

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

A review of potential risks from iodine in the diets of infants aged 0-12 months and children aged 1 to 5 years.

Introduction

1. The Scientific Advisory Committee on Nutrition (SACN) is undertaking a review of scientific evidence that will inform the Government dietary recommendations for infants and young children. The SACN is examining the nutritional basis for the advice. The COT was asked to review the risk of toxicity of chemicals in the diets of infants and young children. The reviews will identify new evidence that has emerged since the Government recommendations were formulated and will appraise that evidence to determine whether the advice should be revised. The recommendations cover diet from birth to age five years.
2. The UK population's exposure to iodine was measured in the 1997 Total Diet Study (TDS). The dietary exposure of adults to iodine for mean and high level consumers was respectively 0.22 and 0.43 mg/day¹. The COT reviewed the results from the 1997 TDS and concluded that the estimated total dietary intake of iodine is unlikely to pose a risk to health in normal, healthy individuals². In 2000, the COT reviewed data from a survey of iodine in cows' milk. At that time, the Committee concluded that concentrations of iodine in cows' milk are unlikely to pose a risk to health, even in those children who are high level consumers³. More recently, the Food Standards Agency completed a survey of 15 elements, including iodine, in infant formula, commercial infant foods and other foods. From the measured levels of iodine, the Committee concluded that the current estimated dietary exposures to iodine were not of toxicological concern⁴.
3. The Reference Nutrient Intake (RNI) for iodine was set by COMA in 1991 to be 0.14mg/day for adults and between 0.05 and 0.14mg/day for children⁵ (DH, 1991). The RNI for iodine for infants aged six months and younger in the UK is between 50-60 µg/day (DH, 1991). Data from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) indicated that infants and young children aged 4 to 18 months in the UK show a mean iodine dietary intake (including from supplements) of 94 to 174µg/day (equivalent to approximately 12 to 16 µg/kg bw/day); the corresponding range of 97.5th percentile intakes is 148 to 337 µg/day (equivalent to 19 to 31 µg/kg bw/day) (DH, 2013). Intake data excluding the use of supplements

¹ According to the Expert Group on Vitamins and Minerals available at: <https://cot.food.gov.uk/sites/default/files/vitmin2003.pdf>

² Available at: http://cot.food.gov.uk/sites/default/files/cot/cotcomcocrep_cot.pdf

³ Available at: <https://cot.food.gov.uk/sites/default/files/cot/iodin2.pdf>

⁴ Available at: <https://cot.food.gov.uk/cot-meetings/cotmeets/cot-meeting-5-july-2016>

⁵ RNIs set by COMA in 1991: 0-3 months (formula fed) 50 µg/day; 4-6 months 60 µg/day; 7-9 months 60 µg/day; 10-12 months 60 µg/day; 1-3 years 70 µg/day; 4-6 years 100 µg/day.

were not provided in the DNSIYC report. The mean and 97.5th percentile dietary intake of iodine (including supplements) for 1.5 to 3 years old children estimated from the National Diet and Nutrition Survey (NDNS, Bates *et al* 2014) was reported to be 143 and 303 µg/day, respectively (equivalent to approximately 10 and 21 µg/kg bw/day). Mean and high-level intakes reported in NDNS in the absence of supplement intake were similar: 142 and 303 µg/day, respectively. The milk and milk products food group made the main contribution (64%) to total intake from food in children aged 1.5 to 3 years.

4. There is a significant amount of literature available that suggests that the British population, including pregnant women, is moderately iodine-deficient which may have an implication for development of the fetus (SACN, 2014). However, due to high levels of iodine in British cow's milk, young children are generally considered to have an adequate iodine intake (BNF, 2011).

Background

5. In the environment, iodine is usually found in the form of iodate salts or organo-iodide compounds synthesized by algae and bacteria. Iodate is reduced in the GI tract to iodide which is the biologically active form (SACN, 2014).

6. Iodine is an essential micronutrient in the human diet, necessary for the production of thyroid hormones. These hormones are necessary for cell metabolism, growth and development at all stages of life. The most visible manifestation of iodine deficiency is goitre – an enlargement of the thyroid gland in the neck but other, more subtle effects can be noted in IQ and physical development at lower levels of deficiency (SACN, 2014).

Expert Opinions on Health-Based Guidance Values (HBGVs)

7. The Expert Group on Vitamins and Minerals (EVM) looked in detail at the metabolism of iodine and the effects of excess iodine in 2003⁶. Further information can be found in the background document prepared for the EVM⁷. The EVM concluded that there were insufficient data to set a Safe Upper Level (SUL) for iodine but for guidance they indicated that a level of 0.5mg/day of supplemental iodine in addition to the background intake of 0.43mg/day would be unlikely to cause adverse effects in adults based on slight alterations in thyroid hormone levels at supplemental doses of 0-2mg/day in a range of human studies. Information published since the EVM opinion was published in 2003 was obtained through a literature search in Pubmed using the search terms noted in appendix 1. This information has been included in this paper.

