

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

Discussion paper on the potential risks from chromium in the diet of infants aged 0 to 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's dietary recommendations for infants and young children. The SACN is examining the nutritional basis of the advice. The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) was asked to review the risks of toxicity from chemicals in the diet of infants, most of which has been completed, and young children. The reviews will identify new evidence that has emerged since the Government's recommendations were formulated, and will appraise that evidence to determine whether the advice should be revised. The recommendations cover diet from birth to age five years.

2. This discussion paper provides estimated chromium exposures for infants and young children in the UK aged 0 to 12 months and 1 to 5 years, respectively. There are currently no Government dietary recommendations for infants and young children on chromium.

Background

3. Chromium is a hard, highly lustrous metal that exists in various mineral forms and is present throughout the environment. It is used in a wide variety of processes including tanning, photography, fungicides, ceramics and glass, electroplating, alloy production, paints and pigments, and is present in a wide range of industrial and consumer products, especially stainless steel. Chromium concentrations in the environment reflect both natural and anthropogenic contributions. The most prevalent natural form of chromium is trivalent (Cr^{3+} or Cr(III)). Hexavalent chromium (Cr^{6+} or Cr(VI)) is present in the environment largely as a result of industrial activity.

4. The general population is primarily exposed to chromium via food and drinking water, with inhalation from ambient air and percutaneous exposure acting as minor sources of exposure. Food, being largely a reducing environment, is considered to be a source of Cr(III), whereas drinking water, which is subject to purification with oxidising agents, is a source of Cr(VI). Workers in the steel industry, such as stainless steel welders can be exposed to high respiratory levels of Cr (VI). Smoking cigarettes also makes a large contribution to inhalation exposure to Cr (VI). (EFSA, 2014).

5. Chromium (III) is regarded as an essential dietary mineral that improves the efficiency of glucose metabolism.

Toxicokinetics

Absorption

6. Following oral ingestion in humans, Cr(III) and Cr(VI) are not well absorbed. Gastrointestinal absorption of Cr(III) is low: ATSDR (2012) state that less than 1% of oral Cr(III) and 1 – 2% of Cr(III) infused into the duodenum or jejunum is recovered from human urine. EFSA (2014) quotes a range of 0.4 – 2.8%. Cr(VI) shows slightly greater absorption, at 2 – 8% (WHO, 2013). Absorption depends largely on the solubility of a particular compound.

7. Absorption through the skin is greater for Cr(VI) than for Cr(III) but the presence of sweat appears to reduce Cr(VI) to Cr(III) and thus acts as a protective mechanism (Franken *et al.*, 2015).

8. Trivalent chromium is used as a food supplement complexed with picolinic acid, nicotinic acid or other binding agents. These complexes may have a different uptake mechanism from other salts of this valency form and this complexation may increase absorption from the gastrointestinal tract. However Laschinsky *et al.* (2012) found no effect of Cr(III) complexation on retention of chromium after absorption.

Distribution

9. Cr(III) absorbed into the blood is transported in the plasma since it shows low penetration of biological membranes and enters cells by simple diffusion or phagocytosis (EFSA, 2014). Cr(VI) is absorbed into cells by facilitated diffusion through phosphate and/ or sulphate transporters (Yokel *et al.*, 2006) and thus can be transported in erythrocytes. Once in the erythrocytes the Cr(VI) is reduced to the trivalent form (Davoy *et al.*, 2016), where it binds to proteins. When not sequestered into erythrocytes, chromium is rapidly distributed to liver, kidneys, spleen and bone marrow.

Metabolism

10. Cr(VI) is reduced to Cr(III) by gastric juice, thus limiting the absorption of the hexavalent form. This process is pH dependent, being greater at lower pH, and appears to be the result of the presence of three “pools” of thermostable reducing agents in gastric juice, with different rates and capacities (De Flora *et al.*, 2016; Kirman *et al.*, 2016). Estimates differ regarding how effective a detoxification mechanism this represents (EFSA, 2014). Reduction also takes place in the lungs (ATSDR 2012).

11. It has been suggested that Cr(III) is involved in the efficient functioning of insulin receptors. Vincent (2000) proposed a mechanism where Insulin-receptor binding caused translocation of the iron-binding protein transferrin from internal vesicular membranes to the cell membrane, where it bound Cr(III) and became

internalised. The Cr(III) then dissociated from the transferrin and bound to the protein chromodulin. The Cr(III)-chromodulin complex was then proposed to bind to activated insulin receptors, enhancing their activity. More detailed biochemical schemes have followed to account for the effect of Cr(III) in alleviating insulin resistance (Hua *et al.*, 2012) and promoting adipocyte differentiation (Tsavé *et al.*, 2016) in type 2 diabetes mellitus.

Excretion

12. The majority (98 – 99%) of ingested chromium is egested in the faeces. Chromium (III) within erythrocytes can persist for years whereas that in the plasma is rapidly excreted in the urine. The average half-life of excretion in human urine has been estimated at 39 hours after a 0.05 mg oral dose of Cr(VI) and 36 hours for elimination from plasma following a dose of 0.8 mg 5 times a day for 17 days (ATSDR, 2012).

Toxicology

Acute toxicity

13. In the general population the main concern is chronic effects of Cr(VI), exposure and acute toxicity is largely confined to workers in the metallurgical industries where activities such as stainless steel welding vaporises the metal, which can then be inhaled. Inhalation of Cr(VI) leads to irritation of the respiratory tract and the formation of painless ulcers and perforations of the nasal septum (US EPA, 1969).

14. Acute effects of ingestion of chromium are nausea and vomiting and ulceration of the gastrointestinal tract. Contact with skin and mucus membranes can lead to localised tissue burns sometimes referred to as chrome holes. Some individuals develop dermatitis from skin exposure to chromium salts and this is exacerbated by dietary and inhalation exposure (ATSDR, 2012).

15. Satarma *et al.* (2016) showed that intranasal chromium can induce acute injury to the lungs but also to the brain by absorption through the nasal mucosa, implying that the damage done by inhaling Cr(VI) may begin before it reaches the lungs.

Chronic effects

16. The International Agency for Research on Cancer (IACR) regard Cr(VI) as a carcinogen in humans by inhalation. There are also chronic non-carcinogenic effects on the hepatic, renal and haematopoietic systems. Cr(III), while possibly the ultimate form of the metal involved in carcinogenic mechanisms, is not regarded as a carcinogen because of its poor cellular penetration (IACR 2012).

Oxidative stress

17. Oxidative stress is a biochemical state in which the production of reactive oxygen species (ROS) such as superoxide and hydroxyl radicals, by cellular

processes exceeds the capacity of the cell's antioxidant mechanisms to counteract it. Cr (VI) is reduced intracellularly by single-electron transfer (for example by glutathione) to Cr(V), which then engages in Fenton-type reactions to lead to the production of ROS. The ROS can then lead to the disruption of normal cellular function by inhibiting enzymes, altering lipid metabolism and forming DNA oxidation products (particularly 8-hydroxy-2'-deoxyguanosine) (EFSA, 2014).

Carcinogenicity

18. The IARC have designated chromium (VI) to be a human carcinogen (Group 1) by inhalation on the basis of occupational studies (IACR, 2012). Exposure to chromium by inhalation in the general population has been statistically associated with increased risk of cancer, largely of the lung and to a lesser extent of the paranasal sinuses. Ingested chromium has not been associated with any carcinogenicity in humans. Cr(VI) does not appear to be directly genotoxic but if it escapes reduction outside cells, intracellular reduction by glutathione leads to transient Cr(V) production and oxidative stress (see above) and 2-electron reduction using ascorbate generates Cr(IV), leading to complex Cr(III)-DNA and protein-Cr(III)-DNA adducts (EFSA, 2014).

19. Oral ingestion of Cr(III) and Cr(VI) in experimental animals has resulted in gastrointestinal cancers, but this has not been shown in humans.

