TOX/2017/37

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

Second draft statement on potential risks from cadmium 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.   Public Health England has produced information for the general public on the risks of exposure to cadmium but there are currently no Government dietary recommendations for infants and young children which relate to this metal. The public information concerning exposure to Cd is found at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/569198/Cadmium_general_information.pdf
The general advice suggests that high levels of Cd exposure are only encountered by those involved in industrial applications.

3.   A discussion paper providing estimated cadmium exposures for infants and young children in the UK aged 0 to 12 months and 1 to 5 years, respectively (TOX/2017/14), was presented to the COT in March 2017. At that meeting, Committee members agreed to the use of the Tolerable Weekly intake (TWI) value of 2.5 μg/kg bw/week that was derived in 2009 by the European Food Safety Authority (EFSA), since it had been given a rigorous statistical review and was upheld by EFSA in 2011, rather than the Provisional Tolerable Monthly Intake (PTMI) value of 25 μg/kg bw/month derived in 2011 by the Joint FAO/WHO Committee on Food Additives (JECFA), in the risk characterisation for cadmium.

4.   Since levels of cadmium in other matrices (*viz* drinking water, air, dust and soil) were very much lower than in food, the Committee agreed that the consideration of aggregate exposures was unnecessary.

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~~6.~~5.   A first draft statement (TOX/2017/28) was prepared and presented to the Committee on 4 July 2017. Members requested a number of amendments and typographical corrections be made; these are shown as tracked changes. Of particular note were the Committee's views on the SUREmilk study, the section on the influence of industrial emissions and Cd in the food chain and breast milk and the wording or the overall conclusion to the paper.

Questions for the Committee

1. Does the Committee consider that the issues raised by the first draft statement have been adequately addressed in the second?

2. Does the Committee agree with the overall conclusion of the second draft statement?

3. Do Members have any further comments on the second draft?

Secretariat
August 2017

TOX/2017/28

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

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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.   Public Health England has produced information for the general public on the risks of exposure to cadmium but there are currently no Government dietary recommendations for infants and young children which relate to this metal.

Background

3.   Cadmium is a soft, silver-white or blue-white metal that exists in various mineral forms and is present throughout the environment. It is used in a wide variety of processes including electroplating, alloy production, paints and pigments, and is present in a wide range of industrial and consumer products. Cadmium concentrations in the environment reflect contributions from sources that are natural, for example volcanic activity, and anthropogenic, for example non-ferrous metal smelting.

4.   The general population is primarily exposed to cadmium via food, with drinking water and inhalation from ambient air acting as minor sources of exposure. Food is considered to be an ~~more important~~ appreciable source of ~~oral exposure to cadmium than drinking water~~exposure in non-smokers. Less than 10 % of total exposure of the non-smoking general population is due to inhalation of the low concentrations of cadmium in ambient air and through

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drinking water (EFSA 2009). The main food plant sources of cadmium are crops such as rice and potatoes, arising from the use of phosphate fertilisers since mineral sources of phosphate are associated with Cd ores. Kidney and liver are the main sources in food of animal origin since Cd in animal feed concentrates in these organs. Tobacco leaves accumulate cadmium from the soil and smoking may make a large contribution to intakes in smokers (EFSA 2009)

5.   There are currently no data showing that cadmium is an essential micronutrient for animals, plants or microorganisms. (EFSA, 2009). Only one enzyme, an isoform of carbonic anhydrase in a marine diatom, has been shown to accept use cadmium as a co-factor (Lane & Morel, 2000).

6.   Oral ingestion of cadmium salts in experimental animals has resulted in a wide range of adverse effects including nephrotoxicity, hepatotoxicity and metabolic effects (WHO 2011).

6.7.

Oral bioavailability of cadmium is low, at 3 – 5% from food. Uptake is greater in individuals with low storage levels of iron (Gallagher *et al*., 2011) and is thus greater in pre-menopausal women, especially during pregnancy, than in men (EFSA, 2009). Studies in experimental animals have shown that dietary deficiency of zinc and calcium can also lead to increased Cd uptake (Asagba, 2009). Cadmium and its salts have low vapour pressures so inhalation is generally in the form of respirable particles. whereas byAbsorption from smoke inhalation it is higherhas been estimated to be, at 7 – 50% (EFSA 2009), with, fractional retention of inhaled cadmium depending on particle size: 50-60 % of ultrafine particles would be retained, the remaining part being exhaled with the smoke. and depends upon pre-existing health, iron storage levels (Gallagher *et al*, 2011). .

7.   Cadmium and its salts have low vapour pressures so inhalation is generally in the form of respirable particles, except in the vicinity of industrial sites, for example zinc smelters, where volatilisation of the metal is possible.

8.   Transport of cadmium in the blood is largely in erythrocytes but in the liver Cd binds to the sulphydryl-rich protein metallothionein (MT). This metal-protein complex is released into the blood, filtered by the glomerulus and reabsorbed by the cells of the proximal convoluted tubule. Cadmium thus concentrates primarily in the kidneys and to a lesser extent in the liver. Its biological half-life in the human body is very long, ranging from 10 to 30 years. (EFSA ,2009). Yoshida *et al*. (1993) found that expression of MT falls sharply after birth, then rises until middle age (40 – 60 years of age), in parallel with Cd accumulation, where after it slowly declines. Cd concentrates in the placenta but concentrations in umbilical cord blood are generally lower than in the maternal circulation (EFSA, 2009; Esteban-Vasalio *et al*., 2012).

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9.   Since it is poorly absorbed, Ingested cadmium is largely excreted in the faeces. Cd absorbed into the blood is excreted in the urine. Blood Cd (B-Cd) levels are regarded as representing levels of exposure, whereas urinary Cd (U-Cd) levels, expressed as μg per g creatinine to account for changes in urine volume, are a measure of body burden (EFSA, 2009).

10.   Acute toxicity from cadmium is largely an issue for workers involved in industrial applications. For the general population, chronic effects are of greater concern. The liver and kidney are the major organs of cadmium accumulation. The liver MT–Cd complex in the blood is filtered through the glomerulus and is then reabsorbed by the cells of the proximal tubule, where it is degraded by lysosomes and the Cd is sequestered by renal MT. As this process continues, the proximal tubule cells' capacity to produce MT is exceeded and free Cd causes damage at multiple sites. The protection from Cd toxicity afforded by MT and its exceedance with increasing Cd concentration has been shown *in vitro* (Leierer *et al*., 2016),

11.   An early sign of renal toxicity is low-molecular-weight proteinuria, particularly of β_2-microglobulin, followed by reduced filtration rate, necrosis of the nephron and high-molecular–weight proteinuria. Cadmium-induced kidney damage may be reversible in its early stages (Gao *et al* 2016) but in later stages may be irreversible and progressive, even in the absence of ongoing cadmium exposure

12.   Chronic cadmium exposure can cause osteoporosis and osteomalacia, with deformity and bone fragility either by direct displacement of calcium or by inhibiting the kidney's hydroxylation of vitamin D, causing disruption of calcium and phosphorus metabolism. In Japan, the combination of kidney dysfunction and bone degradation arising from exposure to high levels of environmental cadmium is known as Itai-Itai (ouch-ouch) disease (EFSA, 2009).