8. In 2006, the European Food Safety Authority (EFSA) published an opinion on the tolerable upper intake levels of vitamins and minerals. For iodine, they set a tolerable upper level (TUL) of 600 µg/day for adults, reduced on a body weight basis

⁶ Available at: <https://cot.food.gov.uk/sites/default/files/cot/vitmin2003.pdf>

⁷ Available at:

<http://tna.europarchive.org/20110911090542/http://www.food.gov.uk/multimedia/pdfs/evm0006p.pdf>

for children to 200 µg/day for ages 1-3 years and 250 µg/day for ages 4-6 years. This would be the equivalent of 8.6 µg/kg bw/day (EFSA, 2006). This figure was based on dose/response studies of short duration which showed changes in thyroid hormone levels at dose levels in excess of 600 µg/day and backed up by longer term studies with approximately similar doses that did not show adverse effects, but lacked detailed iodine intake data.

9. In 1989 the Joint Expert Committee on Food Additives (JECFA) set a provisional Maximum Tolerable Daily Intake (PMTDI) of 17 µg/kg bw/day from all sources based on the same longer term studies in adults used by EFSA in 2006 (Saxena et al, 1962; Thomas et al, 1978). No safety factors were used as these studies encompassed a relatively large number of subjects (JECFA, 1989).

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

Sources of iodine exposure

Human breast milk

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

Infant formulae and food

11. Levels of iodine have recently been measured in an FSA survey of metals and other elements in infant formulae and food (FSA, 2016a) and in the composite food samples of the 2014 Total Diet Study (TDS) (FSA, 2016b).

Drinking water

12. Iodine was detected at low levels (8 µg/L) in tap water from the 2014 TDS (FSA, 2016b). No further data were identified.

Environmental

Dust and soil

13. Iodine levels in soil are highly variable. A median value of 5.9 mg/kg and a 90th percentile value of 14.2 mg/kg have been reported for UK soil by the British Geological Society (BGS 2016). No specific value for dust was identified from the literature.

Air

14. No specific data on iodine levels in air was identified from the literature. Air is unlikely to be a major source of exposure to iodine.

Medication

15. Iodine can be used as a topical antiseptic which can be absorbed through the skin. Absorption in infants appears to be greater than in adults (Leung and Braverman, 2014). There are other medications that also contain iodine.

Exposure assessment

16. Consumption data (on a bodyweight basis) from DNSIYC (DH, 2013), and from years 1-4 of the NDNS (Bates et al., 2014) have been used for the estimation of dietary exposures for ages 4 to 18 months, and 18 to 60 months respectively. Bodyweight data used in the estimation of other iodine exposures are shown in Table 1 below.

17. Thorough exposure assessments have been performed for the dietary sources of exposure to iodine. The assessments for the non-dietary sources of exposure (i.e. soil) have been included to give a more holistic view of exposures, but are not as thorough as the focus of this statement is the diet of infants and young children.

Table 1. Average bodyweights used in the estimation of iodine exposures

Age group (months)	Bodyweight (kg)
0 to <4	5.9 ^a
4 to <6	7.8 ^b
6 to <9	8.7 ^b
9 to <12	9.6 ^b
12 to <15	10.6 ^b
15 to <18	11.2 ^b
18 to <24	12.0 ^c
24 to <60	16.1 ^c

^a DH, 1994

^b DH, 2013

^c Bates *et al.*, 2014

Exposure from Breast milk

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

19. Data on breast milk consumption for infants and young children aged 4 to 18 months were available from the DNSIYC and the NDNS, and have been used to estimate exposures at these ages (Table 2), based on a mean iodine concentration of 70 µg/kg (paragraph 10). There were too few records of breast milk consumption for children older than 18 months in the NDNS to allow a reliable exposure assessment, and breast milk is expected to contribute minimally in this age group.

20. Mean exposures to iodine for 4 to 18 month olds were 1.8 to 6.4 µg/kg bw/day, and 97.5th percentile exposures were 3.6 to 11 µg/kg bw/day (Table 2).

Table 2. Estimated iodine exposure in 0 to 18 month old infants and young children from breast milk, containing iodine at 70 µg/kg.

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

^a Based on default consumption values of 800 and 1200 mL for average and high level exclusive consumption of breast milk. .

^b Based on mean and 97.5th percentile consumption of breast milk from DNSIYC (DH,2013) Values rounded to 2 SF

Exposure from Infant formulae and complementary foods

21. Iodine exposure estimates for infant formulae and complementary foods were derived using occurrence data from the Infant Metals Survey (FSA, 2016a). The basis for this survey is explained in Annex A, but in brief, the exposure data derived from the Infant Metals Survey allow estimation of iodine exposure from infant formula, commercial infant foods and the most commonly consumed adult foods ('other foods') as sold.