Expert opinions

20. An expert opinion on exposure to chromium in food and drinking water has been published by the European Food Safety Authority's (EFSA) Panel on Contaminants in the Food Chain (CONTAM) (EFSA, 2014). The COT reviewed chromium in their report on metals in the diet (2003). The World Health Organization (WHO) has reviewed exposures to chromium via drinking water as part of the development of their 'Guidelines for Drinking Water Quality' (WHO, 2011). The IARC has published an evaluation of the carcinogenicity of chromium compounds (IARC, 2012).

EFSA

21. In their 2014 scientific opinion, the EFSA CONTAM Panel stated that mean chronic dietary exposures to chromium in 'Italian infants and children from 0.5 up to 6 years of age ranged from 3.17 to 3.75 µg/kg body weight (bw)/week, while 95th percentile chronic dietary exposures in children aged 0.5 to 12 years of age ranged from 4.95 to 6.08 µg/kg bw/week¹.

22. The EFSA CONTAM Panel considered it unlikely that dietary exposure to chromium results in cancer in humans (EFSA, 2014).

¹ Estimates were only available from one dietary survey.

23. As part of their assessment, the CONTAM Panel established a TDI of 300 µg Cr(III)/kg b.w. per day from a NOAEL of 286 mg/kg b.w. per day of a long-term rat study, with a default uncertainty factor of 100 to account for species differences and individual variability, with an additional uncertainty factor of 10 to allow for inadequate data on reproductive and developmental toxicity.

24. The CONTAM Panel derived a BMDL₁₀ of 1.0 mg Cr(VI)/kg b.w. per day for combined adenomas or carcinomas of the small intestine in male and female mice. For non-neoplastic lesions in experimental animals, the CONTAM Panel derived a BMDL₁₀ value of 0.11 mg Cr(VI)/kg b.w. per day for diffuse epithelial hyperplasia of the duodenum in female mice. For haematological effects, the CONTAM Panel derived a BMDL₀₅ of 0.2 mg/kg b.w. per day for decrease of haematocrit in male rats.

WHO

25. The Joint FAO/WHO Committee on Food Additives (JECFA, 2003) did not establish a health based guidance value for chromium but the value of 0.05 mg/L, which is considered to be unlikely to give rise to significant risks to health, has been retained as a provisional guideline value until additional information becomes available and chromium can be re-evaluated.

IARC

26. The IARC reviewed chromium (III) and chromium (VI) and their compounds, in 2009. Cr(VI) and its compounds have been classified as human carcinogens that cause cancers of the lung, and paranasal sinuses after inhalation (IARC, 2012). However, the potency of the carcinogenic effect depends upon the physicochemical properties of the compound. There is currently no consistency in the data to suggest that Cr(III) compounds cause cancer in humans at concentrations to which people are exposed in food or the wider environment.

EVM

27. The Expert Group on Vitamins and Minerals stated in their statement of 2003 (<https://cot.food.gov.uk/sites/default/files/vitmin2003.pdf>):

“Overall, there are insufficient data from human or animal studies to derive a Safe Upper Level for chromium, although the oral toxicity of poorly absorbed trivalent chromium appears to be low. There are few available data on chromium (III) toxicity in humans by the oral route. Acute chromium toxicity is associated with vomiting, diarrhoea, haemorrhage and blood loss into the gastrointestinal tract resulting in cardiovascular shock. The available animal data are also limited but adverse gastrointestinal, hepatic, renal, immunological, neurological, developmental and reproductive effects have been reported.

The study by Anderson et al. (1997) indicated that 15 mg/kg bw/day chromium (as chromium chloride) was not associated with adverse effects in the rat. Based on this study, and allowing uncertainty factors of 10 for inter-species variation and 10 for inter-individual variation, a total daily intake of about 0.15 mg/kg bw/day (or 10

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

mg/person) would be expected to be without adverse health effects. This value can be used for guidance purposes and applies to trivalent chromium only”.

28. UK Governmental advice states that while ingestion and inhalation of Cr (III) and Cr (VI) are associated with acute and chronic health effects, members of the general public not involved in the industrial uses of chromium would not be expected to be exposed to high enough concentrations to cause concern for health.

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/338691/Chromium_info_incid_mgmt_tox.pdf

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

Sources of chromium exposure

Human breast milk

29. In general, low levels of chromium are found in breast milk (EFSA, 2014).

30. As part of the 2004 SUREmilk study, levels of chromium were measured in breast milk from women in the UK. In 104 samples, chromium was not detected above the limit of quantification (LOQ, 10 µg/l) in any sample, with only 13% being above the limit of detection (LOD, 3 µg/l). These data suggest that negligible risk is presented to breast-fed infants from chromium in breast milk (Woolridge *et al.*, 2004).

31. The COT² noted that the SUREmilk samples were collected primarily to explore the viability of breast milk collection methods and did not constitute a rigorous survey. Nevertheless, it was possible to draw the conclusion that the estimated intakes of metals and other elements associated with the highest detected concentrations in the breast milk samples did not raise toxicological concerns. From reports from other countries, average values vary over three orders of magnitude, from approximately 0.7 µg/l to 148 µg/l; reported maximum values range from 2.5 to 19.4 µg/l Cr. These ranges may reflect the level of environmental emissions of Cr in the country involved at the time of publication, the sensitivity of the detection method and the experimental design. Table 1 gives a range of recent measured levels of Cr in breast milk.

² <http://cot.food.gov.uk/sites/default/files/cot/cotsuremilk.pdf>

Table 1. Concentrations of chromium in breast milk available from the published literature

Country	Number of samples	Average concentration (µg/L)	Minimum concentration (µg/L)	Maximum concentration (µg/L)	Reference
UK	104	-	< 3(LOD)	<10 (LOQ)	Woolridge <i>et al.</i> (2004)
Brazil	-	<u>148</u>	-	-	Cardoso <i>et al</i> (2014)
China	-	-	0.9	7.37	Sun <i>et al.</i> (2013)
Japan	79	1.0	<0.1	18.61	Yoshida <i>et al.</i> (2008)
United Arab Emirates	209	0.69	0.0	2.5	Abdulrazzaq <i>et al.</i> (2008)
Spain			0.2	8.18	Sola-Larañaga <i>et al</i> (2006)
Germany	19	10.8	3.1	19.4	Wappenhorst <i>et al</i> (2002)
Germany		24.3			Krachler <i>et al</i> (2000)

32. In the absence of a suitable UK study of chromium levels in breast milk, data from the German study of Wappenhorst *et al.* (2002) have been used in this paper.

Infant formulae and food

33. Concentrations of chromium have recently been measured in an FSA survey of metals and other elements in infant formulae and foods (e.g. commercial infant foods) (referred to as the Infant Metals Survey), and in the composite food samples of the 2014 Total Diet Study (TDS).

Food contact materials

34. The migration of chromium from food contact materials could represent an additional source for the presence of this metal in food and drinking water. The EU has not set a migration limit for chromium from kitchen utensils that make contact with food.

35. Szydal *et al.* (2016) analysed 172 samples of ceramic ware (84 deep dishes and 88 flat dishes) and 52 samples of decorated glassware from China. Migration of chromium from the ceramic ware into 4% acetic acid over 24 hours at 22°C was below the limit of quantification (LOQ) for the flame atomic absorption spectrometry (FAAS) method used (0.02mg/l). For glassware, migration of chromium into 4%

acetic acid over 24 hours at 22°C or into 0.5% citric acid over 2 hours at 70°C was also below the LOQ of the FAAS.

Drinking water

36. The primary source of Cr(III) in drinking water is leaching from groundwater as a consequence of dissolution from chromium ore-bearing rocks. However EFSA (2014) regard Cr(VI) as much more prevalent in drinking water, originating largely from anthropogenic sources. Moreover, since drinking water is treated with oxidising agents such as ozone to make it potable, any Cr(III) present would be oxidised to the Cr(VI) form.

37. EU legislation sets a value of 50 µg/L for chromium in water intended for human consumption (Directive 98/83/EC). The WHO has also established a guidance level of 50 µg/L for chromium in drinking water (WHO, 2009).

