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

Second 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 first draft statement on arsenic exposures in 0 to 5 year olds (TOX/2016/13) was presented to the COT in April 2016. At that meeting Members requested that the exposures to arsenic via soil be refined if possible, and that further detail be provided about potential exposures from private water supplies. The Committee also requested that the use of the lowest European Food Safety Authority (EFSA) $BMDL_{01}$ (0.3 µg/kg bw/day) rather than the Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives (JECFA) $BMDL_{0.5}$ (3.0 µg/kg bw/day) in the characterisation of potential risks be reconsidered with clear justification provided for whichever BMDL was decided upon.

3. Annex A contains a second draft statement that takes into account previous discussions including amendments to the formatting and presentation of exposure assessments.

4. As part of the refinement of the exposures to arsenic via soil, the data used in the soil exposure assessments has been replaced with data from the Department for Environment, Food and Rural Affairs (Defra) and the British Geological Survey (BGS). In short, in 2011 and 2013, the Defra published normal background concentrations (NBCs) for arsenic in soil in England and Wales (Defra, 2012 and 2013). An NBC is the 95^{th} percentile upper confidence interval of the available data; it is defined as a contaminant concentration that is seen as typical and widespread in topsoils (depth 0 – 15 cm). In order to establish meaningful NBCs, the available soil data were grouped in domains (e.g. principal, ironstone, and mineralisation) 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 BGS project to define the typical background concentrations for soil contaminants.

5. 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*., 2011 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 arsenic. Overall, for England and Wales, the area covered by the principal domains constitutes approximately 97% and 89% of the country respectively. The summary statistics reported for the principal domain in England were a median of 14 mg/kg and a 95^{th} percentile of 32 mg/kg (n = 41,509 samples). The statistics reported for the same domain in Wales were a median of 18 mg/kg and a 95^{th} percentile of 36 mg/kg (n = 1,270 samples). In line with the approach taken with the water concentration data, the higher of the medians and 95^{th} percentiles has been used to estimate the exposures to arsenic from soil.

6. In addition to the data for soil, the use of a single default soil ingestion value has been revised. The soil exposure assessment now starts at 6 months old and uses default soil ingestion values of 60 mg/day for 6 to 12 month olds and 100 mg/day for 1 to 5 year olds. These default values have been taken from a United States Environmental Protection Agency (US EPA) exposure factors handbook published in 2011 (US EPA, 2011a). The default relative bioavailability factor of 60% has been also removed from these assessments and bioavailability has instead been assumed to be 100% as this was the approach taken by the Defra when deriving screening levels for arsenic in soil (personal communication from PHE, April 2016).

7. Further information has been provided on private water supplies and the exposure assessments for air have been revised, using the more recent default ventilation rates available in the 2011 US EPA exposure factors handbook (US EPA, 2011b) (NB. this has not caused any significant changes in the exposure assessment and was done to be consistent with other papers).

8. After comparing the critical studies used by the EFSA (Ferreccio *et al*, 2000) and the JECFA (Chen *et al*, 2010) to derive their BMDLs, it has been decided that the JECFA $BMDL_{0.5}$ of 3.0 µg/kg bw/day should be used in the risk characterisation. This is because the JECFA's critical study was a well-conducted prospective cohort study with good case ascertainment, which provided more robust evidence than the case-control study used by the EFSA. In addition to this, the JECFA risk assessment (FAO/WHO, 2011) is more recent than the EFSA's (EFSA, 2009), and supported by more extensive documentation including more up to date epidemiological literature.

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

Secretariat
May 2016

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

Second 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[1], cardiovascular diseases[2], 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). There are a number of proposed mechanisms of carcinogenicity of inorganic arsenic, including oxidative damage, epigenetic effects and interference with DNA damage repair, but not direct reaction with DNA (FAO/WHO, 2011).

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

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

examination, nutrition, and stimulation. There is a need for more longitudinal 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 (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, 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). The lowest of these $BMDL_{01}$ values was from a case-control study of lung cancer cases in Chile based on 151 cases and 419 matched controls (Ferreccio *et al*. (2000). The COT noted that there were issues with control recruitment and this gave expected direction of bias such that there would be under-estimation of risks for highest exposures at >300 µg/L, under-estimation at 100-300 µg/L and over-estimation at 50-99 µg/L. General issues with the study design are that hospital-based ascertainment of cases may result in under-ascertainment and hospital-based controls may under-estimate odds ratios (as cases and controls are more similar than if using a cohort approach.

