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

Statement on the potential risks from lead in the infant diet

Background

1. The Scientific Advisory Committee on Nutrition (SACN) is undertaking a review of scientific evidence that bears on the Government's dietary recommendations for infants and young children. The review will identify new evidence that has emerged since the Government's current 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, but will be considered in two stages, focussing first on infants aged 0 – 12 months, and then on advice for children aged 1 to 5 years. SACN is examining the nutritional basis of the advice, and has asked that evidence on possible adverse effects of diet should be considered by other advisory committees with relevant expertise. SACN asked COT to review the risks of toxicity from chemicals in the infant diet.

2. This statement gives an overview of the potential risks from lead in the infant diet. None of Government's current dietary recommendations for infants and young children relates to lead.

3. The general population is exposed to lead through food, drinking water, air, soil and dust. Food and water are the major sources of exposure to lead, although in infants and small children, ingestion of soil and dust can also contribute importantly. Lead can be transferred to the infant from the mother in breast milk. (EFSA, 2010).

4. Recently both the European Food Safety Authority (EFSA) and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) published evaluations of lead, which concluded that a provisional tolerable weekly intake (PTWI) of 25 µg/kg bodyweight (bw) previously established by JECFA could no longer be considered protective for health. In making their assessments, EFSA (EFSA, 2010) and JECFA (FAO/WHO, 2011) focussed on the extensive data that were available on adverse effects in humans, thus avoiding uncertainties in extrapolation from animal studies. They calculated benchmark doses (BMDs) and their lower 95% confidence limits (BMDLs) for the effects of lead most likely to be relevant to dietary exposure in different subgroups of the general population.

5. The EFSA concluded that even low exposures to lead in pregnant women, infants and children can adversely affect neurodevelopment (EFSA, 2010). The JECFA reached a similar conclusion, and stressed that their assessment was based on dietary exposure (mainly from food) and that other sources of exposure to lead

also needed to be considered (FAO/WHO, 2011). The conclusions reached by EFSA and JECFA accord with a view previously expressed by the COT[1] that it was not possible to identify a threshold of exposure below which there was no association between lead and decrements in intelligence quotient (IQ).

6. The current statement draws on the EFSA Opinion (EFSA, 2010) and the JECFA evaluation (FAO/WHO, 2011). In addition, a literature review (Annex 1) was conducted to identify any further relevant papers that were not considered in those publications. Data on concentrations of lead in water were provided by the Drinking Water Inspectorate (DWI) (for England and Wales), the Scottish Government and Northern Ireland Water. Measured concentrations of lead in soil and air were obtained from the Department for Environment, Food and Rural Affairs (Defra), and levels of lead in infant formulae and complementary foods were provided by the Food Standards Agency (FSA).

Absorption, distribution and excretion

Absorption

Gastrointestinal absorption

7. The principal site for absorption of lead from the gastrointestinal tract is the proximal duodenum, where the pH is 6 to 6.5. Absorption can occur through both passive and facilitated processes (US EPA, 2009). Lead has an ionic size similar to that of calcium, and it competes with calcium for binding proteins that are involved in its absorption. Other mechanisms of lead uptake may include transport through calcium channels and calcium pumps such as calcium ATPase (Bridges and Zalups, 2005). The efficiency of calcium uptake in the gastrointestinal tract is higher in young children and nursing mothers than in other population groups (Heath *et al*., 2003), and this may explain why they appear also to take up lead more readily (see below), especially if there is a depletion of dietary calcium. Lead may also be transported by divalent metal transporter 1 (DMT1), perhaps because Pb^{2+} mimics Fe^{2+}, and thereby gains access to the intracellular compartment of cells at the site of this transporter (Bridges and Zalups, 2005).

8. Lead absorption has been measured in a number of studies, and in adult humans is approximately 10% of the ingested dose (Rabinowitz *et al*., 1976). Lead absorption from the gastrointestinal tract appears to be higher in infants and children than in adults, with an average lead absorption in infants of about 42% of intake (Ziegler *et al.*, 1978). This is supported by animal studies which indicate that gastrointestinal absorption rates for lead are greater in the very young than at older ages (Forbes *et al*., 1972; McMichael *et al*., 1986).

