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

First draft statement on potential risks from arsenic in the diet of infants aged 0 to 12 months and children aged 1 to 5 years

Introduction

1. The Committee on Toxicity (COT) has been asked to consider the toxicity of chemicals in the diets of infants (0 to 12 months) and young children (1 to 5 years), in support of a review by the Scientific Advisory Committee on Nutrition (SACN) of Government recommendations on complementary and young child feeding. A scoping paper (TOX/2015/32), highlighting some of the chemicals for possible consideration was discussed by the COT in October 2015. Members concluded that a full review of the exposures from arsenic should be completed.

2. A discussion paper on arsenic (TOX/2016/05) was presented to the COT in February 2016. At that meeting Members requested that a range of aggregate exposures be calculated so that a conclusion about the potential risks from all exposures to inorganic arsenic could be reached. The aggregate exposures are included under the ‘Risk Characterisation’ section of the draft statement in Annex A (TOX/2016/13).

3. At the meeting in February Members raised concerns about the assumption that <10% of the total arsenic present in breast milk is inorganic arsenic. In order to address Members’ concerns, a further literature search has been completed to establish whether a more appropriate assumption could be derived. Some of the key studies have been discussed below but in general the results of the literature searches reconfirmed that there are limited data available on the concentration of arsenic in breast milk, and that those data which are available often relate to women with high exposures to arsenic, and rarely determine the species of arsenic present in samples.

4. As part of the SUREmilk study (2004), levels of arsenic were measured in breast milk from women in the UK. The highest concentration in an individual sample was 4.0 µg/kg; at least 42% of the 104 samples had concentrations that were equal to or below a limit of detection (LOD) of 0.5 µg/kg, while approximately 96% of them were equal to or below a limit of quantification (LOQ) of 1.7 µg/kg (Woolridge *et al.*, 2004). The COT[1] noted that the SUREmilk samples were collected primarily to explore the viability of breast milk collection methods (COT, 2004), and not as part of a rigorous

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

survey. On this basis, and due to the lack of more complete summary statistics (i.e. a median or mean), the literature search was expanded to include non-UK data.

5. Concha *et al*. (1998a) reported the concentrations of total arsenic in the breast milk of Argentinian women up to 4.4 months postpartum (pp.). At 2.8 weeks pp. the median concentration of total arsenic in breast milk was 3.0 µg/L (range = 2.3 - 4.8 µg/L, n = 10), at 2.5 months pp. the median concentration was 2.8 µg/L (range = 1.9 - 5.5 µg/L, n = 8), and at 4.4 month pp. the median concentration was 3.4 µg/L (range = 2.3 - 5.5 µg/L, n = 9). Concha *et al*. reported that the total arsenic concentrations in the breast milk samples were too low to perform speciation, and that there was no association between the concentration of arsenic in maternal blood and breast milk. A second similar study by Concha *et al*. (1998b) reported a median concentration of total arsenic in breast milk of 2.3 µg/L (mean = 3.2 µg/L, range = 0.83 - 7.6 µg/L, n = 10) in Argentinian women. Once again, there was no significant association between the concentration of arsenic in maternal blood and breast milk. In this second study, Concha *et al*. also reported a mean total arsenic concentration of 190 µg/L in samples of drinking water from local sources.

6. The data reported by Sternowsky *et al*. (2002) were used as the basis for the breast milk exposure assessments performed by the EFSA in their 2009 scientific opinion. Sternowsky *et al*. collected 187 samples of breast milk from 36 healthy women living in 3 different regions of Germany. The aim of the study was to assess the impact that living in an urban, rural or contaminated region had on the concentration of arsenic in breast milk. The samples were collected from 2 to 90 days pp. and the LOD was 0.3 µg/L. Of the 187 samples, 154 were below the LOD; when performing statistical analysis the arsenic concentration was set to 0.15 µg/L for samples that were below the LOD (i.e. a mid-bound approach). Sternowsky *et al*. reported a geometric mean of 0.2 µg/L, a median of 0.15 µg/L, and a range of 0.15 - 2.8 µg/L; the geometric mean was higher (0.35 µg/L) when more than one fish meal per week was reportedly consumed. Overall, the concentration of arsenic was considered to be low, and did not differ strongly between the 3 different regions.

7. Fängström *et al*. (2008) assessed the concentration of arsenic in the breast milk of 79 Bangladeshi women at 2 to 3 months pp. The LOD for arsenate (As(V)) was 0.2 µg/L while that for arsenite (As(III)), methylarsonic acid, and dimethylarsinic acid was 0.1 µg/L. Fängström *et al*. reported a median total arsenic concentration of 1.0 µg/L (mean = 1.8 µg/L, range = 0.25 - 19 µg/L), and that the arsenic present in the breast milk samples was essentially all inorganic. A breakdown of the arsenic in the breast milk samples shows that mainly As(III) was present, As(V) was above the LOD in 11/79 samples, and methylarsonic acid and dimethylarsinic acid were detected in 19 and 38 of the samples respectively. At low arsenic concentrations only As(III) was detected, at the higher concentrations, dimethylarsinic acid, methylarsonic acid and As(V) were also found. Contrary

to the two studies by Concha *et al*., Fängström *et al*. reported a significant correlation between arsenic concentrations in breast milk and maternal blood.

8. Björklund *et al*. (2012) reported a median concentration of 0.33 µg/L (mean = 0.55 µg/L) for 60 samples of breast milk collected in 2002-2009 from Swedish first-time mothers at 2-3 weeks postpartum. The LOD for total arsenic was 0.007 µg/L, and the minimum and maximum reported concentrations were 0.041 and 4.6 µg/L respectively. Björklund *et al*. performed speciation on the samples of breast milk with the highest arsenic concentrations (3 samples with a range of 2-4 µg/L) according to the protocol described by Fängström *et al*. (2008), the LODs for As(III), As(V), dimethylarsinic acid and methylarsonic acid are therefore the same as those given in paragraph 7. Björklund *et al*. reported that the speciation showed no content of inorganic arsenic or its methylated metabolites in the 3 samples; this would indicate that <10% of the arsenic present in the samples was inorganic. Using the Spearman correlation test, Björklund *et al*. also assessed the association between the elemental concentrations in breast milk and certain dietary components, and reported that the arsenic concentrations were significantly correlated with fish consumption ($r_s = 0.37$, $p = 0.005$, $n = 54$).

9. A recently published study by Carignan *et al*. (2015) assessed the concentrations of total arsenic in 9 samples of breast milk from women in the US. The samples were collected 2 to 7 weeks pp. from a subsample of women who were taking part in a larger study, the New Hampshire Birth Cohort Study (NHBCS). The NHBCS was designed to assess the impact of various factors on the health of pregnant women and their children. Carignan *et al*. noted that although a maximum contaminant level has been established for arsenic in public water supplies, no such level existed for private well water supplies; private well water supplies serve approximately 40% of the population of New Hampshire and could therefore be an important source of arsenic exposure in this area. The mean concentration of total arsenic in samples of tap water from private wells taken for the NHBCS cohort was reported to be 0.44 µg/L. For the samples of breast milk, Carignan *et al*. reported a median total arsenic concentration of 0.31 µg/L and a range of < LOD - 0.62 µg/L; the LOD was 0.22 µg/L and 3/9 samples fell below this level.

10. Due to the inconsistent data on the proportion of inorganic arsenic likely to be present in breast milk, the exposure estimates presented in Annex A have been performed assuming that 100% of the total arsenic is inorganic. The median total arsenic concentration reported by Björklund *et al*. (2012) has been used in the exposure assessments at this was a recent study in a Western population performed with a very low LOD for total arsenic and no samples reported to be below the LOD; the mean concentration from this study has not been used as the data were not normally distributed.

11. At the February meeting Members also requested that consideration be given to exposures to arsenic from private water supplies, as the information considered to date by the Committee was for public water supplies. It has been established that representative data on the concentration of arsenic in private water supplies in the UK are not available. Private water supplies are

not required to be tested in the same manner as public supplies, and where sampling of private supplies has been conducted, it is usually as the result of a risk assessment that has identified the supply as potentially high risk and therefore the results are highly likely to be skewed (personal communication from DWI, February 2016).