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 in the study of Chen *et al*. (2010), 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).

The COT noted that Chen *et al*. (2010) was a well-conducted prospective cohort study of farmers in north-east Taiwan, published after the EFSA assessment. There were 6888 participants followed for 11 years, with 178 lung cancer cases, most of whom drinking water from shallow wells with arsenic contamination of the water. The study was able to look at each of well water concentration, years duration of drinking well water and cumulative exposure. There were relatively few cases at lower levels of exposure (arsenic <100 µg/L water) and, while there was a dose response associations, risk estimates were more precise (statistically significant) at arsenic concentrations >300 µg/L water. Exclusion of those with pesticide exposure (potentially arsenic containing) did not change findings.

15. The COT noted that lung cancer provided the lowest BMDL values in both assessments and concluded that the JECFA $BMDL_{0.5}$ of 3.0 µg/kg bw/day identified for lung cancer should be used in the characterisation of the potential risks from exposure to arsenic. This is because the JECFA risk assessment was based on the more robust evidence provided by the Chen study, which was a well conducted prospective cohort study, with good case ascertainment. Also, the JECFA opinion was more recent and supported by more extensive documentation, including more up to date epidemiological literature, and provides full details of BMDL modelling. The focus of the risk characterisation would be 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 assessments 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 or IMS), 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 (DWI), 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.

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

28. In 2014 Local Authorities held records for approximately 38,700 private water supplies in England, ~14,400 in Wales, ~20,200 in Scotland and ~1,300 in Northern Ireland. Of the private supplies in England and Wales, 67% and 85% served single dwellings respectively. The DWI estimated that in England approximately 570,000 people lived or worked on premises that relied on a private water supply, this figure was ~80,000 for Wales (DWI, 2015a,b).

29. 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, with supplies that serve single dwellings exempt from monitoring unless requested by the owner. Where sampling of private supplies, especially those serving single dwellings, 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). Reports published by the DWI in 2014 indicated that for the period 2011 – 2014, of the 249 samples taken from private water supplies that served single dwellings in England, 5.6% exceeded the maximum limit for arsenic of 10 µg/L. In Wales, for the same period, 8.6% of the 35 samples tested from supplies serving single dwellings exceeded the maximum limit (DWI, 2015a, b).

30. A study by Ander *et al* (2016) reported concentrations of arsenic in samples taken from private water supplies serving single domestic dwellings in Cornwall. A total of 497 samples were tested, having been collected from 497 different properties across Cornwall during spring 2011 and spring 2013. This was a targeted survey that focussed on Cornwall as it is an area known to have high concentrations of arsenic and other elements in the surface environment, which also has a large number of private water supplies (approximately 3,800 in 2014) (Ander *et al*, 2016).

31. Ander *et al* reported a median arsenic concentration of 0.38 µg/L and a 95^{th} percentile concentration of 11.0 µg/L; the LOD was 0.02 µg/L and the minimum and maximum concentrations were <0.02 and 435 µg/L respectively. The authors also reported that 5% of the samples (n=27) exceeded the maximum limit of 10 µg/L for arsenic in water, 4 samples had concentrations above 100 µg/L (Ander *et al*, 2016).

32. Although the data from Ander *et al* (2016) provides useful insight into the potential concentrations of arsenic in private water supplies serving single domestic dwellings in the UK, it is not considered to be representative of such supplies as the survey was performed in an area known to have high concentrations of arsenic due to the underlying geology and historical anthropogenic activities such as smelting and mining.

Environmental

Dust and soil

33. 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).