[1] http://cot.food.gov.uk/pdfs/cotstatementtds200808.pdf

Modulation of absorption

9. Lead species, particle size and pH conditions importantly influence the bioavailability of lead (Heath *et al*., 2003). Lead is more soluble in acidic media, and increasing amounts are precipitated as pH increases (Barton and Conrad, 1981).

10. Humans in a fasting state absorb much larger fractions of lead than people who have recently eaten, and the presence of food in the gastrointestinal tract reduces the absorption of water-soluble lead (Rabinowitz *et al.*, 1980; FAO/WHO, 2011). Thus, for example, in a study by Liu *et al*. (2011), eating breakfast regularly was significantly associated with lower blood lead levels. (Liu *et al.*, 2011)

11. A number of studies have investigated the effects of nutrients on the bioavailability and absorption of lead. Inadequate intakes of calcium, iron and zinc have been associated with higher absorption of lead (Ahamed *et al.*, 2007; Rico *et al.*, 2006; Wang *et al.,* 2012; Wu *et al.*, 2011), and deficiency of magnesium has been linked with higher blood lead levels (Wu *et al*., 2011). However, supplementation with these nutrients did not necessarily lead to a reduction in the amount of lead absorbed (Rico *et al.*, 2006). Increasing the levels of fat in the diet has also been shown to increase blood lead concentrations in humans (Gallichio *et al.*, 2002; Arora *et al*., 2008).

Distribution and excretion

12. Several models have been constructed to simulate the uptake, distribution and excretion of lead, the most widely used being the Integrated Exposure Uptake Biokinetic (IEUBK) model for lead in children (US EPA, 1994; White *et al.*, 1998). The IEUBK model was developed to estimate blood lead levels, and generates graphical displays of modelled probability distributions for blood lead concentrations in relation to specified exposures. It quantitatively simulates relevant physiological processes, using age-specific biokinetic parameters (Figure 1).