38. Levels of chromium in drinking water in 2016/2017 from England and Wales, Northern Ireland and Scotland were provided by the Drinking Water Inspectorate (DWI), Northern Ireland Water and the Drinking Water Quality Regulator (DWQR) for Scotland, respectively. Median and 97.5th percentile values calculated from these data are shown in Table 2. These values have been used to calculate exposures to chromium from drinking water in combination with exposures from food.

Table 2. Median and 97.5th percentile concentrations (µg/L) of chromium in water across the UK for 2016/2017

Country	Number of samples	Limit of Detection (µg/L)	Median concentration (µg/L)	97.5 th Percentile concentration (µg/L)
England and Wales	12369	0.025-2.0*	0.4	1.2
Northern Ireland	393	0.1	0.2	0.4
Scotland	19232	0.2	0.3	1.8

* The DWI noted that the water companies had reported a range of LODs that varied with the analytical method used, and clarified that the relevant drinking water regulations specify that the LOD must not be more than 10% of the prescribed value 50 µg/L for chromium

Environmental

Soil

39. Chromium is a metallic element, present at about 35 mg/kg in the upper continental crust, but is more abundant in basic (250–300 mg/kg) and ultrabasic (2300 mg/kg) igneous rocks and shales (100 mg/kg) than in granites and sandstones (10–35 mg/kg) (Reimann and De Caritat, 1998). It is an essential element for animals at trace levels, but its bioavailability from the soil is generally low because it exists mainly in the insoluble reduced form (Cr III) in soil.

40. Concentrations of chromium were measured in 5,670 topsoil (from a depth of 0 to 15 cm) samples collected between 1978 and 1982 in England and Wales. Samples were analysed 30 years later (Rawlins *et al.*, 2012). The median and 90th percentile concentrations were reported as 68 and 97 mg/kg, respectively.

Dust

41. Harrison (1979) determined the levels of chromium and other metals in outside and domestic dust samples collected in Lancaster, UK. “Available” chromium levels in domestic dust, i.e. those extractable from the dust by 0.07N HCl to mimic gastric acid, were 11.8 ± 6.1 µg/g (Mean \pm SD, n = 4, range 5.0 – 20 µg/g).

Air

42. Data from 23 air sampling sites across the UK have been collected by Defra. The data for 2007 - 2016 have yielded lowest and highest median values of 0.8 and 8.65 and lowest and highest 99th percentiles of 1.4 and 167 ng chromium/m³ across the sites. The highest value measured was 184 ng/m³ from a sampling site near Sheffield.

43. Cr(VI) in the air is reduced in the air to Cr(III) with a half time of 16 hours to 5 days (ATSDR 2012). Since atmospheric transport of respirable particles may cover large distances (WHO 2006) it is possible that a proportion of inhaled particles may contain Cr(VI) as well as Cr(III). However, Cr (VI) is not relevant to the remit of this paper so the chromium in air will be treated solely as Cr(III).

Exposure assessment

44. Consumption data (on a bodyweight basis) from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) (DH, 2013), and the National Diet and Nutrition Survey Rolling Programme (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 chromium exposures are shown in Table 3 below.

45. Thorough exposure assessments have been performed for the dietary sources of exposure to chromium. The assessments for the non-dietary sources of exposure (i.e. dust, soil and air) 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 3. Average bodyweights used in the estimation of chromium 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

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

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

Infants (0 to 12 months)

46. 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 chromium from breastmilk. These estimates were based on minimum and maximum chromium concentrations of 3.1 and 19.4 µg/L, respectively. The ranges of exposure to chromium in exclusively breastfed 0 to 6 month olds were 0.32 to 2.6 and 0.48 to 3.9 µg/kg bw/day in average and high level consumers respectively (Table 4).

Table 4. Estimated chromium exposure from exclusive breastfeeding in 0 to 6 month old infants, with breast milk containing chromium at 3.1 or 19.4 µg/L.

Chromium concentration (µg/L)	Exposure (µg/kg bw/day)			
	Average consumer (800 mL/day)		High consumer (1200 mL/day)	
	0 to <4 months	4 to <6 months	0 to <4 months	4 to <6 months
3.1	0.42	0.32	0.63	0.48
19.4	2.6	2.0	3.9	3.0

Values rounded to 2 significant figures (SF)

47. Data on breast milk consumption for infants aged 4 to 18 months were available from the DNSIYC and the NDNS and have been used to estimate exposures at these ages (Table 5), based on a minimum and maximum concentration of 3.1 and 19.4 µg/L, respectively. 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.

48. Mean exposures to chromium for 4 to 18 month olds were 0.078 to 1.8 µg/kg bw/day, and 97.5th percentile exposures were 0.16 to 3.0 µg/kg bw/day (Table 5).

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

Table 5. Estimated chromium exposure in 4 to 18 month old infants from breast milk, containing chromium at 3.1 and 19.4 µg/L.

Exposure (µg/kg bw/day)	Age group (months)				
	4 to <6	6 to <9	9 to <12	12 to <15	15 to <18
Mean @ 3.1 µg/L	0.29	0.21	0.12	0.091	0.078
97.5th percentile @ 3.1 µg/L	0.48	0.49	0.36	0.23	0.16
Mean @ 19.4 µg/L	1.8	1.3	0.74	0.56	0.49
97.5th percentile @ 19.4 µg/L	3.0	3.1	2.2	1.5	1.0

Values rounded to 2 SF

Infant formulae and complementary foods

49. Chromium exposure estimates for this category were derived using occurrence data from the Infant Metals Survey (FSA, 2016a), based on both lower bound (LB) and upper bound (UB) concentrations. Exposure estimates for 0 to 6 month olds were calculated for exclusive feeding on infant formulae using the default consumption values of 800 and 1200 mL (Table 6). Consumption data from the DNSIYC were used to estimate exposures for 4 to 12 month olds (DH, 2013).

50. In 0 to 6 month olds, exposures to chromium from ready-to-feed formula were 0 to 0.41 µg/kg bw/day in average consumers, and 0 to 0.61 µg/kg bw/day in high level consumers. Exposures to chromium calculated for reconstituted formula incorporating the water concentration from the TDS, and the highest median and 97.5th percentile concentrations for chromium in water reported in Table 7 were 0.36 to 1.6 µg/kg bw/day in average consumers, and of 0.0.53 to 2.5 µg/kg bw/day in high level consumers (Table 6).

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

Infant Formula	Chromium Exposure (LB-UB Range) (µg/kg bw/day)			
	0 to <4 months		4 to <6 months	
	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	0-0.41	0-0.61	0-0.31	0-0.46
Dry Powder ^{b, c}	0.31-0.71	0.46-1.1	0.23-0.54	0.35-0.81
Dry Powder ^c + TDS	1.2-1.6	1.8-2.5	0.93-1.2	1.4-1.9

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

water of <8 µg/L ^d				
Dry Powder ^c + median water of 0.4 µg/L ^d	0.36-0.76	0.53-1.2	0.27-0.58	0.40-0.86
Dry Powder ^c + 97.5 th percentile water of 1.8 µg/L ^d	0.52-0.92	0.77-1.4	0.39-0.70	0.59-1.0

Values rounded to 2 SF

^a Exposure based on first milk infant formula using LB to UB chromium concentrations of 0-3 µg/L

^b Exposure does not include the contribution from water

^c Exposure based on first milk infant formula using LB to UB chromium concentrations of 15-35 µg/kg

^d Calculated assuming reconstituted formula comprises 85% water

51. Total mean exposures (excluding water) to chromium from infant formulae, commercial infant foods, and other foods, for 4 to 12 month olds were 0.32 to 1.3 µg/kg bw/day, and 97.5th percentile exposures were 1.1 to 3.6 µg/kg bw/day (Table 7). Detailed exposure assessments for 4 to 18 month old infants and young children are provided in Annex A. Total mean and 97.5th percentile exposures were also calculated using the highest median and 97.5th percentile concentrations for chromium in water reported in Table 2. The resulting total mean and 97.5th percentile exposures indicated that levels of chromium in water made a negligible contribution to total exposure.

Table 7. Estimated exposures to chromium from infant formulae, commercial infant foods and other foods for 4 to 12 month olds.