34. Concentrations of arsenic in topsoils (0-15 cm) in England and Wales have been published by the Department for Environment, Food and Rural Affairs (Defra) and the British Geological Survey (BGS). The median and 95th percentile concentrations reported for England were 14 mg/kg and 32 mg/kg respectively (n = 41,509 samples) (Defra, 2012 and Ander *et al*., 2011). The median and 95th percentile reported for Wales were 18 mg/kg and 36 mg/kg respectively (n = 1,270 samples) (Defra, 2013 and Ander *et al*., 2013). These statistics represent the concentrations in topsoils in areas which do not contain significantly elevated levels of arsenic due to specific sources of contamination; these areas are known as the principal domains. Overall, for England and Wales, the area of land covered by the principal domains constitutes approximately 97% and 89% of the country respectively. The highest of the medians and 95th percentiles have been used to estimate the exposures to arsenic from soil.

35. 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.

36. As the bioavailability of arsenic in soil varies with soil composition, for the current exposure assessments, it has been assumed that the relative bioavailability is 100%.

Air

37. 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).

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

39. 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 (Defra, 2015). Due to the lack of specification data, it is assumed that all of the arsenic present in air is inorganic.

Exposure assessment

40. 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.

41. Thorough exposure assessments have been performed for the dietary sources of exposure to arsenic. The assessments for the non-dietary sources of exposure (i.e. soil and air) have been included to give a more holistic view of exposures, but are not as thorough as they are not the main focus of this statement.

Table 3. Average bodyweights used in the estimation of arsenic exposures

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

[a] DH, 1994
[b] DH, 2013
[c] Bates *et al.*, 2014

Infants (0 to 12 months)

Breast milk

42. 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

* Values rounded to 2 significant figures (SF)

43. 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.

44. Mean exposures to inorganic arsenic for 4 to 18 month olds were 0.008 to 0.030 µg/kg bw/day, and 97.5^{th} 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 97.5^{th} 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
97.5^{th} percentile	0.051	0.053	0.038	0.025	0.017

* Values rounded to 2 SF

Infant formulae and complementary foods

45. 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 for 0 to 4 month olds 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).

46. 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 97.5^{th} percentile concentrations for arsenic in water reported in Table 2, this results in exposures of 0.064 to 0.280 µg/kg bw/day in average consumers, and of 0.091 to 0.420 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	0.091-0.130
Dry Powder + 97.5th percentile water of 2.1 µg/L [b]	0.250-0.280	0.380-0.420

* Values rounded to 2 SF
[a] Exposure does not include the contribution from water
[b] Calculated assuming reconstituted formula comprises 85% water

47. 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 0.180 µg/kg bw/day, and 97.5th percentile exposures were 0.230 to 0.450 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 0.200 µg/kg bw/day, while the 97.5th percentile exposures including water were 0.230 to 0.540 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	0.210-0.260	0.061-0.089	0.200-0.290	0.057-0.082	0.220-0.310
Other foods	0.009-0.011	0.057-0.063	0.058-0.064	0.280-0.290	0.086-0.096	0.330-0.350
Total (excl. water)	0.054-0.077	0.230-0.280	0.120-0.160	0.350-0.410	0.140-0.180	0.400-0.450

Total (incl. median water of 0.4 µg/L)	0.056-0.079	0.230-0.290	0.130-0.160	0.370-0.420	0.150-0.180	0.410-0.470
Total (incl. 97.5th percentile water of 2.1 µg/L)	0.064-0.087	0.260-0.310	0.140-0.180	0.420-0.480	0.170-0.200	0.480-0.540

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

Children aged 12 to 18 months

48. 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.

49. 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

50. 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 0.140 to 0.170 and 0.420 to 0.470 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 0.140 to 0.200 µg/kg bw/day, while the 97.5th percentile exposures including water were 0.440 to 0.560 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	0.160-0.220	0.019-0.026	0.089-0.130
Other Foods	0.110-0.120	0.370-0.390	0.130-0.140	0.390-0.410
Total (excl. water)	0.140-0.170	0.430-0.470	0.150-0.170	0.420-0.430
Total (incl. median water of 0.4 µg/L)	0.140-0.170	0.450-0.480	0.150-0.170	0.440-0.450
Total (incl. 97.5th percentile water of 2.1 µg/L)	0.170-0.190	0.520-0.560	0.180-0.200	0.510-0.550

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

Exposure estimates based on the TDS

51. 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.