13.   Cadmium inhibits affects the activity of multiple enzymes, transport systems and second messengers, for example neuronal Ca^{2+}channels (Sadiq *et al*., 2012), metal-dependant protein phosphatases (Pan *et al* 2013), ceruloplasmin (Shariat and Alinejad, 2008), LDH, SDH and Na^+-K^+-ATPase Karthikeyan and Bavani, 2009) and the serine/threonine kinase ERK (Martin *et al*., 2009).either by displacing the native metal cofactor, such as zinc, or

13.14. Cadmium indirectly via the induction induces of oxidative stress, which causes damage to membranes, DNA and proteins. Oxidative stress may also form part of the mechanism of kidney and bone damage as well as cadmium-induced carcinogenesis (Nair *et al*., 2013).

14.15. Cd, although classified by IARC as a Group 1 human carcinogen (IARC, 2012), does not appear to be directly genotoxic, but inhibits DNA repair mechanisms and producesand can lead to DNA modifications such as production of 8-oxo-2'-deoxyguanosine DNA adducts (Nair *et al*, 2013) and changes in the degree of 2'-deoxycytosine methylation (Takiguchi *et al*.,

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2003). Other postulated mechanisms of Cd carcinogenicity include cellular proliferation by activation of the Wnt second messenger system (Chakraborty *et al.,*2010) and mimicry of estradiol at estrogen receptors (Aquino *et al.,* 2012; Chmielowska-Bąk *et al.,* 2013).

15.16. The IARC has reviewed cadmium and cadmium compounds multiple times, most recently in 2012, and has classified them as human carcinogens that cause cancers of the lung, prostate and paranasal sinuses after inhalation (IARC, 2012).

16.17. Exposure to cadmium by inhalation in the general population has been statistically associated with a statistically significant increased risk of cancer such as in the lung (Nawrot *et al* 2015), bladder and prostate (Santana *et al.,* 2016). However, Golabek *et al.* (2014) found that although cadmium accumulated in bladder and other tissues with age, patients with urothelial carcinoma of the bladder had statistically significant (p < 0.001) lower levels of Cd in bladder tissues than control patients.

17.18. Cho *et al.* (2013) reported an association between oral exposure to Cd in Western countries and incidence of cancer of the breast, endometrium and ovary. However Adams *et al.* (2014) found no evidence of an association between oral exposure to cadmium, estimated from a dietary survey and known Cd content of various foodstuffs, and cancers of the breast, endometrium or ovary in a study involving over 155 000 postmenopausal women (age 50 – 79).

18.19. There is currently no consistency in the epidemiological data to suggest that cadmium compounds may cause cancer at additional sites or by additional routes, and no increased incidence of tumours have has been observed in oral carcinogenicity studies in experimental animals. (IARC, 2012)
https://monographs.iarc.fr/ENG/Monographs/vol100C/mono100C-8.pdf

19.20. There is some evidence that the toxic effects of Cd may be ameliorated by consuming foods or treatment with substances, with antioxidant properties, for example quercetin and α-tocopherol (Prabu *et al.,* 2010), grape juice concentrate (Pires *et al.,*2013; Lamas *et al.,* 2015) and tetrahydrocurcumin (Sangartit *et al.,* 2014). However, Cd also appears to act synergistically with other environmental toxicants, for example chlorpyrifos (He *et al.,* 2015), inorganic arsenic (Adebambo *et al* 2015) and molybdenum (Yang *et al.,* 2016).

20.21. The response to cadmium-induced toxicity therefore appears to be complex, depending not only on the presence of the metal itself but also on the chemical environment to which cells are exposed.

Toxicological reference point

21. In their 2009 scientific opinion, the EFSA CONTAM Panel stated that mean chronic dietary exposures to cadmium 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/week[1]

22. As part of their 2009 assessment, the CONTAM Panel established a new tolerable weekly intake (TWI) for cadmium. Using a group meta-analysis based on urinary β_2 – microglobulin as a marker for kidney damage, a $BMDL_5$ of 1 μg U-Cd/ g creatinine was calculated. In order for the U-Cd concentration of the population to remain below 1 μg/ g creatinine by the age of 50 years, dietary exposure to Cd should stay below 0.36 μg/kg bw/day or 2.52 μg/kg bw/week. Since Cd has a long biological half- life, CONTAM established a TWI of 2.5 μg/kg bw.

23. The Joint FAO/WHO Committee on Food Additives (JECFA, 2011) established a provisional tolerable monthly intake (PTMI) for cadmium of 25 μg/kg bw, which is equivalent to ~6 μg/kg bw/week or 0.8 μg/kg bw/day. This was a dietary level associated with a urinary level of less than 5.24 μg Cd/g creatinine, which was not associated with increased excretion of β_2-microglobulin in humans.

24. In 2011, EFSA produced a scientific report that compared the approaches taken by itself and JECFA to establish a HBGV for cadmium (EFSA, 2011a). EFSA concluded (EFSA, 2011b) after reviewing the calculations that the major source of variation between the two approaches was the choice of toxicodynamic variability function. EFSA upheld its own justification for the lower HBGV "… in order to ensure a high level of protection of consumers, including subgroups of the population such as children, vegetarians and people living in highly contaminated areas …" but pointed out that adverse effects were unlikely to take place in an individual at current dietary Cd levels.

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

Sources of cadmium exposure

Human breast milk

25. In general, low levels of cadmium are found in breast milk (EFSA, 2009).

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[1] Estimates were only available from one dietary survey.

26. As part of the 2004 SUREmilk study, levels of cadmium were measured in breast milk from women in the UK. In 104 samples, only one had a concentration at the limit of detection (LOD) of 0.3 µg/kg, the remainder being below this value (Woolridge *et al.,* 2004).

The COT[2] previously 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.noted that in the SUREmilk the data were insufficiently accurate for further analysis but were not of toxicological concern. Searches for cadmium in breast milk found a number of other papers more recent than the EFSA opinion of 2009 but the latest result for the UK other than SUREmilk was from 1984. Since only one of these considered data from the UK, the searchesd were widened to include non-UK data. These data are summarised in Table 12 below

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

Country	Number of samples	Average concentration (µg/L)[a]	Maximum concentration (µg/L)	Reference
UK	28	0.40+0.28	1.20	Kolvar *et al,* 1984
UK	104	-	0.3(LOD)	Woolridge *et al.,* 2004
Poland		0.11+ 0.07**	-	Olszowsk *et ali,* 2016
Turkey	107	-1.62*	6.71-	Dursun *et al,* 2016
Poland	323	2.11±6.33	7.36	Winiarska-Mieczan, 2014
China		-	0.23	Sun *et al,* 2013
Turkey	64	4.62 (single sample)	6.35	Gürbay *et al-,* 2012
Taiwan	34	0.35+0.18	-	Chao *et al,* 2014

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[2] http://cot.food.gov.uk/sites/default/files/cot/cotsuremilk.pdf

Spain	30	1.31	-	García-Esquinas *et al*, 2011

** Mean and standard deviation excluding samples below the detection limit of 0.15 µg/**L.**
Average concentration is the mean or median, where it is the median this has been indicated
with *. Where it has been available, the standard deviation has also been provided (as ±…).
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27.   In 1984, Kolvar *et al* collected breast milk from 28 nursing mothers at 5
days postpartum and analysed it for cadmium using atomic absorption
spectro~~photo~~metry after electrothermal excitation in a graphite furnace.
Although demographic and lifestyle data were collected (place of residence
relative to sources of pollution such as major roads and industrial chimneys
and smoking habits) these were not taken into account when the results were
presented.