Food	Chromium Exposure (LB-UB Range) (µg/kg bw/d)					
	4 to <6 Months (n=116)		6 to <9 Months (n=606)		9 to <12 Months (n=686)	
	Mean	97.5 th	Mean	97.5 th	Mean	97.5 th
Infant formula	0.0014 – 0.20	0.025 – 0.42	0.0035 – 0.17	0.0039 – 0.35	0.0033 – 0.13	0.0060 – 0.29
Commercial infant foods	0.30 – 0.40	1.1 – 1.4	0.43 – 0.57	1.5 – 2.0	0.40 – 0.53	1.6 – 2.2
Other foods	0.018 – 0.067	0.12 – 0.28	0.14 – 0.26	0.67 – 0.92	0.25 – 0.43	0.80 – 1.1
Total (excl. water)	0.32 – 0.67	1.1 – 2.1*	0.57 – 1.0	2.2 – 3.3*	0.65 – 1.3	2.4 – 3.6*

Values rounded to 2 SF

* 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

Children aged 12 to 18 months

52. Estimated exposures to chromium from food for children aged 12 to 18 months were calculated using occurrence data from both the Infant Metals Survey (FSA, 2016a), and the 2014 TDS (FSA, 2016b). The exposure data derived from the Infant Metals Survey allow estimation of chromium exposure in infant formula, commercial infant foods and the most commonly consumed adult foods ('other foods') as sold, whereas the results from the TDS are based on analysis of food that is prepared as for consumption. In addition, the Infant Metals Survey included analysis of infant formulae and commercial infant foods which are not included in the TDS. Exposure estimates based on both LB and UB concentrations are provided.

53. The consumption data from the DNSIYC were used for the estimation of exposure for children aged 12 to 18 months (DH, 2013).

Exposure estimates based on the Infant Metals Survey

54. The ranges of total mean and 97.5th percentile exposures (excluding water) to chromium from infant formula, commercial infant foods and other foods were 0.51 to 0.97 and 1.5 to 2.8 µg/kg bw/day, respectively. As for infants, the total mean and 97.5th percentile exposures including water (calculated using the highest median and 97.5th percentile values from Table 2) were equal to those estimated for the total mean exposures excluding water (Table 8).

Table 8. Estimated exposures to chromium from infant formulae, commercial infant foods and other foods in children aged 12 to 18 months.

Food	Chromium Exposure (LB-UB Range) (µg/kg bw/d)			
	12 to <15 Months (n=670)		15 to <18 Months (n=605)	
	Mean	97.5 th	Mean	97.5 th
Infant formula	0.00010 – 0.047	0 – 0.21	0 – 0.026	0 – 0.15
Commercial infant foods	0.22 – 0.30	1.1 – 1.5	0.12 - 0.16	0.68 – 0.90
Other Foods	0.33 – 0.62	0.83 – 1.3	0.39 – 0.68	0.85 – 1.3
Total (excl. water)	0.66 – 0.97	1.9 – 2.8*	0.51 – 0.87	1.5 – 2.4*

Values rounded to 2 SF

* 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

Exposure estimates based on the TDS

55. Table 9 shows the estimated chromium exposures calculated using the TDS data for children aged 12 to 18 months. The chromium concentration for the tap water group in the TDS was reported to be below the limit of detection (LOD) of 8 µg/L. This LOD is higher than that reported for chromium in tap water by the water authorities across the UK (see Table 2). The calculation was therefore also performed using the highest median (0.4 µg/L) and 97.5th percentile (1.8 µg/L) chromium concentration in tap water and are reported in Table 9.

56. Total mean and 97.5th percentile exposures to chromium from a combination of all food groups are in the region of 1.4 to 3.2 and 3.2 to 5.3 µg/kg bw/day respectively (Table 9). These are higher than those estimated from the Infant Metals Survey due to the inclusion of a greater number of foods in the exposure estimate for the TDS. Overall, the figures in Table 9 demonstrate that the chromium content of water has a negligible impact on total dietary exposure to chromium of young children in the UK.

Table 9. Estimated dietary exposure to chromium based on the TDS data in children aged 12 to 18 months, taking into account the contribution from of UK water containing the highest median and 97.5th percentile concentrations of chromium.

Chromium concentration in the water	Chromium Exposure (LB-UB Range) (µg/kg bw/day)			
	12 to <15 Months (n=670)		15 to <18 Months (n=605)	
	Mean	97.5 th	Mean	97.5 th
0.4 µg/L	1.4-2.9	3.4-5.2	1.5-3.2	3.2-5.3
1.8 µg/L	1.4-2.9	3.4-5.2	1.5-3.2	3.2-5.3
8.0 µg/L	1.4-2.9	3.4-5.2	1.5-3.2	3.2-5.3

Values rounded to 2 SF

Children aged 18 months to 5 years

57. Exposure estimates for these age groups were derived using occurrence data from the 2014 TDS and consumption data from the NDNS (Bates *et al.*, 2014).

58. Table 10 shows the chromium exposures that were calculated using the TDS data for children aged 18 months to 5 years. Detailed exposure assessments are presented in Annex B. As described in paragraph 55, the exposures have been estimated using the TDS water concentration (8 µg/L, the LOD), and the highest median (0.4 µg/L) and 97.5th percentile (1.8 µg/L) chromium concentrations in water reported in Table 2. This results in total mean and 97.5th percentile exposures to chromium from a combination of all food groups of 1.5 to 3.6 and 2.9 to 5.9 µg/kg bw/day, respectively (Table 10). Overall the figures in Table 10 demonstrate that the chromium content of water has a negligible impact on total dietary exposure to chromium of young children in the UK.

Table 10. Estimated dietary exposure to chromium based on the TDS data in children aged 12 to 18 months, taking into account the contribution from of UK water containing the highest median and 97.5th percentile concentrations of chromium.

Chromium concentration in water	Chromium Exposure (LB-UB Range) (µg/kg bw/day)			
	18 to <24 Months (n=70)		24 to <60 Months (n=429)	
	Mean	97.5 th	Mean	97.5 th
0.4 µg/L	1.8-3.6	3.3-5.9	1.5-3.0	2.9-4.7
1.8 µg/L	1.8-3.6	3.3-5.9	1.5-3.0	2.9-4.7
8.0 µg/L	1.8-3.6	3.3-5.9	1.5-3.0	2.9-4.7

Values rounded to 2 SF

59. The food groups making the highest contribution to chromium exposure in the TDS were miscellaneous cereals dairy products and canned vegetables (FSA, 2016b).

Environmental

Dust

60. Potential exposures of UK infants aged 6 to 12 months and young children aged 1 to 5 years to chromium in dust were calculated assuming ingestion of 30 or 60 mg/day, respectively (US EPA, 2011a). Younger infants, who are less able to move around and come into contact with dust, are likely to consume less dust than children of these age groups. Median and maximum chromium concentrations in dust of 11.8 and 20 mg/kg, respectively, were used to estimate average and high level exposures (paragraph 41) (Table 11).

Table 11. Possible chromium exposures from dust in infants and young children aged 6 months to 5 years.

Chromium concentration (mg/kg)	Exposure (µg/kg bw/day)					
	Age (months)					
	6 to <9	9 to <12	12 to <15	15 to <18	18 to <24	24 to <60
11.8 (Mean)	0.040	0.037	0.067	0.063	0.059	0.044
20 (Maximum)	0.069	0.063	0.11	0.11	0.10	0.075

Values rounded to 2 SF

Soil

61. Potential exposures of UK infants aged 6 to 12 months and young children aged 1 to 5 years to chromium in soil were calculated assuming ingestion of 30 or 50 mg/day, respectively (US EPA, 2011a). Younger infants, who are less able to move around and come into contact with soil, are likely to consume less soil than children

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

of these age groups. Median and 95th percentile soil concentrations of 68 and 97 mg/kg respectively were used in these exposure estimations (see paragraph 40) (Table 13).

Table 13. Possible chromium exposures from soil in infants and young children aged 6 months to 5 years.