52. 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 0.130 to 0.700 and 0.320 to 1.200 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 0.130 to 0.690 and 0.320 to 1.200 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)	0.130-0.660	0.320-1.200	0.140-0.700	0.330-1.200
TDS (incl. median water of 0.4 µg/L)	0.130-0.630	0.320-1.200	0.140-0.670	0.330-1.100
TDS (incl. 97.5th percentile water of 2.1 µg/L)	0.150-0.650	0.350-1.200	0.160-0.690	0.350-1.100

* Values rounded to 2 SF

53. 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

54. 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).

55. 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 0.120 to 0.790 and 0.260 to 1.200 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 0.130 to 0.780 and 0.260 to 1.200 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)	0.140-0.790	0.290-1.200	0.120-0.650	0.260-1.000

TDS (incl. median water of 0.4 µg/L)	0.150-0.760	0.290-1.200	0.130-0.620	0.260-0.990
TDS (incl. 97.5th percentile water of 2.1 µg/L)	0.170-0.780	0.320-1.200	0.140-0.640	0.280-1.000

* Values rounded to 2 SF

56. 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

57. 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.

58. For infants and young children aged 1 to 5 years, mean and 97.5th percentile exposures range from 0.220 to 0.600 and 0.600 to 1.500 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, 1.500 µg/kg bw/day) is more than double the upper bound mean exposure values 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]	0.360	0.340	0.320	0.220
	High[b]	0.910	0.780	0.860	0.600

97.5th percentile (20 µg/L)	Average[a]	0.600	0.570	0.530	0.360
	High[b]	1.500	1.300	1.400	1.000

* Values rounded to 2 SF
[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

59. 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

60. 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).

61. 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 0.110 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.

62. 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 0.120 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 0.110 µg/kg bw/day, respectively. The highest value of the 97.5[th] percentile range of exposures from infant rice cakes (for >12 to <15 month olds, 0.120 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	**Age group (months)**

and Exposure	>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	1.40	2.00	2.50	2.60	2.10	3.20
97.5th percentile consumption (g/day)	0.47	4.00	6.60	8.00	6.00	5.50	6.40
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	0.110	0.120	0.078	0.070	0.071

* Values rounded to 2 SF

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	1.80	2.40	2.70	2.80	7.20	4.60
97.5th percentile consumption (g/day)	n/a	3.30	5.30	8.80	7.80	12.00	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	1.20	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	0.110	0.058

* Values rounded to 2 SF

Soil/dust

63. Potential exposures of UK infants aged 6 to 12 months and young children aged 1 to 5 years to arsenic in soil were calculated assuming ingestion of 60 or 100 mg/day respectively (US EPA, 2011a). 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 18 and 36 mg/kg respectively were used in these exposure estimations (paragraph 34) (Table 14).

64. 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 6 months to 5 years.

Arsenic 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**
18 (Median)	0.074	0.068	0.102	0.096	0.090	0.067
36 (97.5th percentile)	0.150	0.140	0.200	0.190	0.180	0.130

* Values rounded to 2 SF

Air

65. Potential exposures of UK infants aged 0 to 12 months and young children aged 1 to 5 years to arsenic in air were estimated using the body weights shown in Table 3, and by assuming the mean ventilation rates presented in Table 15; these rates have been derived from the US EPA exposure factors handbook (US EPA, 2011b). The resulting exposures are presented in Table 16.

Table 15. Mean ventilation rates used in the estimation of arsenic exposures from air (derived from US EPA, 2011b)

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

66. 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 39). 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 16. 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 4	4 to 6	6 to 9	9 to 12	12 to 15	15 to 18	18 to 24	24 to 60
0.12 (lowest median value)	0.00007	0.00006	0.00007	0.00007	0.00009	0.00009	0.00008	0.00008
1.09 (highest median value)	0.00065	0.00057	0.00068	0.00061	0.00082	0.00078	0.00073	0.00068
0.12 (lowest 99th percentile value)	0.00007	0.00006	0.00007	0.00007	0.00009	0.00009	0.00008	0.00008
4.92 (highest 99th percentile value)	0.00292	0.00259	0.00305	0.00277	0.00371	0.00351	0.00328	0.00309