28.   In the absence of other UK data on cadmium in breast milk and the fact
that the data from the Kolvar study are ~~within the same~~of a similar order of
magnitude as some of the later studies from around the world, the values from
this study have been used in this paper. ~~It should be borne in mind that t~~This
study had several shortcomings that may have compromised its accuracy
(small sample size, no accounting for demographic data, lower analytical
sensitivity in 1984 than is now available) and that for these reasons it is
possible that these values may be overestimates. ~~for reasons given below~~

~~29.~~   In 2006, a report by AEA Technology for DEFRA, the Welsh Assembly.
Scottish executive and Department of the Environment for Northern Ireland
showed that UK environmental emissions of Cd had fallen by 83% (26.3 to 4.5
tonnes/ year) between 1970 and 2002. The major contributor to emissions,
municipal solid waste incineration, fell from about 9.5 tonnes/ year to about
0.5 tonnes between 1993 and 1997 and was about 0.3 tonnes/ year in 2002.
Emissions from coal and oil industries fell from around 4 tonnes/ year to under
1 tonne/ year and metals industry from 9 to about 2.4 tonnes/ year
between1970 to 2002. ~~Assuming a causal link between Cd emissions into the
environment, its entry into the food chain and thence levels of exposure,
current breast-feeding mothers, who have been exposed to declining Cd
levels, would be expected to have lower amounts of Cd in their milk than was
measured in 1984.~~

29.   The European Environment Agency (2016) reported that Cd emissions
had fallen across most European countries between 1990 and 2014, with the
UK having the third greatest fall at 86% (after Malta and Slovakia). In the

same period, emissions from Spain had fallen by 68%, while those from Poland had fallen by 38%. No absolute values were givenreported.

https://www.eea.europa.eu/data-and-maps/daviz/change-in-cadmium-emissions-3#tab-chart_3

30.   While there appears to be a linear relationship between soil concentration and uptake of cadmium into plants in any particular soil type, the soil mobility of cadmium and hence its percentage uptake varies with soil pH and organic and mineral matter content (Smolders, 2001; McBride *et al.*, 2014). Low pH and lack of sequestering agents in the soil leads to increased uptake of Cd into plants.

31.   Defra's report on the development of Category 4 Screening Levels for assessment of land affected by contamination - SP1010 (http://randd.defra.gov.uk/Default.aspx?Module=More&Location=None&ProjectID=18341) suggests that the range of soil pH may lead to the uptake of cadmium into crops to be under or over estimated by a factor of 10. However, since most soil on allotments, which may be more contaminated than soil used in commercial enterprises, is in the pH range of 6 – 8, there is less of an effect of pH range on uptake. Further factors contributing to the uncertainty of the level of exposure are produce and produce type consumption and the home grown fraction in an individual's diet.

32.   Deposition of Cd from atmospheric emissions appears to make a minor contribution to total Cd levels in crops in areas where deposition is low but can be a major source of Cd in plants where deposition is elevated, for example in the vicinity of a smelting sites. The aerial parts of plants are initially affected but Cd also accumulates in roots and other tissues (Smolders, 2001).

33.   Thus industrial emissions may lead to contamination of crops by cadmium to an extent unrelated to the content of the soil. Uptake from the soil appears to depend upon soil characteristics. Reducing emissions from metallurgical sites may therefore reduce the level of cadmium in the food chain and hence levels in breast milk.

Infant formulae and food

30.34. Concentrations of cadmium 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, FSA

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2016a), and in the composite food samples of the 2014 Total Diet Study (TDS, FSA 2016b).

Food contact materials

31.35. The migration of cadmium from food contact materials could represent an additional source for the presence of cadmium in food and drinking water. The EU, in Council Directive (84/500/EEC) – migration of lead (Pb) and cadmium (Cd) into food contact ceramic articles, has set a migration limit for cadmium from ceramic glazes into liquids contained in fillable articles as follows:

Table 2. Permissible limits of release of Cd from food contact articles

Category of ceramic wares	Permissible limit of Cd release
(1) Articles which cannot be filled and articles which can be filled, the internal depth of which, measured from the lowest point to the horizontal plane passing through the upper rim, does not exceed 25 cm.	0.07 mg/dm^2
(2) All other articles which can be filled	0.3 mg/l
(3) Packaging and storage vessels having a capacity of more than three litres	0.1 mg/l

32.36. Rebeniak *et al*. (2014) analysed cadmium migration into 4% aqueous acetic acid from the decoration on 751 1273 samples of decorated ceramic and glass ware from the EU and Asia. in categories (1) and (2)and 452 samples of glassware from the EU and Asia between 2010 and 2012. In category (2), 51 samples had detectable but permissible levels of migration. Only 7% of the category (1) products showed Cd migration. None exceeded the permissible limit. In category (2), 8.6% of the samples had detectable Cd migration, within the permissible limit. For glassware, 19% of beverage glasses and 7% of wine/vodka glasses exceeded the permissible limit and a further 11% of the samples had detectable levels. However, the authors

pointed out that food contact times in use migration would probably be lower than into the food simulant ~~used (4% aq acetic acid)~~, food contact time would be shorter than those used (24 hours), and migration would decline with each use of the vessel.

Drinking water

~~33.~~37. The primary source of cadmium in drinking water is leaching ~~from~~ into groundwater as a consequence of dissolution from cadmium ore-bearing rocks and anthropogenic sources (WHO, ~~2005 and~~ 2011).

~~34.~~38. In water, cadmium is present as Cd(II). In their assessment, EFSA found the contribution of drinking water to the total exposure to cadmium to be very small across all age groups (EFSA, 2009)

~~35.~~39. EU legislation has ~~sets~~ a value of 5.0 µg/L for cadmium in water intended for human consumption (Directive 98/83/EC), and a maximum level of 3 µg/L in natural mineral waters (Directive 2003/40/EC). The WHO has established a guidance level of 3 µg/L for cadmium in drinking water~~,~~ (WHO, 2011) ~~but has stated that a concentration of 20 µg/L should be achievable by conventional water treatment (WHO, 2011).~~.