22. Exposure estimates for 0 to 6 month olds were calculated for infants exclusively fed on 'first-milk' formulae using the default consumption values of 800 and 1200 mL (Table 3). In 0 to 6 month olds, exposures to iodine from exclusive feeding on ready-to-feed formula were 15 to 19 µg/kg bw/day in average consumers, and 22 to 29 µg/kg bw/day in high level consumers. Exposures to iodine calculated for reconstituted formula incorporating an iodine concentration in tap water taken from the 2014 TDS (paragraph 12) were 16 to 20 µg/kg bw/day in average consumers, and of 23 to 30 µg/kg bw/day in high level consumers (Table 3). The iodine concentration in tap water used for reconstitution of dry formula made a minimal contribution to total exposure from this source.

Table 3. Estimated average and high level exposures to iodine from exclusive feeding on infant formulae for 0 to 6 month olds.

Infant Formula (concentration)	Iodine Exposure ($\mu\text{g}/\text{kg bw}/\text{day}$)			
	0 to <4		4 to <6	
	Average consumer (800 mL/day)	High level consumer (1200 mL/day)	Average consumer (800 mL/day)	High level consumer (1200 mL/day)
Ready-to-Feed ^a	19	29	15	22
Dry Powder ^{b,c}	19	29	15	22
Dry Powder ^b + water at 8 $\mu\text{g}/\text{L}$ ^d	20	30	16	23

^a Exposure based on first milk infant formula using an iodine concentration of 143 $\mu\text{g}/\text{L}$

^b Exposure based on first milk infant formula using an iodine concentration of 948 $\mu\text{g}/\text{kg}$

^c Exposure does not include the contribution from water.

^d Determined by applying a factor of 0.85 to default formula consumption of 800mL and 1,200mL per day for estimating water consumption. Iodine concentration for tap water was from 2014 TDS. Values rounded to 2 SF.

23. Consumption data from the DNSIYC were used to estimate exposures from infant formula and complementary foods for 4 to 18 month olds (DH, 2013), based on upper-bound (UB) and lower-bound (LB) iodine concentrations in groups of complementary foods and levels detected in infant formula. Total mean exposures (excluding water) to iodine from infant formulae, commercial infant foods, and other foods, for 4 to 18 month olds were 8.6 to 11 $\mu\text{g}/\text{kg bw}/\text{day}$, and 97.5th percentile exposures were 18 to 23 $\mu\text{g}/\text{kg bw}/\text{day}$ (Table 4). These values are within the range of total intake of iodine that was reported in the DNSIYC survey for 4 to 18 month old children (DH 2013). Total mean and 97.5th percentile exposures have also been calculated using an iodine concentration of water of 8 $\mu\text{g}/\text{L}$ (paragraph 12). The resulting total mean and high level exposures indicated that iodine levels in tap water made a negligible contribution to total exposure.

Table 4. Estimated exposures to iodine from infant formulae, commercial infant foods and other foods for 4 to 18 month olds

Values rounded to 2 SF

Iodine Exposure (LB-UB Range) (µg/kg bw/day)										
Food	4 to <6 Months (n=116)		6 to <9 Months (n=606)		9 to <12 Months (n=686)		12 to <15 Months (n=670)		15 to <18 Months (n=605)	
	Mean	97.5 th	Mean	97.5 th	Mean	97.5 th	Mean	97.5 th	Mean	97.5 th
Infant formula	9.2	20	6.8	15	4.9	10	2.0	9.0	1.1	6.6
Commercial infant foods	0.35-.40	1.6-1.8	0.44-0.51	1.8-1.9	0.37-0.44	2.0-2.1	0.18-0.22	1.1-1.2	0.087-0.11	0.55-0.65
Other foods	0.52-0.53	3.4	1.7	6.0-6.1	3.1	16	8.6-8.7	23	8.8	19
Total (excl. tap water)	11	21 ^a	9.4-9.5	18 ^a	8.6-8.8	19 ^a	11	23 ^a	9.8-9.9	19 ^a
Total (incl. tap water at a concentration of 8 µg/L) ^b	11	21	9.5-9.6	18	8.7-8.9	20	11	23	9.9-10	19

^a 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

^b. Iodine concentration for tap water was from 2014 TDS.

Exposure estimates based on foods in the TDS

24. Results from the TDS are based on analysis of food that is prepared as for consumption (FSA, 2016b). The consumption data from the DNSIYC were used for the estimation of exposure for children aged 12 to 18 months (DH, 2013) whereas consumption data from NDNS (Bates et al., 2014) were used for estimating exposure in older children. Exposure estimates based on data from the 2014 TDS are presented only as UB, because the few food groups with concentrations below the LOQ or the LOD (green vegetables, fresh fruit and nuts) had a minimal impact on the total dietary exposure. A more detailed breakdown of individual food groups for the TDS can be found in Annex B. Mean and 97.5th percentile exposures to iodine from a combination of all food groups of up to 12 and 26 µg/kg bw/day, respectively were derived (Table 5). These estimates of dietary exposure are comparable to the intake values for iodine which were reported in NDNS (Bates *et al* 2014) for 1.5 to 3 year old children. The food groups making the highest contribution to iodine exposure in the TDS were milk and dairy products (Annex B).

Table 5. Estimated dietary exposure to iodine in children aged 18 months to 5 years.