12. In line with the approach taken in the addendum to the statement on the potential risks from exposure to lead in the infant diet, the bioavailability of arsenic in soil has also been incorporated into the assessments in Annex A. The bioavailability of arsenic in soil varies with soil composition, however the United States Environmental Protection Agency (US EPA) has established a default relative bioavailability factor of 60% for arsenic in soil to be used when site-specific bioavailability data are not available (US EPA, 2012). This default relative bioavailability factor is used when performing human health risk assessments for sites classified as national priorities for clean-up/remediation.

13. Members are asked to comment on the draft statement attached as Annex A.

Secretariat
March 2016

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

First draft statement on potential risks from arsenic 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 influence the Government's dietary recommendations for infants and young children. The SACN is examining the nutritional basis of the advice. The Committee on Toxicity in Food, Consumer Products and the Environment (COT) was asked to review the risks of toxicity from chemicals in the 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. One Government dietary recommendation for infants and young children relates to arsenic, specifying that toddlers and young children (aged 1 to 4.5 years) should not be given rice drinks as a *substitute* for breast milk, infant formula or cows' milk. This is due to the potential for rice drinks to contain high levels of arsenic, and because of this age group's proportionally higher milk consumption and lower bodyweights compared to other consumers (DH, 2009; FSA, 2009a). In addition, the Department of Health (DH) advises that cows' milk or alternatives are not suitable as drinks for infants under 12 months old. Rice drinks are not suitable alternatives for breast milk or formula at any stage of infancy or early childhood as they are considered to be nutritionally inadequate (FSA, 2009b). The advice regarding rice drink consumption provided on NHS choices is more precautionary and states that "*children under five shouldn't have rice drinks as they may contain unsafe levels of arsenic*" (NHS Choices, 2015).

3. The European Commission (EC) has set maximum levels (MLs) for inorganic arsenic in rice and rice-based products. The EC noted that rice is an important ingredient in a broad variety of foods intended for infants and young children, and established a separate ML this commodity when used as an ingredient for the production of such food. The MLs, which are described in Table 1 and are set out in Commission Regulation 2015/1006, applied from the 1st January 2016.

Table 1. Maximum levels of inorganic arsenic (as the sum of As (III) and As (V)) permitted in rice and rice-based products (Commission Regulation (EU) 2015/1006)

Food Group	Maximum Level (μg/kg)
Non-parboiled milled rice (polished or white rice)	200
Parboiled rice and husked rice	250
Rice waffles, rice wafers, rice crackers and rice cakes	300
Rice destined for the production of foods for infants and young children[a]	100

[a] Foodstuffs listed in this category as defined in Commission Directive 96/5/EC of 16 February 1996 on processed cereal-based foods and baby foods for infants and young children (OJ L 49, 28.2.1996, p. 17) as last amended by Directive 2003/13/EC (OJ L 41, 14.2.2003, p. 33).

4. This statement gives an overview of the potential risks from inorganic arsenic in the diets of infants and young children in the UK aged 0 to 12 months and 1 to 5 years, respectively. In this statement, the term 'inorganic arsenic' generally refers to the sum of the species arsenite (As(III)) and arsenate (As(V)), and the monomethylated arsenic forms (MMA as methylarsonous acid (MMA^{III}) and methylarsonic acid (MMA^{V})).

Background

5. Arsenic is a metalloid that occurs in the environment in a variety of forms as the result of both natural and anthropogenic activity. It is generally accepted that inorganic arsenic compounds are more toxic than the organic arsenic compounds that are commonly found in fish, seafood and other marine organisms (arsenobetaine, arsenosugars, and arsenolipids) (EFSA, 2009). The inorganic arsenic present in the environment comprises mainly of species in the trivalent or pentavalent oxidative states, present primarily as the oxoanions arsenite (As(III)) and arsenate (As(V)), but also present as thio complexes. In food samples, inorganic arsenic is often reported as arsenite and arsenate, or as the sum of these, even though it is likely bound to thio groups in peptides or proteins in the food itself (EFSA, 2009).

6. Along with food, drinking water is considered to be one of the most important sources of oral exposure to arsenic. A provisional guideline value of 10 μg of arsenic per litre of drinking water was established by the World Health Organization (WHO) in 1993. This is a pragmatic guideline that was established in view of the practical difficulties in removing arsenic from drinking-water, particularly from small supplies, the practical quantification limit for arsenic, and the fact that in many countries even the provisional guideline would not be attainable. The WHO stated that every effort should be made to keep concentrations as low as reasonably possible (WHO, 2008).

7. Absorption of arsenic compounds varies depending on the chemical species, its solubility, and the matrix in which it is present; soluble arsenicals in water are highly bioavailable. In humans, inorganic arsenic is rapidly cleared from the blood (FAO/WHO, 2011), and is widely distributed to almost all organs (EFSA, 2009). Inorganic arsenic is metabolised primarily by stepwise reduction of arsenate to arsenite, this is followed by oxidative addition of methyl groups, although alternative pathways have also been proposed that include methylated arsenical glutathione metabolites. Ingested inorganic arsenic is excreted as arsenate and arsenite, and as the pentavalent metabolites methylarsonic acid (MMA^{V}) and dimethylarsinic acid (DMA^{V}), with lesser amounts of the trivalent metabolites methylarsonous acid (MMA^{III}) and dimethylarsinous acid (DMA^{III}), and thioarsenical metabolites. Previously it has been assumed that methylation of inorganic arsenic was a detoxification route, it is no longer clear whether this is correct or not as, based on limited data, the simple organic arsenic species MMA^{III} and DMA^{III} appear to be more toxic than inorganic arsenic (arsenite and arsenate), and have high affinity for thiols and cellular proteins (FAO/WHO, 2011). MMA^{III} is not usually detected in foods (MMA^{V} is a trace species found in some seafood and terrestrial foods), while DMA^{III} is a very unstable reactive species that is difficult to measure and is not detected in foods (DMA^{V} is a minor species in seafood and some terrestrial foods) (EFSA, 2009).

8. The results of toxicity studies in animals are not considered to provide a suitable basis for risk characterisation due to the high level of inter-species variability in arsenic metabolism and toxicokinetics. The main adverse effects associated with long-term ingestion of inorganic arsenic in humans are skin lesions, cancer, developmental toxicity, neurotoxicity[2], cardiovascular diseases[3], abnormal glucose metabolism, and diabetes[2] (EFSA, 2009). The International Agency for Research on Cancer (IARC) has reviewed arsenic on a number of occasions concluding that it is a group 1 carcinogen with "*sufficient evidence* in humans for the carcinogenicity of mixed exposure to inorganic arsenic compounds, including arsenic trioxide, arsenite, and arsenate. Inorganic arsenic compounds, including arsenic trioxide, arsenite, and arsenate, cause cancer of the lung, urinary bladder, and skin." (IARC, 2012).

9. There is some evidence for neurobehavioural effects of inorganic arsenic exposure during childhood, at exposure levels occurring in areas with elevated concentrations in drinking water. Most of the available studies have been performed on relatively small numbers of children, and often lack information on early life exposures to arsenic. Furthermore, neurobehavioural outcomes can be influenced by multiple other factors including age at time of examination, nutrition, and stimulation. There is a need for more longitudinal

[2] Mainly associated with acute exposure from deliberate poisoning/suicide, or drinking water with high concentrations (EFSA, 2009).
[3] Evidence in areas with relatively low levels of inorganic arsenic exposure is inconclusive for these adverse effects (EFSA, 2009).

studies to evaluate the type of effects, the critical windows of exposure, and the dose-response relationship (EFSA, 2009; FAO/WHO, 2011).

10. Although few data are available regarding the toxicity of organic arsenic compounds such as arsenobetaine and the arsenosugars and arsenolipids in humans, exposure to such compounds is not generally considered to be of toxicological concern (EFSA, 2009).

11. The COT has commented on arsenic in food a number of times in the past. In general the conclusions have been that dietary exposure to organic arsenic was unlikely to constitute a risk to health, but that dietary exposure to inorganic arsenic should be as low as reasonably practicable (ALARP), because it is genotoxic and a known human carcinogen (COT, 2008).

Toxicological reference point

12. Risk assessments on exposure to arsenic in food have been published by the European Food Safety Authority's (EFSA) Panel on Contaminants in the Food Chain (CONTAM) (EFSA, 2009), and the Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives (JECFA) (FAO/WHO, 2011).