Chromium concentration (mg/kg)	Exposure (µg/kg bw/day)					
	Age (months)					
	6 to <9	9 to <12	12 to <15	15 to <18	18 to <24	24 to <60
68 (Median)	0.23	0.21	0.32	0.30	0.28	0.21
97 (95 th percentile)	0.33	0.30	0.46	0.43	0.40	0.30

Values rounded to 2 SF

Air

62. Potential exposures of UK infants aged 0 to 12 months and young children aged 1 to 5 years to chromium in air were estimated using the body weights shown in Table 3, and by assuming the mean ventilation rates presented in Table 14; these rates have been derived from the US EPA exposure factors handbook (US EPA, 2011b). The resulting exposures are presented in Table 15.

Table 14. Mean ventilation rates used in the estimation of chromium exposures from air (derived from US EPA, 2011b)

Age group (months)	Ventilation rate (m ³ /day)
0 to <4	3.5
4 to <6	4.1
6 to <9	5.4
9 to <12	5.4
12 to <15	8.0
15 to <18	8.0
18 to <24	8.0
24 to <60	10.1

63. The chromium concentrations used in the exposure calculations were the lowest and highest median values and lowest and highest 99th percentile values of 0.8, 8.65, 1.4 and 167 ng/m³, respectively, from monitoring sites in the UK (see paragraph 42).

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

Table 15. Possible exposures to chromium in infants and young children from air

Chromium concentration (ng/m ³)	Exposure (µg/kg bw/day)							
	Ages (months)							
	0 to <4	4 to <6	6 to <9	9 to <12	12 to <15	15 to <18	18 to <24	24 to <60
0.8 (lowest median value)	0.00047	0.00042	0.00050	0.00045	0.00060	0.00057	0.00053	0.00050
8.65 (highest median)	0.0051	0.0045	0.0054	0.00049	0.0065	0.0062	0.0058	0.0054
1.4 (lowest 99 th percentile value)	0.00083	0.00074	0.00087	0.00079	0.0011	0.0010	0.00093	0.00088
167 (highest 99 th percentile value)	0.099	0.088	0.10	0.094	0.13	0.12	0.11	0.10

64. The highest median and highest 99th percentile intakes were a result of the presence of a small number of high values from two monitoring stations in the vicinity of Sheffield, an area with historic steel-making industry.

Risk characterisation

Breast milk

65. 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 chromium from breastmilk. Since ascorbate is present in breast milk it is assumed that the chromium is all in the form of Cr(III), so risk characterisation is relative to the EFSA TDI of 300 µg/kg bw/day. These estimates were based on a mean and 97.5th percentile chromium concentrations of 3.1 and 19.4 µg/L. The ranges of exposure to chromium in exclusively breastfed 0 to 6 month olds were 0.11 to 0.87 and 0.21 to 1.3% of the EFSA TDI for Cr(III) in average and high level consumers respectively (Table 16).

Table 16. Risk characterisation of chromium exposure from exclusive breastfeeding in 0 to 6 month old infants, with breast milk containing chromium at 3.1 and 19.4 µg/L.

Chromium concentration (µg/L)	Chromium intake as percentage of TDI (300 µg/kg bw/day)			
	Average consumer (800 mL/day)		High consumer (1200 mL/day)	
	0 to <4 months	4 to <6 months	0 to <4 months	4 to <6 months
3.1	0.14	0.11	0.21	0.16
19.4	0.87	0.67	1.3	1.0

Values rounded to 2 significant figures (SF)

66. From the above table it appears that the chromium intake of both average and high consuming infants is well below the EFSA TDI for chromium (III) of 300 µg Cr(III)/kg b.w. per day.

67. Mean intakes of chromium for non-exclusively breast fed 4 to 18 month olds relative to the TDI were 0.026 to 0.60 and 97.5th percentile exposures were 0.05 to 1.0% of the TDI (Table 17). These were calculated from the exposure values in Table 6.

Table 17. Chromium intake in 4 to 18 month old infants from breast milk, containing chromium at 1.2 µg/L as a percentage of the EFSA TDI for Cr(III) of 300 µg/kg bw/day.

Exposure (µg/kg bw/day)	Age group (months)				
	Chromium intake as percentage of TDI (300 µg/kg bw/day)				
	4 to <6	6 to <9	9 to <12	12 to <15	15 to <18
Mean @ 31 µg/L	0.097	0.07	0.04	0.03	0.026
97.5th percentile @ 3.1 µg/L	0.16	0.16	0.12	0.071	0.05
Mean @ 19.4 µg/L	0.60	0.4	0.25	0.19	0.16
97.5th percentile @ 19.4 µg/L	1.0	1.0	0.70	0.50	0.33

Values rounded to 2 SF

Infant formulae and complementary foods

68. In 0 to 6 month olds, intakes of chromium from ready-to-feed formula were 0 to 0.14% of the TDI in average consumers, and 0 to 0.2% of the TDI in high level consumers. Mean and high-level exposure to chromium from infant formula reconstituted with water containing chromium up to 8 µg/L (the highest LOD) were up to 0.53 and 0.83% of the TDI, (Table 18).

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

Table 18. Estimated average and high level exposures to chromium from exclusive feeding on infant formulae for 0 to 6 month olds.

Infant Formula	Chromium Intake as percentage of TDI (300 µg/kg bw/day)			
	0 to <4 months		4 to <6 months	
	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	0-0.14	0- 0.20	0-0.10	0-0.15
Dry Powder ^{b, c}	0.10-0.24	0.15-0.37	0.077-0.18	0.12-0.27
Dry Powder ^c + TDS water of <8 µg/L ^d	0.40-0.53	0.60-0.83	0.31-0.40	0.47-0.63
Dry Powder ^c + median water of 0.4 µg/L ^d	0.12-0.25	0.18-0.40	0.090-0.19	0.13-0.29
Dry Powder ^c + 97.5 th percentile water of 1.8 µg/L ^d	0.17-0.31	0.26-0.47	0.13-0.23	0.20-0.33

Values rounded to 2 SF

^a Exposure based on first milk infant formula using LB to UB chromium concentrations of 0-0.2 µg/L

^b Exposure does not include the contribution from water

^c Exposure based on first milk infant formula using LB to UB chromium concentrations of 3-4 µg/kg

^d Calculated assuming reconstituted formula comprises 85% water

69. Total mean intakes (excluding water) to chromium from infant formulae, commercial infant foods, and other foods, for 4 to 12 month olds were 0.11 and 0.43 % of the TDI and the 97.5th percentile intakes were 0.37 to 1.2% of the TDI (Table 19).

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

Table 19. Estimated exposures to chromium from infant formulae, commercial infant foods and other foods for 4 to 12 month olds.

Food	Chromium Intake as percentage of TDI (300 µg/kg bw/day)					
	4 to <6 Months (n=116)		6 to <9 Months (n=606)		9 to <12 Months (n=686)	
	Mean	97.5 th	Mean	97.5 th	Mean	97.5 th
Infant formula	0.00047 – 0.067	0.0083 – 0.14	0.0012 – 0.057	0.0013 – 0.12	0.0011 – 0.043	0.0020 – 0.097
Commercial infant foods	0.10 – 0.13	0.37 – 0.47	0.14 – 0.19	0.50 – 0.67	0.13 – 0.18	0.53 – 0.73
Other foods	0.0060 – 0.022	0.040 – 0.093	0.047 – 0.087	0.22 – 0.31	0.083 – 0.14	0.27 – 0.37
Total (excl. water)	0.11 – 0.22	0.37 – 0.70	0.19 – 0.33	0.73 – 1.1	0.22 – 0.43	0.80 – 1.2

Values rounded to 2 SF

* 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

Children aged 12 to 18 months

Intake estimates based on the Infant Metals Survey

70. The ranges of total mean and 97.5th percentile intakes (excluding water) of chromium from infant formula, commercial infant foods and other foods were 0.17 to 0.37 and 0.32 to 0.74% of the TDI, respectively.

Table 20. Estimated exposures to chromium from infant formulae, commercial infant foods and other foods in children aged 12 to 18 months.