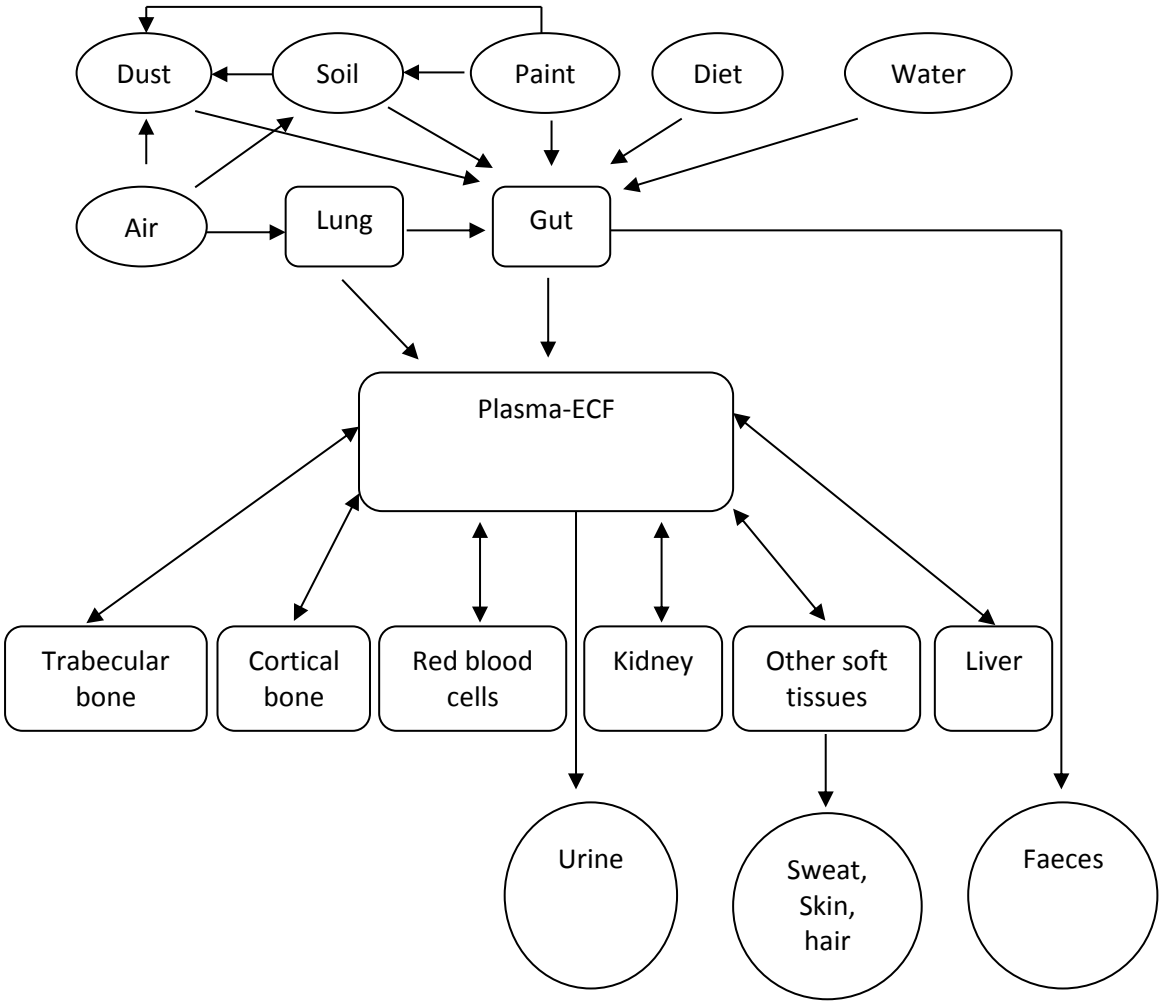

Figure 1. Conceptual diagram of the movement of lead into and through the human body. The oval shapes depict environmental media and pathways of uptake. The rectangular boxes represent the biokinetic compartments of the IEUBK model. The large rectangle is the blood plasma compartment central to the distribution of lead in the body. The circles indicate pathways of elimination. (Taken from White *et al.*, 1998). ECF, extracellular fluid.

13. Modelling exposures of infants from lead in air requires values for the concentration of lead in the air, the ventilation rate (taken as 2-3 m^3/day), indoor/outdoor activity patterns (an assumption of 1-2 hours/day outdoors) and lung absorption (the default value is 32%). Lead exposures from food, drinking water and soil/dust are calculated from intake values and the bioavailability of the source (assumed to be 50% for food and water, and 30% for soil and dust). The IEUBK model assumes that all the lead in the child's body can be assigned to one of seven kinetically homogenous compartments (plasma and extra-vascular or extra-cellular fluids; red blood cells; kidney; liver; other soft tissues; trabecular bone; and cortical bone) and that transfer between compartments occurs through normal physiological processes. (US EPA, 1994a).

14. The biokinetic component of the model calculates the age-dependent quantities of lead in each of the body compartments, based on uptake rates. The

compartmental lead transfer times, blood to plasma-ECF lead mass ratio, tissue to blood lead concentration ratios, fluid volumes and organ weights, compartmental lead masses and blood lead concentration at birth are all considered, and the concentration of lead in the blood is calculated. Urinary, faecal, and soft tissue elimination is also taken into account. (US EPA, 1994b).

15. Rabinowitz, (1976) determined that the mean half-life of lead is about 35 days in blood, approximately 40 days in soft tissue, and much longer in skeletal tissues (Rabinowitz *et al.*, 1976). There is constant low-level interchange of lead between bone and soft tissues (Hernandez-Avila et al., 1998)

16. The concentration of lead in bone increases with age, at rates dependent on the skeletal site and lead exposure (Wittmers *et al.*, 1988). Lead accumulates predominantly in trabecular bone during active growth (childhood) and in both cortical and trabecular bone during adult life (Aufderheide and Wittmers, 1992). Cortical and trabecular bone can accumulate large quantities of lead – at least 60% of the total body burden in children, and over 90% in adults with long exposure histories (White *et al.*, 1998).

17. Maternal bone is mobilised during pregnancy and lactation to meet the demands of fetal mineralisation, and this releases the lead that it contains (Sowers *et al.*, 2000; Tellez-Rojo *et al.*, 2002).

18. Lead in blood is mainly located in the red blood cells (96 to 99%), and most is bound to δ-aminolevulinic acid dehydratase (ALAD). ALAD's lead-binding capacity is approximately 850 µg/L in erythrocytes, corresponding to approximately 400 µg/L in whole blood. Blood lead displays a nonlinear relationship with plasma lead, as would be expected from ALAD's limited binding capacity. (Bergdahl *et al.*, 1998). Lead in the plasma binds with proteins such as albumin and α-globulin (Fleming *et al.*, 1999).