13. The majority of the epidemiological studies have focused on exposures to inorganic arsenic via drinking water, and have not measured or reported total dietary exposure to inorganic arsenic. The EFSA modelled the available dose-response data from key epidemiological studies on cancer, and by selecting a benchmark response of 1% extra risk, calculated a range of values for the 95% lower confidence limit of the benchmark dose ($BMDL_{01}$) of 0.3 to 8 µg/kg bw/day. This range of $BMDL_{01}$ values was identified for cancers of the lung, skin and urinary bladder, as well as skin lesions, taking into account the possible exposures from water and food in the regions studies (EFSA, 2009).

14. The JECFA used a different approach to modelling the dose-response data, including studies in their modelling that had been published after the 2009 EFSA opinion. A BMDL of 3.0 µg/kg bw/day was reported for a 0.5% increased incidence of lung cancer above background, noting that due to the uncertainty in the exposure estimates this $BMDL_{0.5}$ could be in the range of 2.0 to 7.0 µg/kg bw/day (FAO/WHO, 2011).

15. The COT concluded that the lowest available $BMDL_{01}$, 0.3 µg/kg bw/day, should be used in the characterisation of the potential risks from exposure to arsenic in order to be conservative, focussing on inorganic arsenic since this is the form that is carcinogenic.

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

Sources of arsenic exposure

Human breast milk

16. There are limited data available on the concentration of arsenic in breast milk. Those data which are available often relate to women with high exposures to arsenic (e.g. due to the region they live in, or reliance on highly contaminated water) (EFSA, 2014), and rarely determine the species of arsenic present in samples.

17. A literature search has not identified any appropriate data for arsenic concentrations in breast milk in the UK. Therefore a value of 0.33 µg/L, derived from a study by Björklund *et al*. (2012), has been used to estimate exposures to arsenic via breast milk in infants aged 0 to 18 months. This value was the median total arsenic concentration of 60 samples of breast milk collected in 2002-2009 from Swedish first-time mothers at 2-3 weeks postpartum. The limit of detection (LOD) was 0.007 µg/L, and the minimum and maximum reported concentrations were 0.041 and 4.6 µg/L respectively (Björklund *et al*., 2012).

18. Of the studies where arsenic speciation has been performed, there is disparity between the proportion of inorganic arsenic reported to be present in breast milk, with some studies reporting that no inorganic arsenic was detected (Björklund *et al*., 2012), and others reporting that almost all of the arsenic detected was inorganic (Fängström *et al*., 2008). Due to the inconsistent data on the proportion of inorganic arsenic likely to be present in breast milk, the exposure estimates have been performed assuming that 100% of the arsenic is inorganic.

Infant formulae and food

19. Concentrations of inorganic arsenic (defined as the sum of As(III) and As(V), and also MMA if present) 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). With the introduction of MLs for inorganic arsenic in rice and rice-based products, it is possible that some of the exposures from these food products will decrease in time.

20. The mean and 97.5th percentile concentrations of inorganic arsenic (defined as the sum of As(III), As(V) and MMA) in 60 samples of rice drinks tested by the FSA were 12 and 20 µg/kg, respectively (FSA, 2009c). This testing was performed as part of an FSA survey of total and inorganic arsenic in rice drinks, and its results were used in the exposure assessments upon which the recommendations regarding consumption of rice drinks were based. As no new UK data are available, these concentrations have been used in the current exposure assessments for rice drinks.

21. With the introduction of different MLs for inorganic arsenic in rice intended for the production of infant foods, and for inorganic arsenic in rice cakes (i.e. not those intended for infants or young children), questions have been raised about the consumption of rice cakes not specifically marketed for infants (referred to herein as ‘adult’ rice cakes) by those aged 0 to 5 years. Separate exposure assessments have therefore been performed to estimate the level of exposure to inorganic arsenic in infants and young children from the consumption of ‘infant’ and ‘adult’ rice cakes.

22. Concentrations of inorganic arsenic in infant rice cakes have been measured in the Infant Metals Survey. A mean concentration of 150 µg/kg has been derived from the analytical results for 6 types of infant rice cakes (median = 147 µg/kg, range = 74 to 256 µg/kg). It is not possible to determine a concentration for ‘adult’ rice cakes from the TDS as the samples that may have contained rice cakes would have been pooled with other foods for analysis (i.e. there is no ‘rice cakes’ sub-group).

23. A recent study by Signes-Pastor *et al*. (2016) measured the concentration of inorganic arsenic (as As(III) and As(V)) in several rice-based products commonly consumed by infants including baby rice, rice cereals and rice crackers (i.e. rice cakes (confirmed by personal communication with Dr A. Signes-Pastor, January 2016)). The researchers tested 36 samples of infant rice cakes and 61 samples of ‘adult’ rice cakes that were purchased from 36 food shops (15 local shops and 21 big supermarkets) in the UK in 2014. Mean and 97.5th percentile concentrations of 127 and 187 µg/kg, respectively (median = 127 µg/kg), were determined for the infant rice cakes. For the ‘adult’ rice cakes, mean and 97.5th percentile concentrations of 96 and 197 µg/kg, respectively (median = 98 µg/kg) were determined (personal communication with Dr A. Signes-Pastor, January 2016). It is noted that these data do not support the concern that arsenic levels in ‘adult’ rice cakes would be higher than in infant rice cakes.

24. The mean inorganic arsenic concentration reported in the Infant Metals Survey has been used in the exposure assessment for infant rice cakes (150 µg/kg). This concentration was used as it was relatively consistent with that reported by Signes-Pastor *et al.*, albeit slightly higher. For the assessment of exposures from ‘adult’ rice cakes, the mean concentration reported by Signes-Pastor *et al*. has been used (96 µg/kg) as it was not possible to derive a value from the TDS.

Drinking water

25. In water, arsenic is most likely to be present as arsenate (As(V)) if the water is oxygenated, and arsenite (As(III)) under reducing conditions (WHO, 2011). Drinking water can therefore be a major contributor to inorganic arsenic exposure, especially in areas with high natural levels, and when factoring in its use in the preparation of other beverages and food (EFSA, 2009; WHO, 2011)).

26. EU legislation sets a maximum limit of 10 µg/L for arsenic in water (Directive 98/83/EC).

27. Levels of arsenic in drinking water in 2014 from England and Wales, Northern Ireland and Scotland were provided by the Drinking Water Inspectorate, Northern Ireland Water and the Drinking Water Quality Regulator for Scotland, respectively. Median and 97.5th percentile values calculated from this data are shown in Table 2. These values represent the concentration of arsenic in public water supplies, and have been used to calculate exposures to arsenic from drinking water in combination with exposures from food.

28. Representative data on the concentration of arsenic in private water supplies in the UK were not available. Private water supplies are not required to be tested in the same manner as public supplies, and where sampling of private supplies has been conducted, it is usually as the result of a risk assessment that has identified the supply as potentially high risk and therefore the results are highly likely to be skewed (personal communication from DWI, February 2016).

Table 2. Median and 97.5th percentile concentrations (µg/L) of inorganic arsenic in water across the UK for 2014, all arsenic in water is assumed to be inorganic.

Country	Number of samples	Median concentration (µg/L)	97.5th Percentile concentration (µg/L)
England and Wales	12479	0.22	2.10
Northern Ireland	392	0.40	0.70
Scotland	1500	0.20	0.90

Environmental

Dust and soil

29. Arsenic can be present in soil both naturally (depending on the type of bedrock etc.), and as the result of anthropogenic activity (e.g. mining or the use of phosphate fertilisers) (Rawlings *et* al., 2012; EFSA, 2009).

30. Concentrations of arsenic in soil were measured in 453 soil samples collected as part of the Environment Agency's Soil and Herbage Pollutant Survey (EA, 2007). The samples were collected from urban and rural sites across the UK between 2001 and 2002 (SHS, 2007). The median and 97.5th percentile concentrations of arsenic in the samples were 7.5 and 32.1 mg/kg, respectively.

31. No relevant data were available for arsenic concentrations in dust. As the proportion of inorganic arsenic in soil varies depending on local

geology and anthropogenic sources, it has been assumed that all of the arsenic present in soil is inorganic.

32. The bioavailability of arsenic in soil varies with soil composition. The United States Environmental Protection Agency (US EPA) has established a default relative bioavailability factor of 60% for arsenic in soil to be used when specific data are not available (US EPA, 2012). This default relative bioavailability factor has been applied in the current exposure assessments.

Air

33. Both natural (e.g. volcanic eruptions or microbial reduction) and anthropogenic (e.g. coal-fired power generation and smelting) activities release arsenic into the atmosphere, mainly as As_2O_3 particles or bound to particulate matter (EFSA, 2009).