Risk Characterisation

67. 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 $BMDL_{0.5}$ value of 3.0 µg/kg bw/day, to estimated exposures from dietary and non-dietary sources. The Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the

Environment (COC) has advised that for genotoxic carcinogenogens, an MOE of less than 10,000 based on a BMDL for a 10% increased incidence of tumours in an animal carcinogenicity may be a concern. However, there is no precedent for interpretation of MOEs based on epidemiological studies of human cancer, which frequently relate to a lower cancer incidence. The COC has advised that such MOEs should be considered on a case-by-case basis (COC, 2012). In interpreting MOEs calculated for arsenic, it should be noted that the BMDL is for a 0.5% increased cancer risk in a human epidemiological study. Furthermore, arsenic does not appear to exhibit direct genotoxicity.

68. Table 17 summarises the estimated exposures to inorganic arsenic from the diet of infants and young children aged 0 to 5 years. Based on dietary exposures alone, the MOEs for 0 to 4 month olds that are either exclusively breastfed or exclusively fed ready-to-feed infant formula range from 40 to 100 at average and high level exposure. The MOEs for 0 to 4 month olds that are exclusively fed with reconstituted dry infant formula are between 20 and 50 for that reconstituted with water with the median concentration of arsenic, but are equal to or less than 10 for that reconstituted using water with the 97.5th percentile arsenic concentration.

69. Dietary exposures estimated using the Infant Metals Survey (IMS) generate MOEs from 20 to 50 for average consumers aged 4 to 18 months when water is taken into account at both the median and 97.5th percentile arsenic concentrations. Based on the IMS, the MOEs are equal to or less than 10 for high level consumers in the same age group.

70. Using the TDS to estimate dietary exposures for infants aged 12 to 18 months, and young children aged 18 months to 5 years, generates MOEs for median and 97.5th percentile arsenic concentrations in water that are between 4 and 20 for average consumers, and between 3 and 10 for high level consumers.

71. Overall, the ranges of MOEs that have been derived based on the median and 97.5th percentile concentrations of arsenic in water for each age group are generally the same; this demonstrates that the arsenic content of water has a negligible impact on total dietary exposure to inorganic arsenic of UK infants and young children.

Table 17. Summary of estimated dietary exposures to inorganic arsenic, and corresponding MOEs compared to the $BMDL_{0.5}$ of 3.0 µg/kg bw/day

		Exclusive breast milk	Exclusive infant formula			Total diet including water with median arsenic level (0.4 µg/L)					Total diet including water with 97.5th percentile arsenic level (2.1 µg/L)				
			Ready to feed	Dry powder reconstituted[c] with water with arsenic at Median (0.4 µg/L)	Dry powder reconstituted[c] with water with arsenic at 97.5th percentile (2.1 µg/L)										
Survey/Consumption data		N/A	IMS	IMS	IMS	IMS/ DNSIYC	IMS/ DNSIYC	TDS/ DNSIYC	TDS/ NDNS	TDS/ NDNS	IMS/ DNSIYC	IMS/ DNSIYC	TDS/ DNSIYC	TDS/ NDNS	TDS/ NDNS
Age (months)		0 to 4	0 to 4	0 to 4	0 to 4	4 to 12	12 to 18	12 to 18	18 to 24	24 to 60	4 to 12	12 to 18	12 to 18	18 to 24	24 to 60
Estimated dietary exposures (µg/kg bw/day)[a]	Average consumer	0.045	0.000-0.027	0.064-0.087	0.250-0.280	0.056-0.180	0.140-0.170	0.130-0.670	0.150-0.760	0.130-0.620	0.064-0.200	0.170-0.200	0.150-0.690	0.170-0.780	0.140-0.640
	High level consumer	0.067	0.000-0.041	0.091-0.130	0.380-0.420	0.230-0.470	0.440-0.480	0.320-1.200	0.290-1.200	0.260-0.990	0.260-0.540	0.510-0.560	0.350-1.200	0.320-1.200	0.280-1.000
MOE[b]	Average consumer	70	100	30-50	10	20-50	20	4-20	4-20	5-20	20-50	20	4-20	4-20	5-20
	High level consumer	40	70	20-30	7-8	6-10	6-7	3-9	3-10	3-10	6-10	5-6	3-9	3-9	3-10

[a] Values are rounded to 2SF and are the lowest lower bound and highest upper bound estimates for the age range
[b] The MOE is calculated by dividing the $BMDL_{0.5}$ of 3.0 µg/kg bw/day by the respective dietary exposure and rounding to 1 SF. The range relates to the upper bound to lower bound estimates of exposure, only one MOE is shown when the estimated dietary exposures generated the same value.
[c] Based on the assumption that reconstituted infant formula comprises 85% water

72. 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 18 to 20 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.