UB iodine exposure (µg/kg bw/day)							
12 to <15 Months (n=670)		15 to <18 Months (n=605)		18 to <24 Months (n=70)		24 to <60 Months (n=429)	
Mean	97.5 th	Mean	97.5 th	Mean	97.5 th	Mean	97.5 th
11	24	11	22	12	26	8.4	17

Values rounded to 2 SF

Soil/dust

25. Potential exposures to iodine in soil and dust were calculated assuming combined soil and dust ingestion of 60 or 100 mg/day, for 6 to 12 month olds and 1 to 5 year old children, respectively (US EPA, 2011). Children of these age groups are likely to consume more soil and dust than younger infants who are less able to move around and come into contact with soil and dust. The median and 90th percentile values mentioned in paragraph 13 were used for deriving the exposures reported in Table 7. Data specific to dust were not available and therefore for the purposes of this evaluation, it is assumed that they could be the same as soil, (Table 7). The exposures in infants and young children based on the median and 90th percentile concentration of iodine in soil range from 0.036 to 0.056 µg/kg bw/day and 0.088 and 0.13 µg/kg bw/day respectively. These exposures are at least an order of magnitude lower that overall exposures from dietary sources.

Table 6. Potential iodine exposures (µg/kg bw/day) from soil and dust in infants and young children aged 6 to 60 months.

Iodine concentration	Age (months)					
	6 to	9 to	2 to	5 to	8 to	4 to

	<9	<12	<15	<18	<24	<60
Median (5.9 mg/kg)	0.041	0.037	0.056	0.053	0.049	0.036
90 th percentile (14.2 mg/kg)	0.097	0.088	0.13	0.13	0.12	0.088

Values rounded to 2 SF.

ADME and new data from animal studies

26. Iodine metabolism is complex, especially in times of excess. Iodine is used in the thyroid to produce about 80 µg/day thyroxine which corresponds to about 52 µg of iodine per day.

27. One of the acute effects of iodide excess is to impair the conversion of iodine to organic iodine (this is called the Wolff-Chaikoff effect). Excess iodine also causes inhibition of hormone secretion, thyroid blood flow, glucose and amino acid transport and protein and RNA biosynthesis. As most of the inhibitory effects of iodine are reversed by thionamides like methimazole and propylthiouracil it has been proposed that organic iodine compounds are responsible for these inhibitory effects – most likely iodolipids (Gartner, 2009).

28. Recent studies have shown the presence of the sodium-iodide symporter (NIS) in the gastric mucosa of rats with evidence suggesting that this served to move iodine from the blood stream into the lumen of the GI tract – suggesting a role in iodine excretion as well as iodine absorption. However, others have suggested that this NIS activity could be attributable to the antimicrobial properties of iodine – helping to reduce chances of infection in the GI tract (Joseffson, 2006). The kidneys have also been shown to be important in iodine excretion (Spitzweg, 2001).

29. In a study in female Sprague-Dawley rats administered methylnitrosourea to induce tumours, thyroid and mammary tissue were found to vary considerably in their uptake of iodine depending on the form in which the iodine is found and the status of the tissue (lactating, tumoral or normal in the case of mammary tissue). Thyroid tissue showed 300 times and lactating mammary tissue 4 times higher rate of iodine uptake via the NIS than tumoral and normal mammary tissue. (Anguiano et al, 2007).

Human studies and case studies with excess iodine

30. One of the most accurate methods of assessing iodine status is to test urinary iodine but this can vary considerably depending on short term iodine intake and fluid consumption and therefore whole day urine analysis with standardised fluid consumption is far more representative of total iodine intake than single sample concentrations (Andersen et al, 2009).

31. A study in four provinces of China looking at the iodine status of children aged 6-12 and pregnant women residing in areas receiving high iodine drinking water found that with water iodine levels of less than 100µg/L, children were receiving adequate iodine and Mean Urinary Iodine (MUI) levels were between 200 and 299

µg/L. When water levels exceeded 100µg/L, MUI's were high (above 300µg/L) in children. Given their higher iodine requirements, the MUI's in pregnant women were predictably lower than the children given the same water levels. Although the surveyed groups were receiving relatively high iodine intakes; the rate of goitre was found to be low, with 5% of individuals consuming water containing more than 300µg/L iodine demonstrating some degree of thyroid enlargement (Liu et al, 2014).

32. A number of studies have noted the relatively lower incidence of prostate and breast cancer in the Japanese population and the higher intake of seaweed consumption amongst this group. Seaweed is one of the richest dietary sources of iodine and the average iodine intake for the Japanese population is 5280 µg/day vs. 166 and 209 µg/day in the UK and the USA (Aceves and Anguiano, 2009). Iodine has been shown to have an anti-oxidant effect in several organs of the body including breast and prostate tissue.