34. EU legislation sets a target value of 6 ng/m^3 for arsenic in air (Directive 2004/107/EC).

35. Arsenic in particulate matter less than 10 µm (PM_{10}) was measured at 23 sites and as metal deposition was measured at 4 sites across the UK in 2014. Median values from these sites ranged from 0.12 to 1.09 ng/m^3 and 99th percentile values ranged from 0.12 to 4.92 ng/m^3. Due to the lack of specification data, it is assumed that all of the arsenic present in air is inorganic.

Exposure assessment

36. Consumption data from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) (DH, 2013), and from years 1-4 of the National Diet and Nutrition Survey Rolling Programme (NDNS) (Bates *et al.*, 2014) have been used for the estimation of dietary exposures. Bodyweight data used in the estimation of arsenic exposures are shown in Table 3 below.

Table 3. Average bodyweights used in the estimation of arsenic exposures (DH, 2013; Bates *et al*., 2014)

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

Infants (0 to 12 months)

Breast milk

37. As no consumption data were available for exclusive breastfeeding in infants aged 0 to 6 months, the default consumption values used by COT in its evaluations of the infant diet of 800 and 1200 mL for average and high level consumption (EFSA, 2009) have been used to estimate exposures to inorganic arsenic from breastmilk based on a median total arsenic concentration of 0.33 µg/L and the assumption that 100% of this is inorganic arsenic (paragraph 18). The ranges of exposure to inorganic arsenic in exclusively breastfed 0 to 6 month olds were 0.034 to 0.045 and 0.051 to 0.067 µg/kg bw/day in average and high level consumers respectively (Table 4).

Table 4. Estimated inorganic arsenic exposure from exclusive breastfeeding in 0 to 6 month old infants, estimated for average and high level consumption of breast milk containing total arsenic at 0.33 µg/L.

Arsenic 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
0.33	0.045	0.034	0.067	0.051

38. Data on breast milk consumption were available from the DNSIYC and the NDNS, and have been used to estimate exposures for infants aged 4 to 18 months (Table 5) based on the assumed median inorganic arsenic concentration of 0.33 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.

39. Mean exposures to inorganic arsenic for 4 to 18 month olds were 0.008 to 0.030 µg/kg bw/day, and 97.5th percentile exposures were 0.017 to 0.053 µg/kg bw/day (Table 5).

Table 5. Estimated inorganic arsenic exposure in 4 to 18 month old infants from breast milk, estimated for mean and 97.5th percentile level consumption of breast milk containing total arsenic at 0.33 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	0.030	0.022	0.013	0.010	0.008

97.5th percentile	0.051	0.053	0.038	0.025	0.017

Infant formulae and complementary foods

40. Exposure estimates for this category were derived using occurrence data from the Infant Metals Survey, based on both lower bound (LB) and upper bound (UB) concentrations. Exposure estimates were calculated for 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) (Table 7).

41. In 0 to 4 month olds, exposures to inorganic arsenic from ready-to-feed formula were 0.000 to 0.027 µg/kg bw/day in average consumers, and 0.000 to 0.041 µg/kg bw/day in high level consumers (Table 6). When exposures to inorganic arsenic are calculated for reconstituted formula incorporating the highest median and 97.5th percentile concentrations for arsenic in water reported in Table 2, this results in exposures of 0.064 to 0.277 µg/kg bw/day in average consumers, and of 0.091 to 0.415 µg/kg bw/day in high level consumers.

Table 6. Estimated average and high level exposures (µg/kg bw/day) to inorganic arsenic from exclusive feeding on infant formulae for 0 to 4 month olds.

Infant Formula	**Inorganic As Exposure (LB-UB Range) (µg/kg bw/d)**	
	Average consumer (800 mL/day)	**High level consumer (1200 mL/day)**
Ready-to-Feed	0.000-0.027	0.000-0.041
Dry Powder [a]	0.014-0.037	0.021-0.055
Dry Powder + median water of 0.4 µg/L [b]	0.064-0.087	0.091-0.125
Dry Powder + 97.5th percentile water of 2.1 µg/L [b]	0.254-0.277	0.381-0.415

[a] Exposure does not include the contribution from water
[b] Calculated assuming reconstituted formula comprises 85% water

42. Total mean exposures (excluding water) to inorganic arsenic from infant formulae, commercial infant foods, and other foods, for 4 to 12 month olds were 0.054 to 0.178 µg/kg bw/day, and 97.5th percentile exposures were 0.226 to 0.451 µg/kg bw/day. Total mean and 97.5th percentile exposures have also been calculated using the highest median and 97.5th percentile concentrations for arsenic in water reported in Table 2. The total mean exposures including water were 0.056 to 0.203 µg/kg bw/day, while the 97.5th

percentile exposures including water were 0.232 to 0.536 µg/kg bw/day (Table 7).

Table 7. Estimated mean and 97.5th percentile exposures (µg/kg bw/day) to inorganic arsenic from infant formulae, commercial infant foods and other foods (excluding water) for 4 to 12 month olds.

	Inorganic As Exposure (LB-UB Range) (µg/kg bw/d)					
Food	**4 -5.99 Months (n=116)**		**6-8.99 Months (n=606)**		**9-11.99 Months (n=686)**	
	Mean	**97.5th**	**Mean**	**97.5th**	**Mean**	**97.5th**
Infant formula	0.000-0.014	0.001-0.031	0.000-0.014	0.001-0.031	0.000-0.011	0.006-0.027
Commercial infant foods	0.044-0.064	0.214-0.264	0.061-0.089	0.201-0.287	0.057-0.082	0.216-0.306
Other foods	0.009-0.011	0.057-0.063	0.058-0.064	0.284-0.293	0.086-0.096	0.333-0.345
Total (excl. water)	0.054-0.077	0.226-0.279	0.122-0.156	0.352-0.411	0.144-0.178	0.395-0.451
Total (incl. median water of 0.4 µg/L)	0.056-0.079	0.232-0.285	0.126-0.160	0.365-0.424	0.149-0.183	0.411-0.467
Total (incl. 97.5th percentile water of 2.1 µg/L)	0.064-0.087	0.257-0.310	0.142-0.176	0.423-0.482	0.169-0.203	0.480-0.536

* 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

43. Estimated exposures to inorganic arsenic from food for children aged 12 to 18 months were calculated using occurrence data from both the Infant Metals Survey, and the 2014 TDS. The exposure data derived from the Infant Metals Survey allow estimation of inorganic arsenic 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 lower bound (LB) and upper bound (UB) concentrations are provided.

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

Exposure estimates based on the Infant Metals Survey

45. The ranges of total mean and 97.5th percentile exposures (excluding water) to inorganic arsenic from infant formula, commercial infant foods and other foods were 0.139 to 0.166 and 0.416 to 0.466 µg/kg bw/day, respectively. The total mean exposures including water (calculated using the highest median and 97.5th percentile values in Table 2) were 0.144 to 0.196 µg/kg bw/day, while the 97.5th percentile exposures including water were 0.435 to 0.555 µg/kg bw/day (Table 8).

Table 8. Estimated mean and 97.5th percentile exposures (µg/kg bw/day) to inorganic arsenic from infant formulae, commercial infant foods and other foods (excluding water) for 12 to 18 month olds.

Food	**Inorganic As Exposure (LB-UB Range) (µg/kg bw/d)**			
	12-14.99 Months (n=670)		**15-17.99 Months (n=605)**	
	Mean	**97.5th**	**Mean**	**97.5th**
Infant formula	0.001-0.006	0.011-0.028	0.001-0.003	0.009-0.022
Commercial infant foods	0.033-0.047	0.162-0.219	0.019-0.026	0.089-0.132
Other foods	0.106-0.121	0.372-0.387	0.128-0.143	0.385-0.413
Total (excl. water)	0.139-0.165	0.428-0.466	0.147-0.166	0.416-0.432
Total (incl. median water of 0.4 µg/L)	0.144-0.170	0.445-0.483	0.153-0.172	0.435-0.449
Total (incl. 97.5th percentile water of 2.1 µg/L)	0.166-0.192	0.517-0.555	0.177-0.196	0.513-0.546

* 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

46. Table 9 shows the estimated inorganic arsenic exposures that were calculated using the TDS data for children aged 12 to 18 months. These are higher than those estimated from the Infant Metals Survey due to the inclusion of a larger number of foods in the exposure estimate for the TDS.