~~36.~~40. Levels of cadmium in drinking water in 2014/2015 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 this data are shown in Table 3. These values have been used to calculate exposures to cadmium from drinking water in combination with exposures from food.

Table 3. Median and 97.5th percentile concentrations (µg/L) of cadmium in water across the UK for 2014/2015.

Country	Number of samples	Limit of Detection (µg/L)	Median concentration (µg/L)	97.5th Percentile concentration (µg/L)
England and Wales	13325	0.01-0.10*	0.04	0.25
Northern Ireland	392	0.01	<0.01	0.16
Scotland	1500	0.02	<0.02	0.40

* 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 (5 µg/L for cadmium).

Environmental

Dust

37.41. Harrison (1979) determined the levels of cadmium and other metals in outside and domestic dust samples collected in Lancaster. "Available" cadmium levels in domestic dust, ie those extractable from the dust by 0.07N HCl to mimic gastric acid, were 7.3 $\pm$ 6.2 μg/g (Mean $\pm$ SD, n = 4, range 1.0 – 14.0 μg/g).

42.   Turner and Simmonds (2006) determined the concentration of cadmium in 32 household dust samples from 4 regions of the UK (Birmingham , Plymouth and rural areas within 50 km of each of these cities) by ICP-MS. Across all of the samples, the median and maximum values were 1.1 and 4.9 μg/g respectively. These values will be used in the exposure assessment.

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Soil

39.43. Cadmium is present at about 0.1 mg/kg in the Earth's upper continental crust (Rawlins *et al.*, 2012). It occurs naturally at high levels in some types of rock, and is released to soils from anthropogenic activities such as smelting. A total concentration of 10 mg/kg (for sandy loam soil) was adopted as the Soil Guideline value for residential soils (Environment Agency, 2009) and is well above the concentration found in most soils.

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40.44. Concentrations of cadmium 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 0.33 and 0.88 mg/kg, respectively.

41.45. In 2012 and 2013, the Defra published normal background concentrations (NBCs) for cadmium in soil in England and Wales (Defra, 2012 and 2013). An NBC is the 95th percentile upper confidence interval of the available data; it is defined as a contaminant concentration that is seen as typical and widespread in top-soils (depth 0 - 15 cm). In order to establish meaningful NBCs, the available soil data were grouped in domains (e.g. principal, urban, and ultrabasic) that were defined by the most significant controls on a contaminant's high concentrations and distribution. The NBCs for each domain in England and Wales were published following a Defra-commissioned British Geological Survey (BGS) project to define the typical background concentrations for soil contaminants.

42.46. As part of the BGS project, summary statistics were derived from topsoil data from 2 or 3 core datasets held for England and Wales (Ander *et al.*, 2012 and 2013). Although the NBCs and summary statistics were derived for several domains for England and Wales, the most significant domain for each country was the principal domain. The principal domains are areas which do not contain significantly elevated levels of cadmium. Overall, for England and Wales, the area covered by the principal domains constitutes approximately 99% and 94% of each country respectively. The summary statistics reported for the principal domain in England were a median of 0.31 mg/kg and a 95th percentile of 1.0 mg/kg (n = 4418 samples). The statistics reported for the same domain in Wales were a median of 0.33 mg/kg and a 95th percentile of 1.2 mg/kg (n = 685 samples).

43.47. Between 2004 and 2006, 6,862 samples of rural surface soil (depth 5 – 20 cm) were collected from sites in Northern Ireland as part of the Tellus survey. The samples were collected on a systematic basis and following the protocols set out in the BGS's Geochemical Baselines Survey of the Environment (G-BASE) programme. The limit of detection (LOD) used was 0.5 mg/kg (Smyth and Johnston, 2013). The median and 95th percentile concentrations derived from the data[x] are 0.50 and 1.0 mg/kg, respectively.

44.48. The median value of 0.5 mg/kg (the LOD) and the highest 95th percentile concentration value for cadmium in soil from the Defra-commissioned BGS project on NBCs (1.2 mg/kg) have been used to estimate exposures to soil in this assessment. These data have been used as

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they are recent, and represent a relevant domain for estimating exposure for the general population.

Air

45.49. In the atmosphere cadmium occurs mainly as fine respirable particles (<1 µm) and is eventually suspended onto particulate matter from sea spray, industrial emissions and the burning of fossil fuels. Metallic cadmium has a very low vapour pressure and thus would not be expected to make much contribution to atmospheric levels except in the vicinity of smelting works where vaporisation could occur. Anthropogenic sources account for more than 80% of the atmospheric cadmium burden, with the remainder accounted for by natural sources such as soil dust, volcanoes and forest fires (EFSA, 2009).

46.50. The EU Fourth Daughter Directive (2004/107/EC) defined the 'target value' for, cadmium in the PM10 particulate fraction of ambient air as 5 ng/m^3. The DEFRA Technical report on UK supplementary assessment under the Air Quality Directive (2008/50/EC), the Air Quality Framework Directive (96/62/EC) and Fourth Daughter Directive (2004/107/EC) for 2012 found no exceedances of the target value for Cd.

47.51. Data from 22 air sampling sites across the UK (2 in Northern Ireland, 2 in Scotland and the rest distributed across England and Wales) are collected annually by Defra .The latest data, for 2015 have yielded median values across the sites of 0.0238 to 1.18 ng/m^3 and maximum values of 0.0418 to 16.8 ng/m^3. The latter maximum value and a value of 10.3 ng/m^3 were both from a sampling site near Walsall and the only samples to exceed the 5 ng/m^3 limit set by the 4th Daughter directive.

48.52. While infants are very unlikely to actively smoke tobacco, the presence of second-hand smoke in the home is a possible route of exposure to cadmium. In a study in Korea, Jung *et al*. (2015) found a significant positive relationship between B-Cd levels and exposure to second-hand smoke in non-smoking women at work (p < 0.001) and at home (p< 0.04) after $\geq$ 1 hour of exposure. However, Richter *et al*. (2009) in the USA found no relationship between second-hand smoke exposure and urinary Cd concentrations in 776 6 -12 year-old children, although levels increased in non-smokers' urine with age.

Exposure assessment

49.53. Consumption data (on a bodyweight basis) from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) (DH, 2013), and the

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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 cadmium exposures are shown in Table 4 below.

50.54.   Thorough exposure assessments have been performed for the dietary sources of exposure to cadmium. 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 detailed as since the focus of this statement is the diet of infants and young children.

Table 4. Average bodyweights used in the estimation of cadmium exposures where individual body weights are unavailable

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

Infants (0 to 12 months)

Breast milk

51.55. 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 cadmium from breastmilk. These estimates were based on a mean cadmium concentration of 0.4 µg/L and a maximum of 1.2 µg/L. The ranges of exposure to cadmium in exclusively breastfed 0 to 6 month olds were 0.041 to 0.16 and 0.062 to 0.24 µg/kg bw/day in average and high level consumers respectively (Table 5).