Food	Chromium Intake as percentage of TDI (300 µg/kg bw/day)			
	12 to <15 Months (n=670)		15 to <18 Months (n=605)	
	Mean	97.5 th	Mean	97.5 th
Infant formula	0.000033 – 0.016	0 – 0.070	0 – 0.0087	0 – 0.05
Commercial infant foods	0.073 – 0.10	0.037 – 0.5	0.040 – 0.053	0.23 – 0.30
Other Foods	0.11 – 0.27	0.28 – 0.43	0.13 – 0.27	0.28 – 0.43
Total (excl. water)	0.18 – 0.37	0.32 – 0.49	0.17 – 0.33	0.51 – 0.74

Values rounded to 2 SF

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

* 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

Intake estimates based on the TDS

71. Table 21 shows the estimated chromium intakes calculated for children aged 12 to 18 months. Total mean and 97.5th percentile intakes of chromium from a combination of all food groups are in the region of 0.47 to 1.1 and 1.1 to 1.8% of the TDI respectively (Table 21).

Table 21. Estimated dietary intake of chromium based on the TDS data in children aged 12 to 18 months.

Chromium concentration in the water	Chromium intake as percentage of the TDI (300 µg/kg bw/day)			
	12 to <15 Months (n=670)		15 to <18 Months (n=605)	
	Mean	97.5 th	Mean	97.5 th
0.4 µg/L	0.47-0.97	1.1-1.7	0.50-1.1	1.1-1.8
1.8 µg/L	0.47-0.97	1.1-1.7	0.50-1.1	1.1-1.8

Values rounded to 2 SF

Children aged 18 months to 5 years

Intake estimates based on the TDS

72. Table 22 shows the chromium intakes that were calculated using the TDS data for children aged 18 months to 5 years. Total mean and 97.5th percentile intakes of chromium from a combination of all food groups were 0.60 to 1.2 and 1.1 to 2.0 % of the TDI respectively (Table 22).

Table 22. Estimated dietary intake of chromium in children aged 18 months to 5 years.

Chromium concentration in water	Chromium intake as percentage of the TDI (300 µg/kg bw/day)			
	18 to <24 Months (n=70)		24 to <60 Months (n=429)	
	Mean	97.5 th	Mean	97.5 th
0.4 µg/L	0.60-1.2	1.1-2.0	0.50-1.0	1.0-1.6
1.8 µg/L	0.6-1.2	1.1-2.0	0.55-1.0	1.0-1.6

Values rounded to 2 SF

Environment

Dust

73. Potential intakes of UK infants aged 6 to 12 months and young children aged 1 to 5 years to chromium in dust were 0.012 to 0.038% of the TDI respectively (Table 23).

Table 23. Possible chromium intakes from dust in infants and young children aged 6 months to 5 years.

Chromium concentration (mg/kg)	Chromium intake as percentage of the TDI (300 µg/kg bw/day)					
	Age (months)					
	6 to <9	9 to <12	12 to <15	15 to <18	18 to <24	24 to <60
11.8 (Mean)	0.013	0.012	0.022	0.021	0.020	0.015
20 (Maximum)	0.023	0.021	0.038	0.036	0.033	0.025

Values rounded to 2 SF

Soil

74. Potential intakes of UK infants aged 6 to 12 months and young children aged 1 to 5 years to chromium in soil were 0.070 to 0.15% of the TDI respectively.

Table 24. Possible chromium exposures from soil in infants and young children aged 6 months to 5 years.

Chromium concentration (mg/kg)	Chromium intake as percentage of TDI (300 µg/kg bw/day)					
	Age (months)					
	6 to <9	9 to <12	12 to <15	15 to <18	18 to <24	24 to <60
68 (Median)	0.077	0.070	0.11	0.10	0.093	0.070
97 (95 th percentile)	0.11	0.10	0.15	0.14	0.13	0.10

Values rounded to 2 SF

Air

75. Potential exposures of UK infants aged 0 to 12 months and young children aged 1 to 5 years to chromium in air, relative to the TDI are shown in Table 25. Exposures ranged from 0.00014 to 0.040% of the TDI

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

Table 25. Possible exposures to chromium in infants and young children from air

Chromium concentration (ng/m ³)	Chromium intake as percentage of TDI (300 µg/kg bw/day))							
	Ages (months)							
	0 to <4	4 to <6	6 to <9	9 to <12	12 to <15	15 to <18	18 to <24	24 to <60
0.8 (lowest median value)	0.00016	0.00014	0.00017	0.00015	0.00020	0.00019	0.00018	0.00017
8.65 (highest median)	0.0017	0.0015	0.0018	0.00016	0.0022	0.0031	0.0019	0.0018
1.4 (lowest 99 th percentile value)	0.00027	0.00025	0.00029	0.00026	0.00104	0.0003	0.00031	0.00029
167 (highest 99 th percentile value)	0.033	0.029	0.030	0.031	0.036	0.040	0.036	0.033

Questions for the committee

1. Does the Committee consider that it would be appropriate to cover Chromium in the overarching statement since the chromium concentration in the diet of infants and young children is around 1% of the TDI or less?
2. Does the Committee consider that aggregate exposures will not significantly add to estimated dietary intakes in this population?
3. Does the Committee have any other comments on this paper?

Secretariat

August 2017

References

- Agency for Toxic Substance and Disease Registry (ATSDR) 2012 Toxicological profile for chromium. US department for health and human services
- Abdulrazzaq YM, Osman N, Nagelkerke N, Kosanovic M, Adem A Trace element composition of plasma and breast milk of well-nourished women. *J Environ Sci Health A Tox Hazard Subst Environ Eng.* 2008 Feb 15; **43**(3):329-34. doi: 10.1080/10934520701792878.
- Anderson RA¹, Bryden NA, Polansky MM Lack of toxicity of chromium chloride and chromium picolinate in rats. *J Am Coll Nutr.* 1997 Jun; **16**(3):273-9.
Bates
- De Flora S, Camoirano A, Micale RT, La Maestra S, Savarino V, Zentilin P, Marabotto E, Suh M, Proctor DM. Reduction of hexavalent chromium by fasted and fed human gastric fluid I. Chemical reduction and mitigation of mutagenicity. *Toxicology and Applied Pharmacology* 2016 **306** : 113 – 119.
- Davoy J, Gehin A, Müller S, Melczer M, Remy A, Antoine C, Sponne I. Evaluation of chromium in red blood cells as an indicator of exposure to hexavalent chromium: An *in vitro* study. *Tox. Lett.* 2016 **255**: 63 – 70.
- Department of Health (DH) (1994). The COMA report on Weaning and the Weaning Diet. Report on Health and Social Subjects 45. The Stationary Office London
- DH (2013). Diet and Nutrition Survey of Infants and Young Children (DNSIYC), 2011. Available at: <http://transparency.dh.gov.uk/2013/03/13/dnsiyc-2011/>
- EFSA (2014) Scientific opinion on the risks to public health related to the presence of chromium in food and drinking water. *EFSA Journal* 2014; **12**(3):3595
- Franken A, Eloff FC, Du Plessis J, Du Plessis JL. The *in vitro* permeation of metals through human skin: a review and recommendations. *Chem. Res. Toxicol* 2015. **28**:2237 - 2249
- FSA (2016a) 'Survey of metals and other elements in infant foods' (to be published)
- FSA (2016b) 'Metals and other elements in the 2014 Total Diet Study' (to be published)
- Harrison RM. Toxic metals in street and household dust. *Science of the total environment* 1979 **11**(1): 89 – 97.
- Hua Y, Clark S, Ren J, Sreejayan N. Molecular mechanisms of chromium in alleviating insulin resistance *J. Nutr. Biochem.* 2012. **23**(4): 313 – 319.
- IARC (2012) Chromium (VI) compounds IARC Monographs 100C: 147 – 167
- Kirman CR, Suh M, Hays SM, Gürleyük , Gerads R, De Flora S, Parker W, Lin S, Haws LC, Harris MA, Proctor DM. Reduction of hexavalent chromium by fasted and

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

fed human gastric fluid II. *Ex vivo* gastric reduction modelling. Toxicology and Applied Pharmacology 2016 **306**: 120 – 133

Krachler M, Prohaska T, Koellensperger G, Rossipal E, Stingeder G. Concentrations of selected trace elements in human milk and in infant formulas determined by magnetic sector field inductively coupled plasma-mass spectrometry. Biol Trace Elem Res. 2000 Aug;**76**(2):97-112.