33. There are a number of iodine-containing pharmaceuticals, of which currently the most commonly used are Povidone iodine (PVP-I) solution (a broad spectrum antiseptic), radiographic contrast media and amiodarone (an antiarrhythmic agent). All of these have been associated with drug induced thyroid dysfunction but this is primarily only in people with underlying or former thyroid disease or in neonates and infants. Patients with reduced iodine clearance via the kidneys are prone to thyroid disease. Drug induced thyroid dysfunction appears to be more common in population groups who generally have low iodine intakes (Nobukuni, 2009). Amiodarone, in particular, has a history of inducing thyroid dysfunction due to its high iodine content although the majority of patients receiving amiodarone remain euthyroid. A study comparing West Tuscany in Italy (an area of moderately low iodine intake) and Worcester, Massachusetts (an area of sufficient iodine intake) found the incidence of Amiodarone-induced-hypothyroidism to be 22% in Worcester and 5% in Tuscany. The prevalence of amiodarone-induced thyrotoxicosis was found to be 9.6% in Tuscany and 2% in Worcester (Basaria and Cooper, (2005). In a systematic review of exposure to iodine-based topical antiseptics in infants born following <32 weeks gestation, the authors concluded that there was a greater risk of thyroid dysfunction in this group, although the mechanism is not known (Aitken & Williams, 2014)

34. SACN recently published a scoping paper on Iodine and Health. In their conclusions, SACN state "Intake data from the National Diet and Nutrition Survey (NDNS) suggest that children aged ten years and younger and adults aged 19 years and older in the UK generally have adequate iodine intakes, in relation to the Reference Nutrient Intake (RNI), although 21% of girls aged 11-18 years have intakes below the Lower Reference Nutrient Intake (LRNI). However, insecurities surrounding food composition data for iodine and the phenomena of underreporting in dietary assessments are sources of error and uncertainty in the estimation of iodine intakes." The RNIs can be found in Table 8.

35. SACN conclude by stating that it is appropriate to examine data gathered in the NDNS on the UIC (Urinary Iodine Concentration) of the general UK population, provisionally available in 2015, before a full risk assessment on iodine and health is considered. The Committee will keep a watching brief on the arising evidence to inform future research in this area and any updates to the public health guidance on iodine for the UK population (SACN, 2014)

Risk characterisation

36. In 2003, the EVM set a guidance level of 500 µg/day for supplemental iodine (in addition to dietary iodine) that would not be expected to result in significant adverse effects in adults. They calculated that including the contribution from dietary sources, a total intake of 15 µg/kg bw/day would not be expected to cause adverse effects in the majority of the population. It should be noted that this is a guidance level only and is based primarily on data from adults; therefore its applicability to infants and young children is uncertain.

37. The EVM concluded that it is often difficult to distinguish toxic effects from effects that are the result of iodine feedback mechanisms designed to accommodate fluctuation in iodine intake. This makes it difficult to set a Safe Upper Level for iodine.

38. The EFSA tolerable upper level (TUL) was 600 µg/day for adults, reduced on a body weight basis for children to 200 µg/day for ages 1-3 and 250 µg/day for ages 4-6. This would be the equivalent of 8.6 µg/kg bw/day (EFSA, 2006).

39. The JECFA provisional Maximum Tolerable Daily Intake (PMTDI) was 17 µg/kg bw/day from all sources based on the same longer term studies in adults used by EFSA in 2006.

Table 8: Exposures for iodine in children up to 5 years old.

Age		0-<4 months	4-<6 months	6-<9 months	9-<12 months	12-<15 months	15-<18 months	18-<24 months	24-<60 months
Mean bodyweight for age group		5.9	7.8	8.7	9.6	10.6	11.2	12.0	16.1
Mean exposure s (µg/kg bw/day)	Breastfed	9.5a	7.2a	9.5-9.6c	8.7-8.9c	11d	9.9-11d	12e	8.4e
	Exclusively formula fed	20b	16b						
	Weaning diet and formula	-	11c						
97.5th percentile exposure s (µg/kg bw/day)	Breastfed	14a	11a	18c	20c	23-24d	19-22d	26e	17e
	Exclusively formula fed	30b	23b						
	Weaning diet and formula	-	21c						

Exposure to soil and dust has not been included in this table as their contribution to total exposure is minimal.

Ranges are based on upper bound and lower bound figures for iodine concentration in foods.

- a) Taken from Table 2 in this document.
- b) Taken from Table 4 in this document.
- c) Taken from Table 5 in this document.
- d) Taken from Tables 5 & 6 in this document.
- e) Taken from Table 6 in this document.

40. As outlined in Table 8, the range of mean iodine intakes was found to be 7.2-20 µg/kg bw/day and the high level intakes was found to be 11-30 µg/kg bw/day. The group with the highest intake is the exclusively formula-fed infants with a 97.5th percentile intake of 30 µg/kg bw/day – an intake of two times the guidance level set by the EVM. Apart from breast-fed infants, high level consumers (97.5th percentile) at all age groups were found to exceed the PMTDI level set by the JECFA. Infants below 6 months of age and exclusively formula-fed also exceeded the guidance level set by the EVM. Nearly all groups exceeded the TUL set by the EFSA in 2006.