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Table 5. Estimated cadmium exposure from exclusive breastfeeding in 0 to 6 month old infants, with breast milk containing cadmium at 1.2 μg/L..

Cadmium 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
Mean 0.4	0.054	0.041	0.081	0.062
Max 1.2	0.16	0.12	0.24	0.18

Values rounded to 2 significant figures (SF)

52.56. 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 6), based on a mean cadmium concentration of 0.4µg/L and maximum concentration at 1.2 µg/L. There were too few records of breast milk consumption for children older than 18 months in the NDNS to allow a reliable exposure assessment, and breast milk is expected to contribute minimally in this age group.

53.57. Mean exposures to cadmium for 4 to 18 month olds were 0.010 to 0.037 µg/kg bw/day at 0.4 µg Cd/L and 0.03 to 0.11 µg/kg bw/day at 1.2 µg Cd/L, and The 97.5th percentile exposures were 0.021 to 0.062 µg/kg bw/day at 0.4 µg Cd/L and 0.063 to 0.20 µg/kg bw/day at 1.2 µg Cd/L (Table 6).

Table 6. Estimated cadmium exposure in 4 to 18 month old infants from breast milk, containing cadmium at 0.4 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 @0.4 µg Cd/l	0.037	0.027	0.015	0.012	0.010
97.5th percentile @0.4 µg Cd/l	0.062	0.067	0.046	0.030	0.021
Mean @1.2 µg Cd/l	0.11	0.081	0.048	0.036	0.030
97.5th percentile @1.2 µg Cd/l	0.19	0.20	0.14	0.090	0.063

Values rounded to 2 SF

Infant formulae and complementary foods

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54.58. Cadmium 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 7). Consumption data from the DNSIYC were used to estimate exposures for 4 to 12 month olds (DH, 2013).

55.59. In 0 to 6 month olds, exposures to cadmium from ready-to-feed formula were 0 to 0.03 µg/kg bw/day in average consumers, and 0 to 0.04 µg/kg bw/day in high level consumers. Exposures to cadmium calculated for reconstituted formula incorporating the water concentration from the TDS, and the highest median and 97.5[th] percentile concentrations for cadmium in water reported in Table 3 were 0.06 to 0.22 µg/kg bw/day in average consumers, and of 0.08 to 0.33 µg/kg bw/day in high level consumers (Table 7).

Table 7. Estimated average and high level exposures to cadmium from exclusive feeding on infant formulae for 0 to 6 month olds.

Infant Formula	Cadmium 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]	0-0.03	0-0.04	0-0.02	0-0.03
Dry Powder [b, c]	0.06-0.08	0.09-0.12	0.05-0.06	0.07-0.09
Dry Powder [c] + TDS water of <1.2 µg/L [d]	0.19-0.22	0.30-0.33	0.15-0.16	0.23-0.25
Dry Powder [c] + median water of 0.04 µg/L [d]	0.07-0.09	0.10-0.13	0.06-0.07	0.08-0.10
Dry Powder [c] + 97.5[th] percentile water of 0.4 µg/L [d]	0.11-0.13	0.16-0.19	0.10-0.11	0.12-0.14

Values rounded to 2 SF
[a] Exposure based on first milk infant formula using LB to UB cadmium concentrations of 0-0.2 µg/L

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[b] Exposure does not include the contribution from water
[c] Exposure based on first milk infant formula using LB to UB cadmium concentrations of 3-4 µg/kg
[d] Calculated assuming reconstituted formula comprises 85% water

~~56.~~60. Total mean exposures (excluding water) to cadmium from infant formulae, commercial infant foods, and other foods, for 4 to 12 month olds were 0.12 to 0.28 µg/kg bw/day, and 97.5[th] percentile exposures were 0.45 to 0.62 µg/kg bw/day. ~~Detailed exposure assessments for 4 to 18 month old infants and young children are provided in Annex A~~. Total mean and 97.5[th] percentile exposures were also calculated using the highest median and 97.5[th] percentile concentrations for cadmium in water reported in Table 3. The resulting total mean and 97.5[th] percentile exposures indicated that levels of cadmium in water made a negligible contribution to total exposure (Table 8).

Table 8. Estimated exposures to cadmium from infant formulae, commercial infant foods and other foods for 4 to 12 month olds.

Food	Cadmium 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	0-0.01	0.01-0.03	0-0.01	0-0.03	0-0.01	0.01-0.02
Commercial infant foods	0.05-0.06	0.23	0.08	0.29-0.30	0.08	0.32-0.33
Other foods	-0.06	0.31	0.14	0.45	0.20	0.52
Total (excl. water)	0.12-0.13	0.45-0.48	0.22-0.23	0.55	0.27-0.28	0.60-0.62

Values rounded to 2 SF
* Determined from a distribution of consumption of any combination of categories rather than by summation of the respective individual 97.5[th] percentile consumption value for each of the three food categories

Children aged 12 to 18 months

~~57.~~61. Estimated exposures to cadmium 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 cadmium 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.

58.62. 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

59.63. The ranges of total mean and 97.5[th] percentile exposures (excluding water) to cadmium from infant formula, commercial infant foods and other foods were 0.26 to 0.27 and 0.54 to 0.58 µg/kg bw/day, respectively. As for infants the total mean and 97.5[th] percentile exposures including water (calculated using the highest median and 97.5[th] percentile values in Table 3) were equal to those estimated for the total mean exposures excluding water (Table 9).

Table 9. Estimated exposures to cadmium from infant formulae, commercial infant foods and other foods in children aged 12 to 18 months.

Food	Cadmium 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	0-0.004	0-0.02	0 – 0.002	0-0.01
Commercial infant foods	0.04	0.21-0.22	0.02	0.14
Other Foods	0.22-0.23	0.54-0.55	0.24-0.25	0.53
Total (excl. water)	0.26-0.27	0.56-0.58	0.26-0.27	0.54

Values rounded to 2 SF
* Determined from a distribution of consumption of any combination of categories rather than by summation of the respective individual 97.5[th] percentile consumption value for each of the three food categories

Exposure estimates based on the TDS

60.64. Table 10 shows the estimated cadmium exposures calculated using the TDS data for children aged 12 to 18 months. The cadmium concentration for the tap water group in the TDS was reported to be below the limit of detection (LOD) of 1.2 µg/L. This LOD is higher than that reported for cadmium in tap water by the water authorities across the UK (Table 3). The calculation was therefore also performed using the highest median (0.04 µg/L) and 97.5[th] percentile (0.40 µg/L) cadmium concentration in tap water reported in Table 3.

61.65. Table 10 refers to dietary intakes of Cd based on the Total Dietary Survey and illustrates that concurrent intake of UK water, whether at the highest recorded median or highest 97.5[th] percentile Cd concentration (see Table 3) has a negligible impact on the amount taken in with food. Total mean and 97.5[th] percentile exposures to cadmium from a combination of all food groups are in the region of 0.29 to 0.55 and 0.60 to 0.93 µg/kg bw/day, respectively (Table 10). 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.

