TWI 1.3 µg/kg bw	0.19
Molybdenum*	SCF TUL 0.1 mg/day (to 0.5 mg/day) (for 1+ year olds)	6.9 (to 34.2)**
Nickel	EFSA TDI 2.8 µg/kg bw	2.8
Palladium	N/A	N/A
Platinum	N/A	N/A
Rhodium	N/A	N/A
Ruthenium	N/A	N/A
Selenium*	SCF UL 60 µg/day (for 1-3 year olds)	4.1** (SCF)
Strontium	WHO TDI 0.13 mg/kg bw	130
Tin	(JECFA PTWI 14 mg/kg bw – see note)	(2000)
Titanium	N/A	N/A
Zinc*	JECFA PMTDI 0.3-1.0 mg/kg bw or SCF UL 7 mg/day (1-3 year olds)	300-1000 (JECFA) or 479.5** (SCF)

* Essential trace elements
** Converted to a body weight basis using a body weight of 14.6kg (Bates, 2014)
*** Corresponding dietary intake value
$BMDL_{01}$ = Benchmark dose level of a 1% extra risk in key toxicological endpoint
N/A = None available

PMTDI = Provisional maximum tolerable daily intake
PTMI = Provisional tolerable monthly intake
PTWI = Provisional tolerable weekly intake
TDI = Tolerable daily intake
TUL = Tolerable upper level
TWI = Tolerable weekly intake
UL = Upper level

Notes on the health-based guidance values presented in Table 1

1. Aluminium – The Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives (JECFA) has set a provisional tolerable weekly intake (PTWI) of 2 mg/kg body weight (bw) (JECFA, 2011a).

2. Antimony – The World Health Organization (WHO) has set a tolerable daily intake (TDI) of 6 µg/kg bw (as stated in the 4th edition of their guidelines for drinking water quality, WHO, 2011a). This was based on a no observed adverse effect level (NOAEL), of 6 mg/kg bw, from a sub-chronic rat study so an uncertainty factor of 1000 was applied when the TDI was established (10 for inter-species, 10 for intra-species and 10 because it was not a chronic study). The endpoints seen at the NOAEL were decreased body weight and food and water intake, these are not generally considered signs of toxicity. See WHO, 2003 for more details.

3. Inorganic arsenic – No tolerable intake level has been established, but the European Food Safety Authority (EFSA) has identified a range of values for the 95% lower confidence limit of the benchmark dose of a 1% extra risk for each key toxicological endpoint ($BMDL_{01}$). The overall $BMDL_{01}$ range was 0.3-8 µg/kg bw/day; the EFSA concluded that this range of values should be used instead of a single reference point in the risk characterisation for inorganic arsenic (EFSA, 2009b).

4. Barium – The WHO has set a TDI of 20 µg/kg bw (WHO, 2001).

5. Cadmium – The European Food Safety Authority (EFSA) has set a tolerable weekly intake (TWI) of 2.5 µg/kg bw (EFSA, 2009a), while the JECFA has set a provisional tolerable monthly intake (PTMI) of 25 µg/kg bw (~5.8 µg/kg bw/week; JECFA, 2011b).

6. Chromium – The EFSA has set a TDI of 0.3 mg/kg bw for Cr(III) (EFSA, 2014); the EFSA assumed that all chromium in food was present as Cr(III) but that in bottled water was Cr(VI).

7. Copper – The JECFA established a provisional maximum tolerable daily intake (PMTDI) of 50-500 µg/kg bw/day (JECFA, 1982a), while the Scientific Committee on Food (SCF) set an upper level (UL) of 1 mg/day for 1-3 year olds (SCF, 2003a).

a. Nutrition requirements (SCF, 2013):
    i. 0<6 months 0.3 mg/day
    ii. 6<12 months 0.3 mg/day
    iii. 12<36 months 0.4 mg/day

8. Iodine – The SCF has set a UL of 200 µg/day for 1-3 year olds (SCF, 2002).
    a. Nutrition requirements (SCF, 2013):
        i. 0<6 months 90 µg/day
        ii. 6<12 months 90 µg/day
        iii. 12<36 months 90 µg/day

9. Iron – The EFSA said insufficient data to set a tolerable upper level (TUL) (SCF, 2013).
    a. Nutrition requirements (SCF, 2013):
        i. 0<6 months 0.3 mg/day
        ii. 6<12 months 8 mg/day
        iii. 12<36 months 8 mg/day

10. Lead – No longer has a tolerable intake level as there is no evidence for a threshold for critical lead-induced effects. The EFSA has derived several BMDLs from data on human blood lead levels; the most sensitive and appropriate (for this review) of these BMDLs is the $BMDL_{01}$ of 12 µg/L derived from blood lead levels relating to the critical effect of developmental neurotoxicity in young children, this BMDL corresponds to a dietary intake value of 0.5 µg/kg bw/day (EFSA, 2013).

11. Manganese – The WHO has set a TDI of 60 µg/kg bw (WHO, 2011b) but this was set with the possibility in mind that the bioavailability of manganese is increased when ingested via water, and was not used in the 2006 Total Diet Study (TDS); the SCF said insufficient data to set a UL (SCF, 2000a).
    a. Nutrition requirements (SCF, 2013):
        i. 0<6 months 3 µg/day
        ii. 6<12 months 0.02 - 0.5 mg/day (20-500 µg/day)
        iii. 12<36 months 0.5 mg/day (500 µg/day)

12. Mercury – The EFSA has set a TWI of 4 µg/kg bw expressed as mercury (EFSA, 2012).

13. Methylmercury – The form most often present in fish and seafood, also the most common organic form, the EFSA has set a TWI of 1.3 µg/kg bw, expressed as mercury (EFSA, 2012).

14. Molybdenum – SCF set a TUL of 0.1 mg/day for 1-3 year olds (and 0.2 mg/day for 4-6 year olds) (SCF, 2000b).
    a. Nutrition requirements (SCF, 2013):
        i. 0<6 months 2 µg/day

ii. 6<12 months 10 µg/day
iii. 12<36 months 15 µg/day

15. Nickel – The EFSA has set a TDI of 2.8 µg/kg bw (EFSA, 2015).

16. Selenium – The SCF set a UL of 60 µg/day for 1-3 year olds (SCF, 2000c).
    a. Nutrition requirements (SCF, 2013):
        i. 0<6 months. 12.5 µg/day
        ii. 6<12 months 15 µg/day
        iii. 12<36 months 20 µg/day

17. Strontium – The WHO has set a TDI of 0.13 mg/kg bw (WHO, 2010).

18. Tin – Not shown to be an essential nutrient but the EFSA (EFSA, 2005) stated that insufficient data were available to set a UL; the JECFA has established a PTWI of 14 mg/kg bw but later stated that the basis for this was unclear and that it may have been derived from intakes associated with acute effects (JECFA, 2006).

19. Zinc – The JECFA has established a PMTDI of 0.3-1.0 mg/kg bw (JECFA, 1982b); while the SCF set a UL of 7 mg/day for 1-3 year olds (SCF, 2003b).
    a. Nutrition requirements (SCF, 2013):
        i. 0<6 months 2 mg/day
        ii. 6<12 months 4 mg/day
        iii. 12<36 months 4 mg/day

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