47. Using the TDS data (which includes tap water and bottled water), total mean and 97.5th percentile exposures to inorganic arsenic from the combination of all food groups in the TDS ranged from 0.126 to 0.702 and 0.316 to 1.243 µg/kg bw/day, respectively. The inorganic arsenic

concentration identified for tap water in the TDS was <1 µg/L. In order to determine the possible impact of arsenic concentrations in water from different regions, this has been replaced by the highest median (0.4 µg/L) and 97.5th percentile (2.1 µg/L) for arsenic levels in water reported in Table 2. This results in total mean and 97.5th percentile exposures to inorganic arsenic from a combination of all food groups of 0.129 to 0.692 and 0.323 to 1.195 µg/kg bw/day, respectively (Table 9), demonstrating that the arsenic content of water has a negligible impact on total dietary exposure to inorganic arsenic of UK infants and young children.

Table 9. Estimated dietary exposure to inorganic arsenic based on the TDS data in children aged 12 to 18 months.

Food Group	**Inorganic As Exposure (LB-UB Range) (µg/kg bw/day)**			
	12-14.99 Months (n=670)		**15-17.99 Months (n=605)**	
	Mean	**97.5th**	**Mean**	**97.5th**
TDS (incl. TDS water at <1 µg/L)	0.126-0.659	0.316-1.243	0.137-0.702	0.327-1.162
TDS (incl. median water of 0.4 µg/L)	0.129-0.634	0.323-1.169	0.142-0.673	0.332-1.130
TDS (incl. 97.5th percentile water of 2.1 µg/L)	0.146-0.651	0.349-1.195	0.161-0.692	0.350-1.141

48. In general, the food groups with the highest contribution to inorganic arsenic exposure were miscellaneous cereals (including rice and some rice products) and potatoes.

Children aged 18 months to 5 years

49. 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).

50. Table 10 shows the possible inorganic arsenic exposures that were calculated using the TDS data for children aged 18 months to 5 years. Total mean and 97.5th percentile exposures to inorganic arsenic from the combination of all food groups in the TDS ranged from 0.123 to 0.786 and 0.256 to 1.182 µg/kg bw/day, respectively. The inorganic arsenic concentration identified for tap water in the TDS <1 µg/L. In order to determine the possible impact of arsenic concentrations in water from different regions, this has been replaced by the highest median (0.4 µg/L) and 97.5th percentile (2.1 µg/L) for arsenic levels in water reported in Table 2. This results in total mean and 97.5th percentile exposures to inorganic arsenic from

a combination of all food groups of 0.127 to 0.776 and 0.259 to 1.175 µg/kg bw/day, respectively (Table 10), demonstrating that the arsenic content of water has a negligible impact on total dietary exposure to inorganic arsenic of UK infants and young children.

Table 10. Estimated dietary exposure to inorganic arsenic based on the TDS data in children aged 18 months to 5 years.

Food Group	Inorganic As 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
TDS (incl. TDS water at <1 µg/L)	0.144-0.786	0.291-1.182	0.123-0.650	0.256-1.021
TDS (incl. median water of 0.4 µg/L)	0.149-0.757	0.291-1.161	0.127-0.624	0.259-0.992
TDS (incl. 97.5th percentile water of 2.1 µg/L)	0.168-0.776	0.316-1.175	0.144-0.641	0.282-1.001

51. As with the younger children, the food groups with the highest contribution to inorganic arsenic exposure in the TDS were miscellaneous cereals (including rice and some rice products) and potatoes.

Exposures from the consumption of rice drinks

52. This assessment has considered exposures in infants and young children aged 1 to 5 years only as the DH advise that cows' milk and alternatives (i.e. rice drinks) are not suitable for infants under 12 months old (paragraph 2). There are very few consumers of rice drinks recorded in the DNSIYC and the NDNS (5 in total for 1 to 5 year olds). Therefore the exposure estimates have been based on the consumption of cows' milk, assuming that there is complete replacement of cows' milk with rice drinks. Mean and 97.5th percentile inorganic arsenic concentrations of 12 and 20 µg/kg in rice drinks (FSA, 2009b), have also been used.

53. For infants and young children aged 1 to 5 years, mean and 97.5th percentile exposures range from 0.218 to 0.604 and 0.600 to 1.516 µg/kg bw/day, respectively (Table 11). The highest value for the 97.5th percentile range of exposures from rice drinks (for >12 to <15 month olds, 1.516 µg/kg bw/day) is more than double the upper bound mean exposure value estimated from the TDS data for this age range (Table 9). The highest values for the 97.5th percentile range of exposures for the remaining age groups (15 to 60 month olds) were between 1.5 and 2 times higher than the upper bound mean exposure values estimated from the TDS data for the same age groups (Tables 9 and 10).

Table 11. Estimated inorganic arsenic exposures from rice drinks for infants and young children aged 1 to 5 years, using consumption data for cows' milk as a proxy.

Inorganic arsenic concentration	Consumption level	Exposure (µg/kg bw/day)			
		Age group (months)			
		>12 to <15	>15 to <18	>18 to <24	>24 to <60
Mean (12 µg/L)	Average[a]	0.362	0.344	0.316	0.218
	High[b]	0.910	0.774	0.863	0.600
97.5th percentile (20 µg/L)	Average[a]	0.604	0.573	0.526	0.363
	High[b]	1.516	1.290	1.438	1.000

[a] Based on mean consumption from the DNSIYC and the NDNS
[b] Based on 97.5[th] percentile consumption from the DNSIYC and the NDNS

54. Based on upper bound mean exposures for the total diet (calculated with the highest median water concentration), and on the mean occurrence value for inorganic arsenic in rice drinks (12 µg/L), consumption of up to about 50 mL of rice drink per day would result in less than a 10% increase in background exposure from the total diet for this age group.

Exposures from the consumption of rice cakes

55. Exposures have been estimated using consumption data from the DNSIYC (DH, 2013) and the NDNS (Bates *et al*., 2014); separate consumption data were available for infant and 'adult' rice cakes. Rice cakes marketed for infants have an approximate weight of 2 g per cake while the weight of one 'adult' rice cake is ~10 g. A mean inorganic arsenic concentration of 150 µg/kg has been used in the assessment of infant rice cake consumption (Table 12), while a mean concentration of 96 µg/kg has been used for the assessment of 'adult' rice cakes (Table 13) (paragraph 24).

56. For infants aged <6 months, mean and 97.5[th] percentile exposures to inorganic arsenic from the consumption of infant rice cakes were 0.006 and 0.011 µg/kg bw/day, respectively, although these values are based on a very limited number of consumers. For infants aged 6 to 12 months mean and 97.5[th] percentile exposures to inorganic arsenic from the consumption of infant rice cakes range from 0.023 to 0.031 and 0.068 to 0.109 µg/kg bw/day, while those from the consumption of 'adult' rice cakes range from 0.018 to 0.025 and from 0.035 to 0.057 µg/kg bw/day, respectively. There were no consumers of 'adult' rice cakes aged < 6 months.

57. For young children aged 1 to 5 years, mean and 97.5[th] percentile exposures from the consumption of infant rice cakes range from 0.026 to

0.035 and 0.070 to 0.122 µg/kg bw/day, while those from the consumption of 'adult' rice cakes range from 0.025 to 0.066 and from 0.058 to 0.113 µg/kg bw/day, respectively. The highest value of the 97.5th percentile range of exposures from infant rice cakes (for >12 to <15 month olds, 0.122 µg/kg bw/day) is ~20% of the upper-bound mean exposures estimated from the TDS data for this age group (Table 9).

Table 12. Estimated inorganic arsenic exposures from infant rice cakes for infants and young children aged 4 months to 5 years.

Consumption and Exposure	**Age group (months)**						
	>4 to <6	**>6 to <9**	**>9 to <12**	**>12 to <15**	**>15 to <18**	**>18 to <24**	**>24 to <60**
Mean consumption (g/day)	0.30	1.38	1.97	2.45	2.59	2.05	3.20
97.5th percentile consumption (g/day)	0.47	4.00	6.59	8.01	6.00	5.50	6.44
Mean consumption (g/kg bw/day)	0.04	0.16	0.21	0.23	0.23	0.18	0.20
97.5th percentile consumption (g/kg bw/day)	0.07	0.45	0.73	0.81	0.52	0.47	0.47
Mean exposure (µg/kg bw/day)	0.006	0.023	0.031	0.035	0.035	0.026	0.029
97.5th percentile exposure (µg/kg bw/day)	0.011	0.068	0.109	0.122	0.078	0.070	0.071

Table 13. Estimated inorganic arsenic exposures from 'adult' rice cakes for infants and young children aged 4 months to 5 years.