Table 10. Estimated dietary exposure to cadmium 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 97.5[th] percentile concentrations of cadmium.

Cadmium concentration in the water	Dietary Cadmium 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]
0.04 µg/L[a]	0.29-0.50	0.61-0.93	0.32-0.55	0.60-0.90
0.4 µg/L[b]	0.29-0.50	0.61-0.93	0.32-0.55	0.60-0.90

Values rounded to 2 SF
[a] Highest median concentration in UK drinking water. [b] Highest 97.5[th] percentile concentration in UK drinking water

62.66. In general, the food groups making the highest contribution to cadmium exposure were miscellaneous cereals, bread and potatoes (FSA, 2016b), as shown in Table 11.

Table 11 Contribution to total dietary cadmium exposure by the three food groups containing the highest levels of Cd based on TDS data.

Food Groups	Exposure-LB-UB (µg/kg bw/day)

	12 to <15		15<18	
	Mean	**97.5th Percentile**	**Mean**	**97.5th Percentile**
Bread	0.053	0.15	0.060	0.16
Miscellaneous Cereals	0.090	0.28	0.11	0.32
Potatoes	0.070	0.26	0.065	0.21
Total	0.21	0.69	0.24	0.69

Children aged 18 months to 5 years

63.67. 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).

64.68. Table 12 shows the cadmium 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 629, the exposures have been estimated using the TDS water concentration (1.2 µg/L, the LOD), and the highest median (0.04 µg/L) and 97.5th percentile (0.4 µg/L) cadmium concentrations in water reported in Table 3. This results in total mean and 97.5th percentile exposures to cadmium from a combination of all food groups of 0.32 to 0.59 and 0.52 to 0.92 µg/kg bw/day, respectively (Table 124). Once more the figures in Table 12 demonstrate that the cadmium content of water has a negligible impact on total dietary exposure to cadmium of young children in the UK.

Table 12 Estimated dietary exposure to cadmium based on the TDS data in children aged 18 months to 5 years, taking into account the contribution from of UK water containing the highest median and 97.5th percentile concentrations of cadmium

Cadmium concentration in water	Dietary Cadmium Exposure (LB-UB Range) (µg/kg bw/day)			
	18 to <24 Months (n=70)		24 to <60 Months (n=429)	
	Mean	**97.5th**	**Mean**	**97.5th**
0.04 µg/L[a]	0.34-0.59	0.57-0.92	0.32-0.52	0.52-0.80
0.4 µg/L[b]	0.34-0.59	0.57-0.92	0.32-0.52	0.52-0.80

Values rounded to 2 SF

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[a] Highest median concentration in UK drinking water. [b] Highest 97.5[th] percentile concentration in UK drinking water

65.69. As with the younger children, the food groups making the highest contribution to cadmium exposure in the TDS were miscellaneous cereals, bread and potatoes (FSA, 2016b), shown in Table 13

Table 13 Contribution to total dietary cadmium exposure by the three food groups containing the highest levels of Cd based on TDS data.

Food Groups	Exposure-LB-UB (µgµg/kg bw/day)			
	12 to <15		15<18	
	Mean	97.5th Percentile	Mean	97.5th Percentile
Bread	0.063	0.14	0.072	0.17
Miscellaneous Cereals	0.12	0.24	0.095	0.24
Potatoes	0.067	0.14	0.061	0.18
Total	0.25	0.52	0.23	0.58

Exposure to cadmium from soya-based infant formulae.

66.70. Cadmium has been reported in powdered soya formula at a level of 11 µg/kg , which is higher than in other types of infant formulae (3 - 4 µg/kg for first milk infant formula, FSA, 2016a). This is because soybean plants concentrate cadmium from the soil by active uptake (Cataldo *et al*, 1983), even when grown in soils with permitted levels of the metal.(Zhi *et al.*, 2015) Therefore exposure to cadmium from consumption of soya formula was considered separately. Using the EFSA default values of 800 and 1200 ml for exclusive consumption of infant formula for the 4 to 6 month age group, exposure estimates for cadmium in soya formula would be 0.17 and 0.26 µg/kg bw/day for average and high level consumers, respectively before taking into account water used in reconstitution, i.e. approximately 3 times the exposure for non-soya formula shown in Table 7.

Dust

67.71. Potential exposures of UK infants aged 6 to 12 months and young children aged 1 to 5 years to cadmium 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

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to consume less dust than children of these age groups. Median and maximum cadmium concentrations in dust of 1.1 and 4.9 mg/kg, respectively, were used to estimate average and high level exposures (paragraph 48) (Table 14).

Table 14. Possible cadmium exposures from dust in infants and young children aged 6 months to 5 years.

Cadmium 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
1.1 (Median)	0.0038	0.0034	0.0062	0.0059	0.0055	0.0041
4.9 (Maximum)	0.017	0.015	0.028	0.026	0.025	0.018

Values rounded to 2 SF

Soil

~~68.~~72. Potential exposures of UK infants aged 6 to 12 months and young children aged 1 to 5 years to cadmium 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 of these age groups. Median and 90th percentile soil concentrations of 0.50 and 1.2 mg/kg respectively were used in these exposure estimations (paragraph 54) (Table 15).

Table 15. Possible cadmium exposures from soil in infants and young children aged 6 months to 5 years.

Cadmium 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
0.5 (Median)	0.0017	0.0015	0.0023	0.0022	0.0021	0.0016
1.2 (95th percentile)	0.0041	0.0038	0.0057	0.0054	0.0050	0.0037

Values rounded to 2 SF

Air

~~69.~~73. Potential exposures of UK infants aged 0 to 12 months and young children aged 1 to 5 years to cadmium in air were estimated using the body weights shown in Table 4, and by assuming the mean ventilation rates presented in Table 16; these rates have been derived from the US EPA

exposure factors handbook (US EPA, 2011b). The resulting exposures are presented in Table 17.

Table 16 Mean ventilation rates used in the estimation of cadmium exposures from air (derived from US EPA, 2011b)

Age group (months)	Ventilation rate (m³/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

70.74. The cadmium concentrations used in the exposure calculations were the lowest and highest median values and lowest and highest maximum values of 0.024, 1.2, 2.230.042 and 56.2317 ng/m³, respectively, from monitoring sites in the UK (paragraph 570).

Table 17. Possible exposures to cadmium in infants and young children from air.

Cadmium concentration (ng/m³)	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
(lowest median value)	0.000014	0.000011	0.000015	0.000013	0.000018	0.000017	0.000016	0.000015
(highest median value)	0.00070	0.00062	0.00073	0.00066	0.00089	0.00084	0.00079	0.00074
(lowest maximum value)	0.000025	0.000022	0.000026	0.000024	0.000032	0.000030	0.000028	0.000026
(highest maximum value)	0.010	0.0088	0.010	0.0095	0.013	0.012	0.011	0.011

Risk characterisation

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71.75. COT concluded that previously applied caveats to the use of the use of the EFSA tolerable weekly intake value (TWI) of 2.5 µg/kg bw/week, but concluded that this iswas an acceptable value to use in risk assessment following EFSA's rigorous statistical review of the derivation of its HBGV compared with that of JECFA.