19. The level of lead in the blood is an indicator of recent environmental exposure (approximately the past 30 days). (WHO, 2000). Lead in bone is considered a biomarker of long-term exposure. (ATSDR, 2007).

Hazard identification and characterisation

20. The toxicity of lead differs according to whether it is in organic or inorganic form. In the past, organic lead compounds were used as additives in petrol. However, this use was phased out progressively from the 1970s until by 1998 leaded fuel was unavailable, other than for a few minor specialist uses. Moreover, although the lead added to fuel was in the form of the organometallic compounds, tetramethyl lead and tetraethyl lead, tailpipe emissions were in the form of fine particles of inorganic halide salts (Biggins and Harrison, 1978; 1979). Uncombusted organic lead compounds represented only a small proportion of the emissions, and an even smaller proportion of the environmental burden (Hewitt and Harrison, 1987). Hence the dominant environmental exposure has always been to inorganic lead. This review of toxicity therefore focuses specifically on inorganic lead.

Toxicity in experimental animals/models

21. The acute toxicity of lead salts is low in experimental animals; oral LD_{50} values for lead salts have been reported to be greater than 2,000 mg/kg bw. Repeated dose studies provide evidence of neurotoxicity, neurodevelopmental toxicity, cardiovascular effects and nephrotoxicity. (EFSA, 2010). These findings support the plausibility of observations in epidemiological studies, but are not described in detail here as the available human data are considered more influential for risk assessment.

22. At high doses, various water-soluble and insoluble lead compounds have been shown to induce tumours at different sites (adrenal gland, testes, prostate, lung, pituitary, mammary gland, brain and kidney) in rodents. As lead is not a direct acting genotoxin and the doses that induced tumours in the rodent studies were much higher than human intakes, EFSA concluded that exposure to lead through food is unlikely to represent a significant cancer risk (EFSA, 2010). Inorganic lead also has effects on reproduction, the immune system, the liver, and the haematological system. These effects are apparent only at higher exposures than affect blood pressure, the kidneys and the nervous system, and therefore are not considered further in this statement.

Observations in humans

23. Colic is a characteristic early symptom of acute lead poisoning following high exposures – for example, in the workplace. Other symptoms include constipation, nausea, vomiting and anorexia. High acute exposures can also cause encephalopathy, both in children and in adults. (ATSDR, 2007). However, because lead accumulates in the body, adverse effects can occur from long-term dietary exposures at lower levels, insufficient to cause acute toxicity.

Neurotoxicity in adults

24. EFSA (2010) noted that in a study by Murata *et al.* (2009), $BMDL_{05}$ values, expressed as blood lead levels, were derived for two maximal motor nerve conduction velocity (MCV) parameters – median MCV (two studies) and posterior tibial MCV (one study). These were between 75 and 84 µg/L, with a mean (weighted by sample size) of 80 µg/L which was based on data from a total of 150 occupationally exposed adults. However these data were not used for the current risk assessment since effects have been observed at lower levels in neurodevelopmental studies in children. (EFSA, 2010).

Neurodevelopmental effects

25. The developing brain seems to be more vulnerable to lead exposure than the mature brain. Encephalopathy, decreased nerve conduction velocity and cognitive deficits have been observed at lower blood lead concentrations in children than in adults. A wide range of neurobehavioural tests have been applied to assess the effects of lead exposure on central nervous system (CNS) functions. The most widely used measure of cognitive ability has been general intelligence. Intelligence tests incorporate tasks probing various aspects of cognition such as memory, verbal

and spatial reasoning, planning, learning, and the comprehension and use of language. (EFSA, 2010).

26. Negative associations between blood lead and psychometric performance have been reported in several prospective and cross-sectional studies of children. From studies available in the mid-1990s, WHO (1995) concluded that each 100 µg/L increment in blood lead concentration was likely to be associated with a deficit of 1 to 3 intelligence quotient (IQ) points (at ages 4 and above).

27. In several more recent studies, both IQ and other outcomes, such as measures of sustained attention, were lower in children with higher blood lead levels, the relationship applying even at blood lead concentrations less than 100 µg/L. Moreover, decline in IQ for a given increase in blood lead concentration was greater at these low concentrations than at higher levels.