41. These HBGVs are based on limited data. In all cases the relevant studies on which the HBGV are set did not allow an accurate estimation of dietary intakes. The response high iodine intakes can be highly variable between individuals and will depend on iodine status. Individuals with a low iodine status who are suddenly exposed to high iodine levels are more likely to experience adverse effects than those with an adequate iodine status.

42. It is difficult to distinguish between adverse effects and normal homeostatic changes in the case of iodine and the RNI and the guidance levels/tolerable daily intakes are of a similar order of magnitude. These two factors along with the fact that the available studies are all in adult populations make it difficult to identify a safe upper level which is applicable for all infants and children.

Questions for the Committee:

43. Members are invited to comment on the information provided in this paper and to consider the following questions:

- i. What are Members thoughts on the current Health Based Guidance Values (HBGVs) and which may be considered most appropriate for this age group?
- ii. Do Members consider the estimates of dietary exposure to iodine from a) breast milk b) infant formula and c) dietary sources indicate a concern for the health of infants?
- iii. Do Members have recommendations for additional information that should be obtained in order to reach conclusions?

**Secretariat
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Appendix 1

Literature search terms

In order to update our knowledge on iodine, we carried out a literature search using Pubmed for new data published since the EVM reviewed iodine toxicity in 2003 with emphasis on data in children aged 1-5 years.

Search terms:

Iodine toxicity
Iodine safety
Iodine in drinking water, UK
Iodine in soil, UK
Iodine in breastmilk

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

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

Possible iodine exposure from dietary sources in children aged 4 to 18 months

Two surveys were conducted during 2014 which measured the concentrations of elements in food consumed by infants (4 to 18 months) and young children (18 months to 5 years). The first survey was a survey on types of foods eaten by infants (referred to as the Infant Metals Survey), the other was a total diet study (TDS) which focused on sampling foods eaten by young children. Both studies measured the concentrations of iodine.

The Infant Metals Survey measured the concentrations of metals and other elements in food 'as sold', in the following categories: infant formula (Table A1) commercial infant foods (Table A2), and groups of food comprising the top 50 most commonly consumed varieties of foods not specifically marketed for infants (Table A3). 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) to estimate dietary exposures for children aged 4 to 18 months.

The TDS consisted 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 concentrations of 26 elements, including iodine, were measured in the 2014 TDS. The composite samples for 27 food groups (Table A4) were collected from 24 UK towns and analysed for their levels of iodine and other elements. Where appropriate, tap water was used in the preparation and cooking of food samples. The results from this survey were also used together with food consumption data from the DNSIYC (DH, 2013) to estimate dietary exposures for children aged 4 to 18 months.

Table A1. Infant formula

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	
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Table A2. 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 A3. Other foods commonly eaten by infants.

Other Foods	
Beverages	Fruit Products
Bread	Green Vegetables
Canned Vegetables	Meat Products
Cereals	Milk
Dairy Products	Other Vegetables
Eggs	Potatoes
Fish	Poultry/Chicken
Fresh Fruit	

Table A4. The 27 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 Assessments

Infant Metals Survey

Tables A5, A6 and A7 summarise lower- (LB) and upper-bound (UB) total dietary exposures to iodine calculated using results from the infants Metal Survey for ages 4 to 18 months.

Table A5: Estimated iodine exposure from infant formula in children aged 4 to 18 months using data from the Infant Metals Survey

Food Groups	Infant Formula - Iodine LB to UB (ug/kg bw/day)									
	4 to <6		6 to <9		9 to <12		12 to <15		15 to <18	
	Mean	97.5th Percentile	Mean	97.5th Percentile	Mean	97.5th Percentile	Mean	97.5th Percentile	Mean	97.5th Percentile
Comfort	0	0	0.016	0	0.055	0	0	0	0	0
First Milk: From Birth (Powder)	0.053	1.1	0.077	0	0.021	0	0	0	0	0
Follow On Milk: 6 Months (Powder)	0	0	0.043	0	0.076	0.52	0.0039	0	0.010	0
Growing Up Milk: 12 Months (Powder)	0	0	0	0	0	0	0.033	0	0.012	0
Goat Milk Formula	0	0	0.029	0	0	0	0	0	0	0
Hipp Organic	0	0	0.0054	0	0.0030	0	0.0010	0	0	0
Soy	0.096	0	0.048	0	0.049	0	0.014	0	0.0085	0
First Milk: From Birth (Ready to Feed)	8.2	20	3.4	15	1.5	9.4	0.21	4.0	0.049	0
Follow on: 6 Months (Ready to Feed)	0.89	9.2	3.2	11	3.1	10	0.77	6.5	0.39	4.2
Growing up Milk: 12 Months (Ready to Feed)	0	0	0.0069	0	0.11	0	0.97	7.7	0.63	6.0
Total	9.2	20	6.8	15	4.9	10	2.0	9.0	1.1	6.6

Table A6: Estimated iodine exposure from commercial infant foods in children aged 4 to 18 months using data from the Infant Metals Survey