Laschinsky N, Kottwitz K, Freund B, Dresow B, Fischer R, Nielsen P. Bioavailability of chromium(III)-supplements in rats and humans. Biometals. 2012 **25**(5):1051-60. doi: 10.1007/s10534-012-9571-5. Epub 2012 Jul 20.

Reimann, C, and DeCaritat, P. 1998. *Chemical elements in the environment*. (Berlin: Springer Verlag

Salama A, Hegazy R, Hassan A. Intranasal chromium induces acute brain and lung injuries in rats: assessment of different potential hazardous effects of environmental and occupational exposure to chromium and introduction of a novel pharmacological and toxicological animal model. PLOS One 2016 doi:10.1371/journal.pone.0168688

Szynal T, Rebeniak M, Mania M. Migration studies of nickel and chromium from ceramic and glass tableware into food simulants. Roczn. Panstw. Zaki. Hig 2016 **67**(3):247 – 252

Sola-Larrañaga C, Navarro-Blasco Chromium content in different kinds of Spanish infant formulae and estimation of dietary intake by infants fed on reconstituted powder formulae. Food Addit Contam. 2006 Nov;**23**(11):1157-68.

Sun Z, Yue B, Yang Z, Li X, Wu Y, Yin S. Determination of 24 minerals in human milk by inductively coupled plasma mass spectrometry and microwave digestion. Wei Sheng Yan Jiu 2013 May;**42**(3):504 -9 [Abstract only – article in Chinese]

Tsave O, Yavropoulou MP, Katantari M, Gabriel C, Yovos JC, Salifoglou A. The adipogenic potential of Cr(III). A molecular approach exemplifying metal-induced enhancement of insulin mimesis in diabetes mellitus II. J Inorg Biochem. 2016.**163**:323-331

US EPA 1969 Air pollution aspects of chromium and its compounds. Review prepared for the National Air Pollution Control Administration Consumer Protection and Environmental Health Service by Ralph J. Sullivan.

US EPA (2011a) 'Exposure Factors Handbook Chapter 5: Soil and Dust Ingestion' Available at:
https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252&CFID=69447188&CF_TOKEN=21916199

US EPA (2011b) 'Exposure Factors Handbook Chapter 6: Inhalation Rates' Available at:
https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252&CFID=69447188&CF_TOKEN=21916199

Vincent JB. The Biochemistry of Chromium. J. Nutr. 2000 **130**:715 – 718

Wappelhorst O, Kühn I, Heidenreich H, Markert B Transfer of selected elements from food into human milk. Nutrition. 2002 Apr;**18**(4):316-22.

World Health Organization (WHO) 2003 Chromium in Drinking-water. Background document for Guidelines for drinking-water quality, 2nd ed. Vol. 2.

World Health Organization (WHO) 2006 Health risks of particulate matter from long-range transboundary air pollution. Joint WHO / Convention Task Force on the Health Aspects of Air Pollution

World Health Organization (WHO) 2013. Inorganic Chromium(VI) Compounds International Programme On Chemical Safety Concise International Chemical Assessment Document 78

Yamawaki N, Yamada M, Kan-no T, Kojima T, Kaneko T, Yonekubo A. Macronutrient, mineral and trace element composition of breast milk from Japanese women. J Trace Elem Med Biol. 2005;**19**(2-3):171-81. Epub 2005 Oct 24.

Yokel RA, Lasley SM, Dorman DC. J. Toxicol. Environ. Health B Crit. Rev 2006, **9**(1) 63 – 85

Yoshida M, Takada A, Hirose J, Endô M, Fukuwatari T, Shibata K. Molybdenum and chromium in breast milk from Japanese women. Biosci. Biotechnol. Biochem 2008 **72**(8): 2247 - 2250

Search terms

Chromium AND Breast milk

- Toxicology
- Toxicokinetics
- Food contact
- Dust
- House dust
- Domestic dust
- Air
- Indoor air
- Cancer
- Carcinogenesis
- Oxidative stress

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

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

Possible Chromium 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 Chromium.

The Infant Metals Survey measured the concentrations of metals and other elements in food 'as sold', in the following categories: infant formula (Table B1) commercial infant foods (Table B2), and groups of food comprising the top 50 most commonly consumed varieties of foods not specifically marketed for infants (Table B3). 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 Chromium, were measured in the 2014 TDS. The composite samples for 27 food groups (Table B4) were collected from 24 UK towns and analysed for their levels of Chromium 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 12 to 18 months.

Table B1. 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	

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

Comfort Milk	
--------------	--

Table B2. 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 B3. 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 B4. The 27 food groups used for analysis of Chromium and other 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

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

Exposure Assessments

Infant Metals Survey

Tables B5, B6 and B7 summarise lower- (LB) and upper-bound (UB) total dietary exposures to Chromium calculated using results from the infants Metal Survey for ages 4 to 18 months.

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

Table B5. Estimated Chromium exposure from infant formula in children aged 4 to 18 months using data from the Infant Metals Survey

Infant Formula	Chromium 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
Comfort	0	0	0.00080-0.0015	0	0.0027-0.0053	0	0	0	0
First Milk: From Birth (Powder)	0.00080-0.0020	0.017-0.040	0.0012-0.0028	0	0.00030-0.00080	0	0	0	0
Follow On Milk: 6 Months (Powder)	0	0	0-0.0012	0	0-0.0021	0-0.014	0-0.00010	0	0-0.000
Growing Up Milk: 12 Months (Powder)	0	0	0	0	0	0	0-0.0011	0	0-0.000
Goat Milk Formula	0	0	0.0012-0.0014	0	0	0	0	0	0
Hipp Organic	0	0	0-0.00020	0	0-0.00010	0	0	0	0
Soy	0.00060-0.0062	0	0.00030-0.0031	0	0.00030-0.0031	0	0.00010-0.00090	0	0-0.000

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

First Milk: From Birth (Ready to Feed)	0-0.17	0-0.42	0-0.071	0-0.32	0-0.031	0-0.20	0-0.0045	0-0.084	0-0.001
Follow on: 6 Months (Ready to Feed)	0-0.023	0-0.24	0-0.084	0-0.29	0-0.082	0-0.26	0-0.020	0-0.17	0-0.010
Growing up Milk: 12 Months (Ready to Feed)	0	0	0-0.00010	0	0-0.0023	0	0-0.021	0-0.17	0-0.013
Total	0.0014-0.20	0.025-0.42	0.0035-0.17	0.0039-0.35	0.0033-0.13	0.0060-0.29	0.00010-0.047	0-0.21	0-0.026

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

Table B6. Estimated Chromium exposure from commercial infant foods in children aged 4 to 18 months using data from the Infant Metals Survey

Infant food	Chromium 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	Me
Cereal Based Dishes	0.020-0.027	0.097-0.13	0.023-0.032	0.12-0.16	0.017-0.023	0.11-0.14	0.0069-0.0094	0.069-0.093	0.0
Dairy Based Dishes	0.029-0.041	0.28-0.40	0.029-0.041	0.26-0.37	0.018-0.025	0.19-0.26	0.0094-0.013	0.13-0.18	0.0
Fruit Based Dishes	0.076-0.095	0.58-0.73	0.11-0.14	0.63-0.79	0.11-0.13	0.57-0.72	0.066-0.083	0.49-0.61	0.0
Meat Based Dishes	0.094-0.13	0.61-0.85	0.15-0.21	0.77-1.1	0.14-0.20	0.73-1.0	0.085-0.12	0.59-0.82	0.0
Drinks	0-0.0097	0-0.096	0-0.013	0-0.13	0-0.011	0-0.10	0-0.0054	0-0.081	0-0
Other savoury based dishes	0.058-0.070	0.38-0.46	0.084-0.10	0.48-0.58	0.089-0.11	0.62-0.75	0.035-0.043	0.34-0.42	0.0
Snacks - sweet and savoury	0.021	0.13	0.031	0.16	0.03	0.16	0.022	0.15	0.0
Total	0.30-0.40	1.1-1.4	0.43-0.57	1.5-2.0	0.40-0.53	1.6-2.2	0.22-0.30	1.1-1.5	0.1