28. An analysis by Lanphear *et al*. (2005), was used by both EFSA and JECFA for dose-response modelling of neurodevelopmental effects (EFSA, 2010; FAO/WHO, 2011). This was a pooled analysis of data from seven prospective cohort studies concerning the quantitative relationship between performance on IQ tests and measures of blood lead concentration, among children followed from infancy. The primary outcome measure was full-scale IQ, assessed at an age between four years 10 months and 10 years. This was related to four measures of blood lead: concurrent blood lead (the most recent measurement before IQ was assessed), maximum blood lead (the highest concentration of blood lead that had been measured at any time before IQ was assessed), average lifetime blood lead (the mean of blood lead measurements from age 6 months up to the time that IQ was assessed) and early childhood blood lead (the mean of measurements between 6 and 24 months of age). After adjustment for covariates, IQ was inversely related to each of these measures of blood lead. (Lanphear *et al.*, 2005).

Cardiovascular effects

29. An association between blood lead and elevated blood pressure has been observed both in cross-sectional and in longitudinal studies, and it has been estimated that systolic pressure is approximately 1 mm Hg higher for each doubling of blood lead, without any clearly identifiable threshold. (EFSA, 2010). It is possible that the relationship is mediated, at least in part, by effects on the kidney, since an inverse association has been observed between blood lead and glomerular filtration rate (GFR) (see paragraphs 31-34 below).

30. In its dose-response modelling for cardiovascular effects, EFSA selected as a benchmark response, a 1% change in systolic blood pressure, corresponding to an increase of 1.2 mm Hg from a baseline value of 120 mm Hg in a normotensive adult, since this was within the range of observed effects and could have significant consequences for human health at a population level. EFSA (2010) calculated an average $BMDL_{01}$ of 36 µg/L blood lead from two longitudinal and two cross-sectional studies (Glenn *et al.*, 2003; Vupputuri *et al.*, 2003; Nash *et al.*, 2003; Glenn *et al.*, 2006). This blood lead BMDL value was converted into a corresponding BMDL for dietary lead exposure of 1.5 µg/kg bw/day.

Renal effects

31. Reduced GFR, as indicated by lower creatinine clearance or higher serum creatinine concentration, has been observed in association with exposures resulting in average blood lead levels <200 µg/L, after allowance for age and other covariates that might contribute to glomerular disease. In subjects with blood lead levels below 100 µg/L, serum creatinine has been estimated to increase by 1.4 mg/L per 10-fold increase in blood lead. (EFSA, 2010).

32. Several factors have been suggested to modify the association between blood lead and renal function, although the evidence is inconsistent. Among these are certain genetic polymorphisms, including in the genes for ALAD, the vitamin D receptor and nitric oxide synthase (FAO/WHO, 2011). Decrements in glomerular filtration rate may contribute to elevations in blood pressure, and elevated blood pressure may predispose people to glomerular disease (U.S. ATSDR, 2007). However, renal disease does not lead to excessive retention of lead in the body (Batuman *et al*., 1983; Sánchez-Fructuoso *et al.*, 1996).

33. The association between lead exposure and renal function in children has been little studied. The few data available suggest that paradoxically, higher blood lead levels are associated with increased GFR (as estimated by serum creatinine or cystatin C levels). (FAO/WHO, 2011)

34. EFSA selected as a benchmark response for renal effects, a 10% increase in the prevalence of chronic kidney disease. A $BMDL_{10}$ of 15 µg/L blood lead was calculated using data from a cross-sectional study conducted in the USA (Navas-Acien *et al*., 2009). This was converted into a corresponding dietary lead exposure of 0.63 µg/kg bw/day.

Allergenicity

35. No reports were identified of allergenicity from dietary exposure to lead. Consistent data from studies in both humans and several animal species (rodents, chicken) indicate that lead exposure can result in immune dysregulation. Findings are generally consistent with alteration of the immune system's homeostasis to favour development of IgE-mediated allergies, including down-regulation of TH1 cytokines such as IFN-γ and up-regulation of TH2 cytokines such as IL-4 (Dietert *et al.,* 2004). In a recent study, Hsiao *et al.* (2011) found differences in blood concentrations of IFN-γ, IL-12, IL-4 and IL-5 in young children who had allergies, but only among those who were living in the vicinity of an oil refinery. However because of inadequate documentation of recruitment methods and response rates, and limitations of the statistical analysis, no useful conclusions can be drawn from this observation.