Breast milk

72.76.   Cadmium intake in average and high level exclusively breast-fed UK infants from 0 to < 6 months of age is shown in Table 18 below. Values range from 11 – 687% of the EFSA TWI of 2.5 µg/kg bw/week.

Table18. Risk characterisation of cadmium intake from exclusive breastfeeding in 0 to 6 month old infants, with breast milk. .

| Cadmium concentration (µg/L) | Percentage of EU TWI (2.5 µg/kg bw/week) | | | |
| | 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
Mean0.4	15	11	232	17
Max 1.2	4546	34	6768	5052

73.77. Intakes of cadmium for mean and 97.5[th] percentile breast milk consumers from infants of 4 to < 18 months of age who are fed milk as only part of their diet are shown in Table 19 below. Mean and 97.5[th] percentile intakes of cadmium were 4.2 2.8 to 19 % of the EU TWI at 0.4 mg Cd/l and 8.4 to 56% at 1.2 mg Cd/l.

Table 19. Estimated cadmium intake in 4 to 18 month old infants from breast milk, containing cadmium at 1.2 µg/L..

| Breast milk consumption | Percentage of EU TWI (2.5 µg/kg bw/week) | | | | |
| | Age group (months) | | | | |
	4 to <6	6 to <9	9 to <12	12 to <15	15 to <18

Mean@0.4 mg Cd/lMean	10	7.6	4.2	3.4	2.8
97.5th percentile @0.4 mg Cd/l97.5th percentile	17	19	13	8.4	5.9
Mean@1.2 mg Cd/l	31	23	13	10	8.4
97.5th percentile @1.2 mg Cd/l	52	56	39	25	18

Infant formulae and complementary foods

74.78. Cadmium intake estimates for 0 to 6 month olds fed on infant formula of different make-up are shown in Table 20 below. Average consumer intakes of cadmium were 0 to 45 62 % of the EU TWI. High level consumer intakes were from 0 to 92% of the EU TWI.

Table 20. Estimated dietary intake of cadmium from exclusive feeding on infant formulae for 0 to 6 month olds relative to HBGV

Infant Formula	Percentage of EU TWI (2.5 µg/kg bw/week)			
	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]	0-8.4	0-11	0-5.6	0-8.4
Dry Powder [b, c]	17-22	25-34	14-17	20-25
Dry Powder [c] + TDS water of <1.2 µg/L [d]	53-62	84-92	42-45	64-70
Dry Powder [c] + median water of 0.04 µg/L [d]	20-25	28-36	17-20	22-28
Dry Powder [c] + 97.5th	31-36	45-53	28-31	34-39

percentile water of 0.4 µg/L [d]				

75.79. Intakes of cadmium from infant formulae, commercial infant foods, and other foods, for 4 to 12 month olds are shown in Table 21. Mean total intakes were 34 to 78% µg/kg bw/day, and 97.5[th] percentile total intakes were 130 to 170 % for the EU TWI. Intakes of cadmium from exclusive consumption of soya-based infant formulae are 47% and 71% of the EU TWI! for the mean and 97.5[th] percentile consumers respectively.

Table 21.Estimated Intake of cadmium from infant formulae, commercial infant foods and other foods for 4 to 12 month olds relative to HBGV.

Food	Percentage of TWI (2.5 µg/kg bw/week)					
	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	0.11-3.9	1.4-7.8	0.14-3.4	0.36-7.6	0.14-2.5	1.5-5.3
Commercial infant foods	15-15	64	22-23	81-84	21-22	90-92
Other foods	17-17	87	39	130	56	150
Total (excl. water)	34-36	130	62-64	150	76-78	170

Children aged 12 to 18 months

Intake estimates based on the Infant Metals Survey

~~76.~~80. For the EU TWI, the ranges of total mean and 97.5[th] percentile intakes (excluding water) to cadmium from infant formula, commercial infant foods and other foods were 73 to 79 and 150 to160% respectively (Table 22).

Table 22. Estimated dietary intake of cadmium from infant formulae, commercial infant foods and other foods in children aged 12 to 18 months relative to HBGV.

| Food | Percentage of EU TWI (2.5 µg/kg bw/week) | | | |
| | 12 to <15 Months (n=670) | | 15 to <18 Months (n=605) | |
	Mean	97.5[th]	Mean	97.5[th]
Infant formula	~~0.028-1.1~~0 - 11	0-~~5~~6	~~0.028-0.64~~0.6	0-~~3.9~~2.8
Commercial infant foods	~~12~~11	59-62	~~6.2-6.4~~5.6	39
Other Foods	62-64	~~150-155~~150	67-70	150
Total (excl. water)	73-76	160	73-76	15~~0~~1

~~77.~~81. Table 23 refers to dietary intakes of Cd based on the Total Dietary Survey and illustrates that concurrent intake of UK water, whether at the highest recorded median or highest 97.5[th] percentile Cd concentration (see Table 3) has no significant effect on the amount taken in with food. Relative to the EU TWI , mean intakes were ~~90~~81 to 15~~7~~0% and 97.5[th] percentile intakes were 1~~7~~50 to 260%.

Table 23. Estimated dietary intake of cadmium based on the TDS data in children aged 12 to 18 months, relative to the HBGV, taking into account the contribution from of UK water containing the highest median and 97.5[th] percentile concentrations of cadmium.

| Cadmium concentration in the water | Percentage of the EU TWI (2.5 µg/kg bw/week) | | | |
| | 12 to <15 Months (n=670) | | 15 to <18 Months (n=605) | |
	Mean	97.5[th]	Mean	97.5[th]
0.04 µg/L[a]	81-140	170-260	90-150	170-250
0.4 µg/L[b]	81-140	170-260	90-150	170-250

Values rounded to 2 SF

[a] Highest median concentration in UK drinking water. [b] Highest 97.5[th] percentile concentration in UK drinking water

78.82. In general, the food groups making the highest contribution to cadmium exposure were miscellaneous cereals, bread and potatoes (FSA, 2016b)., as shown in Table 24.

Table 24. Contribution to total dietary cadmium intake by the three food groups containing the highest levels of Cd based on TDS data.

| Food Groups | Percentage of EU TWI (2.5 µg/kgbw/week) | | | |
| | 12 to <15 | | 15<18 | |
	Mean	97.5th Percentile	Mean	97.5th Percentile
Bread	15	42	17	45
Miscellaneous Cereals	25	78	31	90
Potatoes	21	73	18	59
Total	58	193	67	193

Children aged 18 months to 5 years

79.83. The total mean and 97.5[th] percentile intake values including water (calculated using the highest median and 97.5[th] percentile values in Table 3) were equal to those estimated for the total mean exposures excluding water (Table 22).