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

Table B7. Estimated Chromium exposure from other foods commonly eaten by children aged 4 to 18 months using data from the Infant Metals Survey

Food Groups	Other Food - Chromium 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
Beverages	0-0.0012	0-0.018	0-0.0033	0-0.026	0-0.0025	0-0.033	0-0.0022	0-0.025	0-0.0012
Bread	0.0022-0.0035	0.032-0.050	0.020-0.032	0.13-0.21	0.057-0.089	0.23-0.36	0.087-0.14	0.29-0.45	0.09-0.14
Canned Vegetables	0.0022-0.0038	0.029-0.049	0.010-0.017	0.11-0.18	0.024-0.041	0.17-0.30	0.036-0.062	0.20-0.35	0.03-0.04
Cereal	0.0056-0.0060	0.067-0.071	0.093-0.099	0.51-0.55	0.14-0.15	0.63-0.67	0.17-0.19	0.71-0.75	0.22-0.24
Dairy Products	0-0.015	0-0.090	0-0.032	0-0.14	0-0.039	0-0.15	0-0.040	0-0.14	0-0.015
Egg	0-0.00020	0-0.00020	0-0.0016	0-0.016	0-0.0033	0-0.026	0-0.0053	0-0.032	0-0.0020
Fish	0.00040-0.00080	0.0023-0.0047	0.0030-0.0061	0.029-0.057	0.0065-0.013	0.043-0.086	0.0084-0.017	0.040-0.081	0.0040-0.0080
Fresh fruit	0-0.0061	0-0.042	0-0.012	0-0.055	0-0.018	0-0.073	0-0.025	0-0.087	0-0.0061
Fruit products	0-0.0027	0-0.044	0-0.0042	0-0.044	0-0.0042	0-0.043	0-0.0069	0-0.064	0-0.0027
Green vegetables	0-0.0031	0-0.0264	0-0.0066	0-0.031	0-0.0074	0-0.049	0-0.0071	0-0.035	0-0.0031
Meat products	0	0	0.0041	0.074	0.01	0.098	0.021	0.14	0.02
Milk	0-0.0014	0-0.015	0-0.0075	0-0.041	0-0.019	0-0.16	0-0.079	0-0.22	0-0.0014
Other vegetables	0.0078-0.018	0.057-0.13	0.010-0.024	0.048-0.11	0.0095-0.022	0.040-0.092	0.0064-0.015	0.028-0.064	0.0078-0.018
Potato	0-0.0040	0-0.028	0-0.0088	0-0.041	0-0.012	0-0.048	0-0.013	0-0.058	0-0.0040
Poultry	0-0.00090	0-0.0059	0-0.0027	0-0.022	0-0.0035	0-0.025	0-0.0037	0-0.021	0-0.00090
Total	0.018-0.067	0.12-0.28	0.14-0.26	0.67-0.92	0.25-0.43	0.80-1.1	0.33-0.62	0.83-1.3	0.39-0.53

Total Diet Study

Table B8 summarise lower- and upper-bound total dietary exposures to Chromium 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 B8. Estimated Chromium exposure from food eaten by young children aged 12 months to 18 months using data from the TDS Groups.

Food Groups	12 to <15		15 to <18	
	Mean	97.5th Percentile	Mean	97.5th Percentile
Bread	0-0.10	0-0.28	0-0.11	0-0.31
Miscellaneous Cereals	0.67	2.1	0.82	2.4
Carcase meat	0-0.038	0-0.20	0-0.048	0-0.24
Offal	0-0.00010	0	0-0.0010	0
Meat products	0.048	0.25	0.059	0.27
Poultry	0.021	0.091	0.023	0.10
Fish	0.056	0.26	0.052	0.26
Fats and oils	0-0.0053	0-0.021	0-0.0063	0-0.023
Eggs	0-0.014	0-0.071	0-0.014	0-0.073
Sugars	0.027	0.16	0.040	0.20
Green vegetables	0-0.020	0-0.090	0-0.022	0-0.084
Potatoes	0-0.14	0-0.52	0-0.13	0-0.43
Other vegetables	0-0.13	0-0.48	0-0.13	0-0.44
Canned vegetables	0.10	0.53	0.10	0.47
Fresh fruit	0-0.23	0-0.78	0-0.28	0-0.80
Fruit products	0.074	0.53	0.085	0.56
Non alcoholic beverages	0-0.24	0-1.1	0-0.29	0-1.4
Milk	0-0.52	0-1.5	0-0.53	0-1.3
Dairy products	0.30	1.6	0.25	1.1
Nuts	0.0046	0.020	0.0021	0.019
Alcoholic drinks	0-0.00020	0-0.0011	0-0.00010	0
Meat substitutes	0.00080	0	0.0021	0.026

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

Snacks	0.014	0.092	0.021	0.15
Desserts	0.034	0.30	0.047	0.34
Condiments	0.023	0.14	0.026	0.13
Tap water	0-0.079	0-0.30	0-0.090	0-0.36
Bottled water	0- 0.0041	0-0.036	0- 0.0054	0-0.083
Total	1.4-2.9	3.4-5.2	1.5-3.2	3.2-5.3

Secretariat
November 2016
References

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

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

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

Possible Chromium 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 Chromium 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 Chromium, were measured in the 2014 TDS. The composite samples for 27 food groups (Table C1) were collected from 24 UK towns and analysed for their levels of Chromium 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 C1. Food groups used for analysis of Chromium and other 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 C2 summarises lower- and upper-bound total dietary exposures to Chromium 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 C2. Estimated Chromium exposure from food eaten by young children aged 18 months to 5 years using data from the TDS Groups.

Food Groups	Exposure-LB to UB			
	18 to <24		24 to <60	
	Mean	97.5th Percentile	Mean	97.5th Percentile
Bread	0-0.120	0-0.27	0-0.14	0-0.32
Miscellaneous Cereals	0.87	1.8	0.71	1.8
Carcase meat	0-0.053	0-0.27	0-0.032	0-0.17
Offal	0-0.00020	0	0-0.00030	0
Meat products	0.070	0.32	0.085	0.28
Poultry	0.027	0.076	0.023	0.098
Fish	0.069	0.28	0.053	0.20
Fats and oils	0-0.0085	0-0.027	0-0.0076	0-0.025
Eggs	0-0.011	0-0.059	0-0.011	0-0.061
Sugars	0.047	0.22	0.068	0.29
Green vegetables	0-0.019	0-0.11	0-0.020	0-0.080
Potatoes	0-0.13	0-0.28	0-0.12	0-0.35
Other vegetables	0-0.081	0-0.27	0-0.084	0-0.30
Canned vegetables	0.17	0.66	0.11	0.41
Fresh fruit	0-0.34	0-0.89	0-0.25	0-0.65
Fruit products	0.19	0.73	0.17	0.83

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

Non-alcoholic beverages	0-0.40	0-1.6	0-0.38	0-1.1
Milk	0-0.49	0-1.5	0-0.35	0-1.0
Dairy products	0.27	1.3	0.15	0.61
Nuts	0.0011	0.0016	0.0034	0.047
Alcoholic drinks	0-0.00020	0	0-0.00020	0
Meat substitutes	0.00050	0.0093	0.0024	0.036
Snacks	0.025	0.15	0.028	0.15
Desserts	0.071	0.39	0.079	0.38
Condiments	0.018	0.090	0.028	0.15
Tap water	0-0.089	0-0.47	0-0.081	0-0.30
Bottled water	0-0.0027	0-0.028	0-0.0071	0-0.076
Total	1.8-3.6	3.3-5.9	1.5-3.0	2.9-4.7

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