Food Groups	Commercial Infant Foods - Iodine LB to UB (ug/kg bw/day)									
	4 to <6		6 to <9		9 to <12		12 to <15		15 to <18	
	Mean	97.5th Percentile	Mean	97.5th Percentile	Mean	97.5th Percentile	Mean	97.5th Percentile	Mean	97.5th Percentile
Cereal Based Dishes	0.10	0.48-0.49	0.11-0.12	0.58-0.60	0.082-0.084	0.52-0.54	0.034-0.035	0.34-0.35	0.014	0.15-0.16
Dairy Based Dishes	0.10	1.0	0.10	0.92-0.94	0.063-0.065	0.66-0.68	0.033-0.034	0.45-0.47	0.012	0.18-0.19
Fruit Based Dishes	0.039-0.048	0.30-0.37	0.057-0.070	0.32-0.40	0.054-0.066	0.29-0.36	0.034-0.042	0.25-0.30	0.021-0.026	0.18-0.22
Meat Based Dishes	0.038-0.059	0.24-0.38	0.061-0.096	0.31-0.49	0.058-0.091	0.29-0.46	0.034-0.053	0.23-0.37	0.017-0.027	0.14-0.22
Drinks	0-0.0069	0-0.068	0-0.0090	0-0.091	0-0.0078	0-0.070	0-0.0039	0-0.058	0-0.0035	0-0.042
Other savoury based dishes	0.075-0.077	0.49-0.51	0.11	0.62-0.64	0.12-0.12	0.80-0.83	0.046-0.047	0.45-0.46	0.023	0.34-0.35
Snacks - sweet and savoury	0.0011	0.0068	0.0016	0.0085	0.0016	0.0085	0.0012	0.0077	0.00070	0.0045
Total	0.35-0.40	1.6-1.8	0.44-0.51	1.8-1.9	0.37-0.44	2.0-2.1	0.18-0.22	1.1-1.2	0.087-0.11	0.55-0.65

Table A7: Estimated iodine exposure from other foods commonly eaten by children aged 4 to 18 months using data from the Infant Metals Survey

Food Groups	Other Food - Iodine LB to UB (ug/kg bw/day)									
	4 to <6		6 to <9		9 to <12		12 to <15		15 to <18	
	Mean	97.5th Percentile	Mean	97.5th Percentile	Mean	97.5th Percentile	Mean	97.5th Percentile	Mean	97.5th Percentile
Beverages	0-0.0016	0-0.024	0-0.0045	0-0.035	0-0.0034	0-0.044	0-0.0029	0-0.034	0-0.0042	0-0.070
Bread	0.0011-0.0014	0.016-0.020	0.010-0.013	0.067-0.086	0.029-0.037	0.11-0.15	0.043-0.056	0.14-0.19	0.048-0.062	0.16-0.20
Canned Vegetables	0-0.00050	0-0.0061	0-0.0022	0-0.023	0-0.0051	0-0.037	0-0.0077	0-0.043	0-0.0068	0-0.032
Cereal	0.0014-0.0016	0.016-0.019	0.023-0.027	0.13-0.15	0.034-0.041	0.15-0.18	0.042-0.051	0.17-0.21	0.052-0.063	0.18-0.22
Dairy Products	0.36	2.1	0.77	3.2	0.94	3.5	0.95	3.4	0.87	3.0
Egg	0.0075	0.0081	0.076	0.78	0.16	1.2	0.25	1.5	0.26	1.6
Fish	0.012	0.072	0.094	0.88	0.20	1.3	0.26	1.2	0.23	1.2
Fresh fruit	0-0.0040	0-0.028	0-0.0078	0-0.037	0-0.012	0-0.048	0-0.016	0-0.057	0-0.020	0-0.057
Fruit products	0.0014-0.0020	0.022-0.033	0.0021-0.0031	0.022-0.033	0.0021-0.0031	0.021-0.032	0.0034-0.0051	0.032-0.048	0.0049-0.0074	0.037-0.056
Green vegetables	0.0031-0.0034	0.026-0.030	0.0066-0.0074	0.031-0.035	0.0074-0.0082	0.049-0.055	0.0071-0.008	0.035-0.039	0.0074-0.0082	0.036-0.040
Meat products	0	0	0-0.00090	0-0.016	0-0.0023	0-0.022	0-0.0045	0-0.031	0-0.0061	0-0.050
Milk	0.12	1.4	0.67	3.7	1.7	14	7.1	20	7.1	17
Other vegetables	0-0.0061	0-0.045	0-0.0081	0-0.038	0-0.0074	0-0.032	0-0.0050	0-0.022	0-0.0049	0-0.019
Potato	0-0.0020	0-0.014	0-0.0044	0-0.021	0-0.0060	0-0.024	0-0.0065	0-0.029	0-0.0059	0-0.024
Poultry	0.0025	0.017	0.0075	0.061	0.0099	0.070	0.010	0.059	0.0095	0.064
Total	0.52-0.53	3.4	1.7	6.0-6.1	3.1	16	8.6-8.7	23	8.6	19

Total Diet Study

Table A8 summarise lower- and upper-bound total dietary exposures to iodine calculated using the 2014 TDS for ages 12 to 18 months. 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. In addition the total exposure from the diet has also been provided.