Consumption and Exposure	**Age group (months)**						
	>4 to <6	**>6 to <9**	**>9 to <12**	**>12 to <15**	**>15 to <18**	**>18 to <24**	**>24 to <60**
Mean consumption (g/day)	n/a	1.81	2.40	2.68	2.81	7.22	4.56
97.5th percentile consumption (g/day)	n/a	3.34	5.29	8.75	7.83	12.25	7.50
Mean consumption (g/kg bw/day)	n/a	0.19	0.26	0.26	0.26	0.69	0.31

97.5th percentile consumption (g/kg bw/day)	n/a	0.36	0.59	0.80	0.73	1.18	0.61
Mean exposure (µg/kg bw/day)	n/a	0.018	0.025	0.025	0.025	0.066	0.030
97.5th percentile exposure (µg/kg bw/day)	n/a	0.035	0.057	0.077	0.070	0.113	0.058

Soil/dust

58. Potential exposures of UK infants aged >9 to 12 months and young children aged 1 to 5 years to arsenic in soil were calculated assuming ingestion of 100 mg/day (US EPA, 2008; WHO, 2007). Children of these age groups are likely to consume more soil and dust than younger infants who are less able to move around and come into contact with soil and dust. Median and 97.5th percentile soil arsenic concentrations of 7.5 and 32.1 mg/kg respectively were used in these exposure estimations (paragraph 30, EA, 2007) (Table 14). A default bioavailability factor of 60% relative to food has been incorporated into these estimations (paragraph 32).

59. Data specific to dust were not available, however this is not considered an issue as the EPA's default ingestion value is for combined soil and dust ingestion; using only the arsenic concentrations determined for soil would therefore result in a relatively conservative exposure estimate.

Table 14. Possible inorganic arsenic exposures (µg/kg bw/day) from soil in infants and young children aged >9 months to 5 years.

Arsenic concentration (mg/kg)	**Exposure (µg/kg bw/day)**				
	Age (months)				
	>9 to 12	**12 to 15**	**15 to 18**	**18 to 24**	**24 to 60**
7.5 (Median)	0.047	0.042	0.040	0.038	0.028
32.1 (97.5th)	0.201	0.182	0.172	0.161	0.120

Air

60. Potential exposures of UK infants aged 0 to 12 months and young children aged 1 to 5 years to arsenic in air were estimated (Table 15) assuming mean ventilation rates of 3.6, 4.1, 5.4, 8.0, 9.5 and 10.9 m^3/day, respectively for infants and children aged 0 to <3, 3 to <6 and 6 to <12 months and 1 to <2, 2 to <3 and 3 to <6 years (US EPA, 2008). To assess the exposures in these age groups, average bodyweights of 5.9, 7.8, 9.2, 13.5, 15.1 and 19.7 kg, respectively, were used (Bates *et al*., 2014; DH, 2013).

61. The arsenic concentrations used in the exposure calculations were the lowest and highest median values and lowest and highest 99th percentile values of 0.12, 1.09, 0.12 and 4.92 ng/m^3, respectively, from monitoring sites in the UK (paragraph 35). It has been assumed that all of the arsenic present in air is inorganic. These exposures are approximately 2 to 3 orders of magnitude lower than those estimated from other sources.

Table 15. Possible exposures to inorganic arsenic (µg/kg bw/day) in infants and young children from the air.

Arsenic concentration (ng/m^3)	Exposure (µg/kg bw/day)					
	Ages (months)					
	0 to <3	3 to <6	6 to <12	12 to <24	24 to <36	36 to <72
0.12 (lowest median)	0.00007	0.00006	0.00007	0.00007	0.00008	0.00007
1.09 (highest median)	0.00067	0.00057	0.00064	0.00065	0.00069	0.00060
0.12 (lowest 99th percentile)	0.00007	0.00006	0.00007	0.00007	0.00008	0.00007
4.92 (highest 99th percentile)	0.00300	0.00259	0.00289	0.00292	0.00310	0.00272

Risk Characterisation

62. Potential risks from the exposure of infants and young children to inorganic arsenic were characterised by margins of exposure (MOEs), calculated as the ratio of the $BMDL_{01}$ value of 0.3 µg/kg bw/day, to estimated exposures from dietary and non-dietary sources.

63. As toxicity will depend on total exposure to inorganic arsenic from all sources, it is important to consider combined exposures from food, water, and non-dietary sources. Tables 17 to 19 summarise the aggregate exposures and corresponding MOEs for each age group for inorganic arsenic based on exposures from breast milk, the total diet including water, and soil, where these exposures are available. Exposures from water have been taken into account by using the estimates generated for the total diet including water, based on both the highest median and 97.5th percentile water concentrations. Exposures from air have not been incorporated as they are too low to have an impact on the MOEs.

64. The aggregate exposures have been estimated by adding the mean/average exposure estimates from all but one source to the 97.5th percentile/high level exposure estimate for the remaining source. Where a range of exposures from lower bound to upper bound were available, the upper bound estimates have been used.

65. Aggregate exposures have not been calculated for 0 to 4 month olds as this age group were considered to be exclusively breast- or formula-fed, with no exposure to other foods or to soil. Table 16 shows the inorganic arsenic exposures and corresponding MOEs for this age group. The MOEs for exclusively breastfed 0 to 4 month olds are greater than 1 at average and high level exposure. The MOEs for exclusively formula-fed 0 to 4 month olds are greater than 1 at median water concentration of arsenic, but are in the region of or less than 1 at 97.5th percentile water concentration.

Table 16. Estimated exposures to inorganic arsenic in exclusively breast- or formula-fed 0 to 4 month olds, and the corresponding MOEs when they are compared to the $BMDL_{01}$ of 0.3 µg/kg bw/day.

Source of exposure	Exposure level	Exposure (µg/kg bw/day)	MOE[a]
Exclusive breast milk	Average	0.045	6.7
	High	0.067	4.5
Exclusive infant formula reconstituted with water with inorganic As at highest median concentration (0.4 µg/L)[b]	Average	0.087	3.4
	High	0.125	2.4
Exclusive infant formula reconstituted with water with inorganic As at highest 97.5th percentile concentration (2.1 µg/L)[b]	Average	0.277	1.1
	High	0.415	0.7

[a] The MOE is calculated by dividing the $BMDL_{01}$ of 0.3 µg/kg bw/day by the respective exposure
[b] Based on the assumption that reconstituted infant formula comprises 85% water

66. Table 17 shows the aggregate exposure estimates and MOEs for infants aged 4 to 6 and 6 to 9 months. The aggregate exposures for these age groups are based on the exposure estimates for breast milk and the total diet including water. Estimates from exposures via soil were not calculated for this age group as infants <9 months are less able to move around and come into contact with soil. For 4 to 9 month olds, most of the aggregate exposures result in MOEs that are above 1. For a combination of mean breast milk exposures plus 97.5th percentile total diet exposure with the median or 97.5th percentile concentration of inorganic arsenic in the water, the MOEs are equal to or below 1.

Table 17. Aggregate exposures to inorganic arsenic for infants aged 4 to 9 months based on exposures from breast milk and the total diet including water, and the corresponding MOEs when these aggregate exposures are compared to the $BMDL_{01}$ 0.3 µg/kg bw/day.

Exposure combination	Concentration of inorganic arsenic in water	Age (months)			
		4 to 6		6 to 9	
		Exposure (µg/kg	MOE[a]	Exposure (µg/kg	MOE[a]

		bw/day)		bw/day)	
Mean breast milk plus mean total diet (incl. water)	Median (0.4 µg/L)	0.109	2.8	0.182	1.6
	97.5th percentile (2.1 µg/L)	0.117	2.6	0.198	1.5
97.5th percentile breast milk plus mean total diet (incl. water)	Median (0.4 µg/L)	0.130	2.3	0.213	1.4
	97.5th percentile (2.1 µg/L)	0.138	2.2	0.229	1.3
Mean breast milk plus **97.5th percentile total diet (incl. water)**	Median (0.4 µg/L)	0.315	1.0	0.446	0.7
	97.5th percentile (2.1 µg/L)	0.340	0.9	0.504	0.6

[a] The MOE is calculated by dividing the $BMDL_{01}$ of 0.3 µg/kg bw/day by the respective exposure

67. Table 18 shows the aggregate exposure estimates and MOEs for infants aged 9 to 12, 12 to 15, and 15 to 18 months. The aggregate exposures for these age groups are based on the exposure estimates for breast milk, the total diet including water, and soil. For 9 to 18 month olds, all of the aggregate exposures result in MOEs that are in the region of or less than 1.