73. 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 dietary exposures from lower bound to upper bound were available, both estimates have been used.

74. 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. These exposures have been presented in table 17 and discussed in paragraph 68.

75. Table 18 shows the aggregate exposure estimates and MOEs for infants aged 4 to 6 months. The aggregate exposures for this age group are based on the exposure estimates for breast milk and the total diet including water. Estimates from exposures via soil were not included as infants <6 months are less able to move around and come into contact with soil. For 4 to 6 month olds, most of the aggregate exposures result in MOEs that are above 20. 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 marginally below 10.

Table 18. Aggregate exposures to inorganic arsenic for infants aged 4 to 6 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 $BMDL_{0.5}$ of 3.0 µg/kg bw/day

Exposure combination[a]			**Age (months)**	
			4 to 6	
			Exposure (µg/kg bw/day)	**MOE**[b]
Mean breast milk	Mean total diet incl. As in water at	Median conc. (0.4 µg/L)	0.090-0.110	30-40
		97.5th percentile conc. (2.1 µg/L)	0.100-0.120	30
97.5th percentile breast milk	Mean total diet incl. As in water at	Median conc. (0.4 µg/L)	0.110-0.130	20-30
		97.5th percentile conc. (2.1 µg/L)	0.120-0.140	20-30

Mean breast milk	**97.5th percentile total diet** incl. As in water at	Median conc. (0.4 µg/L)	0.270-0.320	9-10
		97.5th percentile conc. (2.1 µg/L)	0.290-0.340	9-10

* Exposures have been rounded to 2 SF, MOEs have been rounded to 1 SF
[a] Breast milk from Table 4, and total diet including water from Table 7
[b] The MOE is calculated by dividing the $BMDL_{0.5}$ of 3.0 µg/kg bw/day by the respective exposure combination. The range relates to the upper bound to lower bound estimates of exposure, only one MOE is shown when the estimated aggregate exposures generated the same value

76. Table 19 shows the aggregate exposure estimates and MOEs for infants aged 6 to 9, 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 6 to 18 month olds, all of the aggregate exposures result in MOEs that are equal to or less than 10.

Table 19. Aggregate exposures to inorganic arsenic for infants aged 6 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 $BMDL_{0.5}$ of 3.0 µg/kg bw/day

Exposure combination[a]			**Age (months)**							
			6 to 9		**9 to 12**		**12 to 15**		**15 to 18**	
			Exposure (µg/kg bw/day)	**MOE[b]**	**Exposure (µg/kg bw/day)**	**MOE[b]**	**Exposure (µg/kg bw/day)**	**MOE[b]**	**Exposure (µg/kg bw/day)**	**MOE[b]**
Mean breast milk plus median soil[c]	Mean total diet incl. As in water at	Median conc. (0.4 µg/L)	0.220-0.260[e]	10	0.230-0.260[e]	10	0.240-0.750[f]	4-10	0.250-0.780[f]	4-10
		97.5[th] percentile conc. (2.1 µg/L)	0.240-0.270[e]	10	0.250-0.280[e]	10	0.260-0.760[f]	4-10	0.270-0.800[f]	4-10
97.5[th] percentile breast milk plus median soil[c]	Mean total diet incl. As in water at	Median conc. (0.4 µg/L)	0.250-0.290[e]	10	0.260-0.290[e]	10	0.260-0.760[f]	4-10	0.260-0.790[f]	4-10
		97.5[th] percentile conc. (2.1 µg/L)	0.270-0.300[e]	10	0.280-0.310[e]	10	0.270-0.780[f]	4-10	0.270-0.810[f]	4-10
Mean breast milk plus median soil[c]	**97.5[th] percentile total diet** incl. As in water at	Median conc. (0.4 µg/L)	0.460-0.520[e]	6-7	0.490-0.550[e]	5-6	0.440-1.300[f]	2-7	0.440-1.200[f]	2-7
		97.5[th] percentile conc. (2.1 µg/L)	0.520-0.580[e]	5-6	0.560-0.620[e]	5	0.460-1.300[f]	2-7	0.450-1.200[f]	2-7
Mean breast milk plus **97.5[th] percentile soil**[d]	Mean total diet incl. As in water at	Median conc. (0.4 µg/L)	0.300-0.330[e]	9-10	0.300-0.330[e]	9-10	0.340-0.850[f]	4-9	0.340-0.870[f]	3-9
		97.5[th] percentile conc. (2.1 µg/L)	0.310-0.350[e]	9-10	0.320-0.350[e]	9	0.260-0.760[f]	4-10	0.360-0.890[f]	3-8