Table A8 Estimated iodine exposure from food eaten by young children aged 12 months to 18 months using data from the TDS Groups.

Food Groups	Total Diet Study - Iodine LB to UB (ug/kg bw/day)			
	12 to <15		15 to <18	
	Mean	97.5th Percentile	Mean	97.5th Percentile
Bread	0.068	0.19	0.077	0.21
Miscellaneous Cereals	0.37	1.1	0.44	1.3
Carcase meat	0.022	0.11	0.028	0.14
Offal	0.00020	0	0.0018	0
Meat products	0.064	0.34	0.079	0.36
Poultry	0.016	0.068	0.017	0.075
Fish	0.75	3.5	0.71	3.6
Fats and oils	0.0061	0.025	0.0072	0.027
Eggs	0.26	1.3	0.26	1.4
Sugars	0.059	0.36	0.089	0.44
Green vegetables	0-0.0051	0-0.023	0-0.0056	0-0.021
Potatoes	0.021	0.077	0.020	0.064
Other vegetables	0.023	0.084	0.023	0.077
Canned vegetables	0.014	0.070	0.013	0.062
Fresh fruit	0-0.028	0-0.097	0-0.035	0-0.10
Fruit products	0.17	1.2	0.19	1.3
Non-alcoholic beverages	0.097	0.46	0.12	0.55
Milk	6.9	20	6.9	17
Dairy products	2.4	13	2.0	8.9
Nuts	0-0.00080	0-0.0033	0-0.00030	0-0.0032
Alcoholic drinks	0.00010	0.00030	0	0
Meat substitutes	0.0010	0	0.0027	0.033
Snacks	0.0094	0.065	0.015	0.10
Desserts	0.060	0.52	0.082	0.60
Condiments	0.014	0.085	0.016	0.083
Tap water	0.079	0.30	0.090	0.36
Bottled water	0.0010	0.0090	0.0014	0.021
Total	11	24	11	21-22

References

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

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

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

Possible iodine exposure from dietary sources in young children aged 18 to 60 months

A Total Diet Study (TDS) was conducted during 2014 which measured the concentrations of iodine by young children (18 months and older).

The TDS consisted 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 concentrations of 26 elements, including iodine, were measured in the 2014 TDS. The composite samples for 27 food groups (Table B1) were collected from 24 UK towns and analysed for their levels of iodine and other elements. Where appropriate, tap water was used in the preparation and cooking of food samples. The results from this survey were also used together with food consumption data from years 1 to 4 of the National Diet and Nutrition Survey Rolling Programme (NDNS) (Bates *et al.*, 2014) to estimate dietary exposures for young children aged 18 months to 5 years.

Table B1. 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 B2 summarises lower- and upper-bound total dietary exposures to iodine calculated using the 2014 TDS for young children aged 18 months to 5 years. 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. In addition the total exposure from the diet has also been provided.

Table B2. Estimated iodine exposure from food eaten by young children aged 18 months to 5 years using data from the TDS Groups.

FOOD GROUP	Total Diet Study - Iodine LB to UB (ug/kg bw/day)			
	18 to <24		24 to <60	
	Mean	97.5th Percentile	Mean	97.5th Percentile
Bread	0.081	0.18	0.092	0.21
Miscellaneous Cereals	0.47	0.99	0.39	0.98
Carcase meat	0.030	0.16	0.018	0.098
Offal	0.00040	0	0.00060	0
Meat products	0.094	0.43	0.11	0.38
Poultry	0.020	0.057	0.017	0.074
Fish	0.93	3.7	0.71	2.7
Fats and oils	0.0098	0.031	0.0088	0.029
Eggs	0.20	1.1	0.20	1.2
Sugars	0.10	0.49	0.15	0.63
Green vegetables	0-0.0048	0-0.029	0-0.0049	0-0.020
Potatoes	0.020	0.042	0.018	0.053
Other vegetables	0.014	0.047	0.015	0.053
Canned vegetables	0.023	0.088	0.014	0.054
Fresh fruit	0-0.043	0-0.11	0-0.031	0-0.081
Fruit products	0.43	1.7	0.39	1.9
Non-alcoholic beverages	0.16	0.66	0.15	0.44
Milk	6.5	20	4.6	13
Dairy products	2.2	10	1.2	4.9
Nuts	0-0.00020	0-0.00030	0-0.00060	0-0.0080
Alcoholic drinks	0.00010	0	0	0
Meat substitutes	0.00070	0.012	0.0031	0.047
Snacks	0.017	0.10	0.020	0.11
Desserts	0.13	0.69	0.14	0.67
Condiments	0.011	0.056	0.018	0.092
Tap water	0.089	0.47	0.081	0.30
Bottled water	0.00070	0.0070	0.0018	0.0191
Total	12	26	8.4	17

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) Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/310995/NDNS_Y1_to_4_UK_report.pdf