Table 18. Aggregate exposures to inorganic arsenic for infants aged 9 to 18 months based on exposures from breast milk, the total diet including water, and soil, and the corresponding MOEs when these aggregate exposures are compared to the $BMDL_{01}$ of 0.3 µg/kg bw/day.

Exposure combination	**Concentration of inorganic arsenic in water**	**Age (months)**					
		9 to 12		**12 to 15**		**15 to 18**	
		Exposure (µg/kg bw/day)	**MOE[a]**	**Exposure (µg/kg bw/day)**	**MOE[a]**	**Exposure (µg/kg bw/day)**	**MOE[a]**
Mean breast milk plus mean total diet (incl. water) plus average soil[b]	Median (0.4 µg/L)	0.243[d]	1.2	0.686[e]	0.4	0.721[e]	0.4
	97.5th percentile (2.1 µg/L)	0.263[d]	1.1	0.703[e]	0.4	0.740[e]	0.4
97.5th percentile breast milk plus mean total diet (incl. water) plus average soil[b]	Median (0.4 µg/L)	0.268[d]	1.1	0.701[e]	0.4	0.730[e]	0.4
	97.5th percentile (2.1 µg/L)	0.288[d]	1.0	0.718[e]	0.4	0.749[e]	0.4
Mean breast milk plus **97.5th**	Median (0.4 µg/L)	0.527[d]	0.6	1.221[e]	0.2	1.178[e]	0.3
	97.5th	0.596[d]	0.5	1.247[e]	0.2	1.189[e]	0.3

percentile total diet (incl. water) plus average soil[b]	percentile (2.1 µg/L)						
Mean breast milk plus mean total diet (incl. water) **plus high level soil**[c]	Median (0.4 µg/L)	0.397[d]	0.8	0.826[e]	0.4	0.853[e]	0.4
	97.5th percentile (2.1 µg/L)	0.417[d]	0.7	0.843[e]	0.4	0.872[e]	0.3

[a] The MOE is calculated by dividing the $BMDL_{01}$ of 0.3 µg/kg bw/day by the respective exposure
[b] Based on ingestion of soil with the median concentration of inorganic arsenic (7.5 mg/kg)
[c] Based on ingestion of soil with the 97.5th percentile concentration of inorganic arsenic (32.1 mg/kg)
[d] This includes the highest upper bound total diet exposure estimate for this age range, based on the results of the IMS
[e] This includes the highest upper bound total diet exposure estimate for this age range, based on the results of the TDS

68. Table 19 shows the aggregate exposure estimates and MOEs for young children aged 18 to 24 and 24 to 60 months. The aggregate exposures for these age groups are only based on the exposure estimates for the total diet including water, and soil, as breast milk is expected to contribute minimally in children older than 18 months. For 18 to 60 month olds, all of the aggregate exposures result in MOEs that are equal to or less than 0.5.

Table 19. Aggregate exposures to inorganic arsenic for young children aged 18 to 60 months based on exposures from the total diet including water, and soil, and the corresponding MOEs when these aggregate exposures are compared to the $BMDL_{01}$ of 0.3 µg/kg bw/day.

Exposure combination	**Concentration of inorganic arsenic in water**	**Age (months)**			
		18 to 24		**24 to 60**	
		Exposure (µg/kg bw/day)	**MOE[a]**	**Exposure (µg/kg bw/day)**	**MOE[a]**
Mean total diet (incl. water) plus average soil[b]	Median (0.4 µg/L)	0.795	0.4	0.652	0.5
	97.5th percentile (2.1 µg/L)	0.814	0.4	0.669	0.4
97.5th percentile total diet (incl. water) plus average soil[b]	Median (0.4 µg/L)	1.199	0.3	1.020	0.3
	97.5th percentile (2.1 µg/L)	1.213	0.2	1.029	0.3
Mean total diet (incl. water) plus	Median (0.4 µg/L)	0.918	0.3	0.744	0.4

high level soil[c]	97.5[th] percentile (2.1 µg/L)	0.937	0.3	0.761	0.4

[a] The MOE is calculated by dividing the $BMDL_{01}$ of 0.3 µg/kg bw/day by the respective exposure
[b] Based on ingestion of soil with the median concentration of inorganic arsenic (7.5 mg/kg)
[c] Based on ingestion of soil with the 97.5[th] percentile concentration of inorganic arsenic (32.1 mg/kg)

Risk characterisation for specific food products

Rice drinks

69. Table 20 summarises the MOEs for the estimated exposures calculated for rice drinks using the mean concentration of inorganic arsenic (12 µg/L), assuming complete replacement of cows' milk with rice drinks. The MOEs for average consumers from all age groups are greater than or in the region of 1, while the MOEs for all high level consumers are equal to or less than 0.5 from this source alone.

Table 20. Range of possible exposures to inorganic arsenic from rice drinks, and the corresponding MOEs when they are compared to the $BMDL_{01}$ of 0.3 µg/kg bw/day.

Consumer	**Age group (months)**					
	12 to 18		**18 to 24**		**24 to 60**	
	Exposure (µg/kg bw/day)	**MOE**[a]	**Exposure (µg/kg bw/day)**	**MOE**[a]	**Exposure (µg/kg bw/day)**	**MOE**[a]
Average	0.362[b]	0.8	0.316	1.0	0.218	1.4
High	0.910[b]	0.3	0.863	0.3	0.6	0.5

[a] The MOE is calculated by dividing the $BMDL_{01}$ of 0.3 µg/kg bw/day by the respective exposure
[b] Based on highest estimate for this age range

70. It has been estimated that, for those aged 1 to 5 years, consumption of about 50mL of rice drink per day would not cause an appreciable increase in background exposure to inorganic arsenic (paragraph 54).

Rice cakes

71. Tables 21 and 22 summarise the MOEs for the estimated exposures from the consumption of infant and 'adult' rice cakes. All of the MOEs from rice cake consumption are greater than 1. The MOEs for infants aged 4 to 18 months from infant rice cake consumption are lower than those from 'adult' rice cake consumption; this is explained by the fact that although the consumption of infant and 'adult' rice cakes by this age group was similar, the

concentration of inorganic arsenic used to assess exposure from infant rice cakes was approximately 50% greater than that used to assess ‘adult’ rice cakes. For 18 to 24 month olds, the MOEs from ‘adult’ rice cake consumption are considerably lower than those from infant rice cake consumption; this is due to the fact that this age group consumed considerably more ‘adult’ rice cakes than they did infant rice cakes (~2 to 3 times greater). The MOEs from the consumption of infant rice cakes and of ‘adult’ rice cakes for young children aged 24 to 60 months are relatively similar.

72. The exposures from the consumption of rice cakes can be considered in addition to those from the total diet, bearing in mind that this would result in a degree of double-counting due to the inclusion of rice cakes in the total diet exposure assessments. Adding the highest of the 97.5th percentile exposures for infants < 12 month olds (0.109 µg/kg bw/day from consumption of infant rice cakes) to the highest mean exposure from the total diet[4] for the same age group (0.183 µg/kg bw/day) would result in an increase of approximately 40% above the mean total diet exposure. Adding the highest of the 97.5th percentile exposures for 1 to 5 year olds (0.122 µg/kg bw/day from 18 to 24 month olds consuming infant rice cakes) to the highest mean exposure from the total diet for the same age group (0.673 µg/kg bw/day) would result in an increase of ~15% above the mean total diet exposure.

Table 21. Range of possible exposures to inorganic arsenic from infant rice cakes, and the corresponding MOEs when they are compared to the lowest $BMDL_{01}$ for inorganic arsenic (0.3 µg/kg bw/day).