* Exposures have been rounded to 2 SF, MOEs have been rounded to 1 SF
[a] Breast milk from Table 5, total diet including water from Tables 7 and 9, and soil from Table 14
[b] The MOE is calculated by dividing the $BMDL_{0.5}$ of 3.0 µg/kg bw/day by the respective exposure combination. The range relates to the upper bound to lower bound estimates of exposure, only one MOE is shown when the estimated aggregate exposures generated the same value
[c] Based on ingestion of soil with the median concentration of inorganic arsenic (18 mg/kg)
[d] Based on ingestion of soil with the 97.5[th] percentile concentration of inorganic arsenic (36 mg/kg)
[e] Based on the results of the IMS
[f] Based on the results of the TDS

77. Table 20 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, the aggregate exposures generally result in MOEs that are equal to or less than 10.

Table 20. 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 $BMDL_{0.5}$ of 3.0 µg/kg bw/day

Exposure combination[a]			**Age (months)**			
			18 to 24		**24 to 60**	
			Exposure (µg/kg bw/day)	**MOE**[b]	**Exposure (µg/kg bw/day)**	**MOE**[b]
Median soil[c]	Mean total diet incl. As in water at	Median conc. (0.4 µg/L)	0.240-0.850	4-10	0.190-0.690	4-20
		97.5th percentile conc. (2.1 µg/L)	0.260-0.870	3-10	0.210-0.710	4-10
Median soil[c]	**97.5th percentile total diet** incl. As in water at	Median conc. (0.4 µg/L)	0.380-1.300	2-8	0.330-1.100	3-9
		97.5th percentile conc. (2.1 µg/L)	0.410-1.300	2-7	0.350-1.100	3-9
97.5th percentile soil[d]	Mean total diet incl. As in water at	Median conc. (0.4 µg/L)	0.330-0.940	3-9	0.260-0.760	4-10
		97.5th percentile conc. (2.1 µg/L)	0.350-0.960	3-9	0.280-0.780	4-10

* Exposures have been rounded to 2 SF, MOEs have been rounded to 1 SF
[a] Total diet including water from Table 10, and soil from Table 14
[b] The MOE is calculated by dividing the $BMDL_{0.5}$ of 3.0 µg/kg bw/day by the respective exposure combination The range relates to the upper bound to lower bound estimates of exposure, only one MOE is shown when the estimated aggregate exposures generated the same value
[c] Based on ingestion of soil with the median concentration of inorganic arsenic (18 mg/kg)
[d] Based on ingestion of soil with the 97.5th percentile concentration of inorganic arsenic (36 mg/kg)

Risk characterisation for specific food products

Rice drinks

78. Table 21 summarises the MOEs for the estimated exposures for 1 to 5 year olds calculated for rice drinks using the mean concentration of inorganic arsenic (12 µg/L), and assuming complete replacement of cows' milk with rice drinks. The MOEs for average consumers from all age groups

are equal to or marginally less than 10, while the MOEs for all high level consumers are equal to or less than 5 from this source alone.