80.84. Table 25 refers to dietary intakes of Cd based on the Total Dietary Survey and illustrates that concurrent intake of UK water, whether at the highest recorded median or highest 97.5[th] percentile Cd concentration (see Table 3) has no significant effect on the amount taken in with food. Relative to the EU TWI, mean intakes were 90 to 170% and 97.5[th] percentile intakes were 150 to 260%.

Table 25. Estimated dietary intake of cadmium based on the TDS data in children aged 18 months to 5 years, relative to the HBGV, taking into account the contribution from of UK water containing the highest median and 97.5[th] percentile concentrations of cadmium.

Cadmium concentration in water	Percentage of the EU TWI (2.5 μg/kg bw/week)			
	18 to <24 Months (n=70)		24 to <60 Months (n=429)	
	Mean	97.5[th]	Mean	97.5[th]
0.04 µg/L[a]	95-170	160-260	90-150	150-220
0.4 µg/L[b]	95-170	160-260	90-150	150-220

Values rounded to 2 SF
[a] Highest median concentration in UK drinking water. [b] Highest 97.5[th] percentile concentration in UK drinking water

81.85. As with the younger children, the food groups making the highest contribution to cadmium exposure in the TDS were miscellaneous cereals, bread and potatoes (FSA, 2016b), shown in Table 26

Table 26 Contribution to total dietary cadmium intake by the three food groups containing the highest levels of Cd based on TDS data.

Food Groups	Percentage of EU TWI (2.5ug5μg/kg bw/week)			
	12 to <15		15<18	
	Mean	97.5th Percentile	Mean	97.5th Percentile
Bread	18	39	20	48
Miscellaneous Cereals	34	67	27	67
Potatoes	19	39	17	50
Total	70	146	64	162

Soya

Using the EFSA default values of 800 and 1200 ml for exclusive consumption of infant formula for the 4 to 6 month age group, intake estimates for cadmium in soya formula would be 48% and 73% of the EU TWI for average and high level consumers, respectively before taking into account water used in reconstitution,

Dust

Table 27 shows that the median Intakes from dust ingestion were at most 1.7% and the maximum intakes 7.8% of the EU TWI.

Table 27. Estimated cadmium intakes from dust in infants and young children aged 6 months to 5 years.

Cadmium concentration (mg/kg)	Percentage of EU TWI (2.5 µg/kg bw/week)					
	Age (months)					
	6 to <9	9 to <12	12 to <15	15 to <18	18 to <24	24 to <60
1.1 (Median)	0.95	0.95	1.7	1.7	1.5	1.1
4.9 (Maximum)	4.8	4.2	7.8	7.3	7.0	5.0

Soil

82.86. Intakes in UK infants aged 6 to 12 months and young children aged 1 to 5 years of cadmium in soil are given in Table 28.

83.87. Relative to the EU TWI , the highest median intake value for cadmium from soil was 0.64% and the highest 95th percentile value was 1.6%.

Table 28 Estimated cadmium intakes from soil in infants and young children aged 6 months to 5 years.

Cadmium concentration (mg/kg)	Percentage of EU TWI (2.5 µg/kg bw/week)					
	Age (months)					
	6 to <9	9 to <12	12 to <15	15 to <18	18 to <24	24 to <60
0.5 (Median)	0.48	0.42	0.64	0.62	0.59	0.45
1.2 (95th percentile)	1.1	1.1	1.6	1.5	1.4	1.0

Air

84.88. Relative to the EU TWI , the highest median intake value for cadmium from the air was 0.25% and the highest maximum value was 3.6% (Table 29).

Table 29. Possible intakes to cadmium in infants and young children from air

Cadmium concentration (ng/m^3)	Percentage of the EU TWI (2.5 µg/kg bw/week)							
	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
(lowest median value)	0.0039	0.0031	00.0042	0.0036	0.0050	0.0048	0.0045	0.0042
(highest median value)	0.20	0.18	0.20	0.18	0.25	0.24	0.22	0.21
(lowest maximum value)	0.0070	0.0062	0.0073	0.0067	0.0090	0.0084	0.0078	0.0073
(highest maximum value)	2.8	2.5	2.8	2.7	3.6	3.4	3.1	3.1

Conclusions

85.89. Cadmium is present in the environment from both natural and anthropogenic sources. Natural sources include volcanic eruptions and erosion of cadmium ore-bearing rocks. Anthropogenic sources include non-ferrous metal smelting, burning fossil fuels, industrial incinerators and use of phosphate fertilisers.

86.90. Chronic exposure to cadmium causes lesions primarily in the kidney and bone and the metal has been classified by IARC as a Group 1 human carcinogen. Cadmium has a biological half-life estimated to be up to 30 years.

87.91. Food is the major source of cadmium for infants up to 12 months and children up to 5 years of age. Foods making the major contribution to cadmium intake in infants and young children are bread, miscellaneous cereals, potatoes and soya. Cadmium intake via drinking water, air, soil and dust make only a minor contribution to total exposure. The highest total exposure to cadmium was found in solid food for 12 - <60 month old children which constituted up to 260% of the EFSA TWI of 2.5 µg/kg bw/week.

92. Although the EFSA Tolerable Weekly Intake of Cd was exceeded by infants in some cases, these exceedances were small in magnitude (260%

33

maximum) and were only relevant over a short period of life, and it would not be expected to remain at this level not over the 50 years of bioaccumulative exposure considered by EFSA in setting the HBGV. The Committee decided concluded that this was therefore not a major cause for concern., However, considering the cumulative nature of cadmium toxicity, any exceedance of the HBGV, no matter how small, is undesirable and dietary exposure of infants to cadmium should be kept as low as reasonably practicableit would be prudent to minimise the exposure of infants to levels as low a level as is reasonably practicable.

88.

Abbreviations

Cd – cadmium

Cd(II) – divalent cadmium ions

bw – body weight

COT – Committee on Toxicity

DEFRA – Department of the Environment, Food and Rural Affairs

DH – Department of Health

DNSIYC – Diet and Nutrition Survey of Infants and Young Children

DWI – Drinking Water Inspectorate

EFSA – European Food Safety Authority

EU – European Union

FAO – Food and Agriculture Organization

FSA – Food Standards Agency

g – grams

HBGV – Health Based Guidance Value (TWI or PTMAPTMI, *qv*)

IARC – International Agency for Research on Cancer

JECFA – Joint FAO/WHO Expert Committee on Food Additives

kg - kilogram

LB – Lower Bound

LOD – Limit Of Detection

µg/kg – micrograms/kilogram

µg/L – micrograms/litre

mg/kg – milligrams/kilogram

mL/day – millilitres/day

MT - metallothionein

NDNS – National Diet and Nutrition Survey

ng/m^3 – nanograms per cubic metre

PTMI – Provisional Tolerable Monthly Intake

SACN – Scientific Advisory Committee on Nutrition

TDS – Total Diet Study

TWI – Tolerable Weekly Intake

UB – Upper Bound

UK – United Kingdom

US EPA – United States Environmental Protection Agency

WHO – World Health Organization

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