Consumer	Age group (months)							
	4 to 12		12 to 18		18 to 24		24 to 60	
	Exposure (µg/kg bw/day)	MOE[a]	Exposure (µg/kg bw/day)	MOE[a]	Exposure (µg/kg bw/day)	MOE[a]	Exposure (µg/kg bw/day)	MOE[a]
Average	0.031[b]	9.7	0.035[b]	8.6	0.026	11.5	0.029	10.3
High	0.109[b]	2.8	0.122[b]	2.5	0.070	4.3	0.071	4.2

[a] The MOE is calculated by dividing the $BMDL_{01}$ of 0.3 µg/kg bw/day by the respective exposure
[b] Based on highest estimate for this age range

Table 22. Range of possible exposures to inorganic arsenic from ‘adult’ rice cakes, and the corresponding MOEs when they are compared to the lowest $BMDL_{01}$ for inorganic arsenic (0.3 µg/kg bw/day).

Consumer	Age group (months)			
	4 to 12	12 to 18	18 to 24	24 to 60

[4] Total diet including the median water concentration

	Exposure (µg/kg bw/day)	MOE[a]	Exposure (µg/kg bw/day)	MOE[a]	Exposure (µg/kg bw/day)	MOE[a]	Exposure (µg/kg bw/day)	MOE[a]
Average	0.025[b]	12	0.025[b]	12	0.066	4.5	0.030	10
High	0.057[b]	5.3	0.077[b]	3.9	0.113	2.7	0.058	5.2

[a] The MOE is calculated by dividing the $BMDL_{01}$ of 0.3 µg/kg bw/day by the respective exposure
[b] Based on highest estimate for this age range

Conclusions

73. Arsenic occurs in the environment in a variety of forms as the result of natural and anthropogenic activity. It is generally accepted that inorganic arsenic compounds are more toxic than the organic arsenic compounds that are commonly found in fish, seafood and other marine organisms (arsenobetaine, arsenosugars, and arsenolipids). The inorganic arsenic present in the environment is present primarily as arsenite (As(III)) and arsenate (As(V)).

74. The general population is exposed to arsenic through food, drinking water, air, soil and dust. Food and water are the most important sources of oral exposure to arsenic. Infants and young children can also be exposed to arsenic via breast milk.

75. Absorption of arsenic compounds varies depending on the chemical species, its solubility, and the matrix in which it is present; soluble arsenicals in water are highly bioavailable. In humans, inorganic arsenic is rapidly cleared from the blood and widely distributed to almost all organs. Inorganic arsenic is metabolised by reduction of As(V) to As(III), followed by oxidative addition of methyl groups. Ingested inorganic arsenic is excreted as As(V) and As(III), and as the metabolites methylarsonous acid (MMA^{III}), methylarsonic acid (MMA^{V}), dimethylarsinous acid (DMA^{III}), and dimethylarsinic acid (DMA^{V}). Previously it has been assumed that methylation of inorganic arsenic was a detoxification route, it is no longer clear whether this is correct or not as, based on limited data, the simple organic arsenic species MMA^{III} and DMA^{III} appear to be more toxic than inorganic arsenic (As(V) and As(III)).

76. The main adverse effects associated with long-term ingestion of inorganic arsenic in humans are skin lesions, cancer, developmental toxicity, neurotoxicity, cardiovascular diseases, abnormal glucose metabolism, and diabetes. The International Agency for Research on Cancer (IARC) has reviewed arsenic on a number of occasions concluding that it is a group 1 carcinogen that causes cancer of the lung, urinary bladder, and skin.

77. Although few data are available regarding the toxicity of organic arsenic compounds such as arsenobetaine and the arsenosugars and arsenolipids in humans, exposure to such compounds is not generally considered to be of toxicological concern.

78. The European Food Safety Authority (EFSA), and the Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives (JECFA) have published risk assessments on exposure to arsenic in food. Based on the available epidemiological studies, the EFSA calculated a range of values for the 95% lower confidence limit of the benchmark dose ($BMDL_{01}$) of 0.3 to 8 µg/kg bw/day, this range was identified for cancers of the lung, skin and urinary bladder, as well as skin lesions. Using a different approach to modelling the dose-response data, and studies that had been published after the EFSA assessment, the JECFA calculated a BMDL of 3.0 µg/kg bw/day for a 0.5% increased incidence of lung cancer.

79. The Committee concluded that the lowest available $BMDL_{01}$, 0.3 µg/kg bw/day, should be used in the characterisation of the potential risks from exposure to arsenic in order to be conservative, focussing on inorganic arsenic since this is the form that it carcinogenic. A margin of exposure (MOE) approach would be used to compare the exposure estimates to the BMDL.

80. As toxicity would depend on total exposure to inorganic arsenic from dietary and non-dietary sources, aggregate exposures were estimated and assessed for each age group. These aggregate exposures were estimated by adding the average exposure estimates from all but one source to the high level exposure estimate for the remaining source. Exposures from water were taken into account by using estimates generated for the total diet including water, that had been based on both the highest median and 97.5^{th} percentile water concentrations available. Exposures from air were not incorporated as they were considered too low to have an impact on the MOEs.

81. Calculated MOEs for exclusively breastfed or formula-fed 0 to 4 month olds were generally greater than 1. Based on the aggregate exposures, the MOEs for infants aged 4 to 12 months ranged from 0.5 to 2.8, while the MOEs for infants and young children aged 1 to 5 years were all less than 0.5.

82. The Food Standards Agency (FSA) currently recommends that toddlers and young children (aged 1 to 4.5 years) should not be given rice drinks as a *substitute* for breast milk, infant formula or cows' milk due to the potential for rice drinks to contain high levels of arsenic, and because of this age group's proportionally higher milk consumption and lower bodyweights compared to other consumers. The Committee concludes that the current estimates of exposure to inorganic arsenic from rice drinks support the FSA's advice not to use rice drinks as a *substitute*, and that this advice should therefore remain in place. However, Members agreed that consumption of 50 mL of rice drink per day by those aged 1-5 years would not make an appreciable difference to total dietary exposure to inorganic arsenic, contributing less than 10%.

83. Due to the introduction of different maximum levels for inorganic arsenic in rice intended for the production of infant foods including infant rice cakes, and for inorganic arsenic in 'adult' rice cakes (i.e. not those intended for infants or young children), exposure assessments were performed to estimate the level of exposure to inorganic arsenic from the consumption of

infant and ‘adult’ rice cakes by those aged 0 to 5 years. The MOEs calculated based on these exposure estimates were all considerably greater than 1 and do not indicate a risk from consumption of these food products.

84. There are uncertainties in the assessment of risks to infants and young children from exposure to inorganic arsenic because, for some sources of exposure (e.g. breast milk and soil), it has been necessary to assume that all of the arsenic present in that source is inorganic. This has occurred for sources where inorganic arsenic has not been measured, and consistent information about the proportion of inorganic arsenic likely to be present in that source of exposure has not been available. This assumption could potentially result in over-estimation of the exposures to inorganic arsenic.

85. Overall, although the MOEs were low, exposures in the majority of exclusively breastfed infants aged 0 to 4 months were lower than for formula-fed UK infants aged 0 to 4 months. Total exposure to inorganic arsenic in infants and young children aged 4 to 12 months and 1 to 5 years generally generated low MOEs and could therefore pose a risk to health. It is therefore reiterated that exposures to inorganic arsenic should be kept ALARP.

Secretariat
March 2016

Abbreviations

ALARP – As low as reasonably practicable

As – Arsenic

As(III) – Arsenite

As (V) – Arsenate

BMDL – 95% lower confidence limit of the benchmark dose

bw – body weight

COT – Committee on Toxicity

DH – Department of Health

DMA^{III} – Dimethylarsinous acid

DMA^{V} – Dimethylarsinic acid

DNSIYC – Diet and Nutrition Survey of Infants and Young Children

DWI – Drinking Water Inspectorate

EA – Environment Agency

EC – European Commission

EFSA – European Food Safety Authority

EU – European Union

FAO – Food and Agriculture Organization

FSA – Food Standards Agency

g - grams

IARC – International Agency for Research on Cancer

incl. - including

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

ML – Maximum level

MMA^{III} – Methylarsonous acid

MMA^{V} – Methylarsonic acid

MOE – Margin of Exposure

n – number

NDNS – National Diet and Nutrition Survey

ng/m^3 – nanograms/cubic metre

NHS – National Health Service

SACN – Scientific Advisory Committee on Nutrition

SHS – Soil and Herbage Survey

TDS – Total Diet Study

UB – Upper bound

UK – United Kingdom

US EPA – United States Environmental Protection Agency

WHO – World Health Organization

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