Table 21. Range of possible exposures to inorganic arsenic from rice drinks with a mean concentration of inorganic arsenic of 12 µg/L, and the corresponding MOEs when they are compared to the $BMDL_{0.5}$ of 3.0 µg/kg bw/day

Consumer	Age group (months)							
	12 to 15		15 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	0.360	8	0.340	9	0.320	10	0.220	10
High	0.910	3	0.770	4	0.860	3	0.600	5

* Exposures have been rounded to 2 SF, MOEs have been rounded to 1 SF
[a] The MOE is calculated by dividing the $BMDL_{0.5}$ of 3.0 µg/kg bw/day by the respective exposure

79. 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 59).

Rice cakes

80. Tables 22 and 23 summarise the MOEs for the estimated exposures from the consumption of infant and 'adult' rice cakes by infants and young children aged 4 months to 5 years. All of the MOEs from rice cake consumption are greater than 20. The MOEs for infants aged 4 to 18 months from infant rice cake consumption are generally 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 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.

81. 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 97.5^{th} percentile exposures for infants < 12 month olds (0.110 µg/kg bw/day from consumption of infant rice cakes) to the highest mean exposure from the total

diet[3] for the same age group (0.180 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 (0.120 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 (0.670 µg/kg bw/day) would result in an increase of ~15% above the mean total diet exposure.

Table 22. Range of possible exposures to inorganic arsenic from infant rice cakes, and the corresponding MOEs when they are compared to the $BMDL_{0.5}$ of 3.0 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]	100	0.035[b]	90	0.026	100	0.029	100
High	0.110[b]	30	0.120[b]	20	0.070	40	0.071	40

* Exposures have been rounded to 2 SF, MOEs have been rounded to 1 SF
[a] The MOE is calculated by dividing the $BMDL_{0.5}$ of 3.0 µg/kg bw/day by the respective exposure
[b] Based on highest estimate for this age range

Table 23. Range of possible exposures to inorganic arsenic from 'adult' rice cakes, and the corresponding MOEs when they are compared to the $BMDL_{0.5}$ of 3.0 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	0.025[b]	100	0.025[b]	100	0.066	50	0.030	100
High	0.057[b]	50	0.077[b]	40	0.110	30	0.058	50

* Exposures have been rounded to 2 SF, MOEs have been rounded to 1 SF
[a] The MOE is calculated by dividing the $BMDL_{0.5}$ of 3.0 µg/kg bw/day by the respective exposure
[b] Based on highest estimate for this age range

Conclusions

82. Arsenic occurs in the environment in a variety of forms as the result of natural and anthropogenic activity. It is generally accepted that inorganic

[3] Total diet including the median water concentration

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)).

83. 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.

84. 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)).

85. 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 in humans. It does not appear to be directly genotoxic.

86. 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.

87. 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.

88. The Committee concluded that the JECFA $BMDL_{0.5}$ of 3.0 µg/kg bw/day identified for lung cancer should be used in the characterisation of the

potential risks from exposure to arsenic. This was because the JECFA risk assessment was based on more robust and recent evidence than that available to EFSA. The focus of the risk characterisation would be on inorganic arsenic since this is the form that is carcinogenic. A margin of exposure (MOE) approach would be used to compare the exposure estimates to the BMDL.

89. 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, which had been based on both the highest median and 97.5th percentile water concentrations available. Exposures from air were not incorporated as they were considered too low to have an impact on the MOEs.

90. Calculated MOEs for exclusively breastfed or formula-fed 0 to 4 month olds were generally greater than 10. Based on the aggregate exposures, the MOEs for infants aged 4 to 12 months ranged from 5 up to 40, while the MOEs for infants and young children aged 1 to 5 years were generally less than 10.

91. 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%.

92. 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 ranged from 20 to 100 and do not indicate an increased risk from consumption of these food products.

93. 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. Such assumptions could potentially result in over-estimation of the exposures to inorganic arsenic.

94. Overall, the MOEs in exclusively breastfed infants aged 0 to 4 months were higher 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 MOEs of less than 10 and could therefore pose a risk to health. It is therefore reiterated that exposures to inorganic arsenic should be kept ALARP.

Secretariat
May 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

Defra – Department for Environment, Food and Rural Affairs

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

IMS – Infant metals survey

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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