Benchmark dose for developmental neurotoxicity

36. While noting the BMDLs that had been derived by EFSA for cardiovascular and renal effects, the COT concluded that the toxic effect of lead in infants which was most important at low levels of exposure, and which therefore was critical for

risk assessment, was its developmental neurotoxicity. Both EFSA and JECFA have derived BMDLs for effects on neurological development.

37. Budtz-Jørgensen (2010) was commissioned by EFSA to calculate a BMDL for the association of lead with the development of intellectual function, by modelling of data from the pooled analysis by Lanphear *et al.* (2005). The benchmark calculations used regression models with full IQ score as the dependent variable, and adjustment for birth weight, Home Observation for Measurement of the Environment (HOME)[2] score, maternal education and maternal IQ, all of which were significantly associated with IQ in the dataset. BMD and BMDL values were calculated for a 1% change in full scale IQ score (a decrease in IQ by 1 point), taking concurrent blood lead, maximum blood lead, average lifetime blood lead and early childhood blood lead as alternative exposure metrics. The dose-response models applied were logarithmic, linear, and a piecewise linear function with breakpoint at 100 µg/L (Table 1) (Budtz-Jørgensen, 2010).

Table 1. Benchmark doses for neurodevelopmental effects of lead (expressed as µg/L blood lead) from Budtz-Jørgensen (2010).

Dose-response model	Benchmark	
	BMD_{01}	$BMDL_{01}$
Concurrent blood lead		
logarithmic	3.5	2.6
piecewise linear	18	12
linear	56	41
Maximum blood lead		
logarithmic	3.9	2.7
piecewise linear	10	6.9
linear	97	66
Lifetime average blood lead		
logarithmic	3.6	2.5
piecewise linear	15	9.7
linear	64	45
Early childhood blood lead		
logarithmic	5.6	3.4
piecewise linear	37	16
linear	81	52

38. For its assessment of risk, EFSA took as a point of departure, the $BMDL_{01}$ value of 12 µg/L from the piecewise linear dose-response model for concurrent blood lead. Concurrent blood lead concentration exhibited the strongest relationship with IQ, and the piecewise linear model showed a better fit to the data than the linear model. The logarithmic model generally gave an even better fit than the piecewise linear model, but the differences were small, and EFSA preferred the latter because, taking into account the mathematical properties of the logarithmic model, they considered that it provided "less uncertain estimates of the $BMDL_{01}$". Using the

[2] The HOME Inventory is an index that reflects the quality and quantity of emotional and cognitive stimulation in the home environment (Lanphear *et al*, 2005)

IEUBK toxicokinetic model, the blood lead $BMDL_{01}$ of 12 µg/L was estimated to correspond to a dietary lead exposure in infants and children of 0.5 µg lead/kg bw per day (EFSA, 2010).

39. JECFA (FAO/WHO, 2011) also used data from the Lanphear *et al.* (2005) analysis for dose-response modelling. Models were based on concurrent blood lead levels since they showed the highest correlation with IQ. Initially, six different models were considered – four with linear form and two sigmoidal. From these, a bilinear model (unlike the piecewise linear model used by EFSA, this did not constrain the inflexion in the dose-response relationship to be at a pre-specified blood lead concentration) was chosen to characterise the relationship of blood lead to IQ, since it provided a better fit than four of the other models, and it was considered that it would give better estimates of effect than the one other model with similar fit, when non-dietary exposures to lead were unknown or highly variable. Using this model, the chronic dietary exposure of a 20 kg child corresponding to a decrease of 1 IQ point was estimated to be 0.6 µg/kg bw per day with a 90% confidence interval of 0.2-7.2 µg/kg bw per day.

40. The differences between the EFSA and JECFA analyses are small, and reflect inevitable uncertainties in the specification of the mathematical models. The COT noted that both were influenced by an apparently steep dose-response at low levels of lead exposure (blood lead levels less than 75 µg/L), which was based on few data from a single study in Rochester, USA, and may have rendered the BMDL values conservative. In this statement, the COT has based its risk characterisation on the EFSA $BMDL_{01}$, which is between the EFSA BMD_{01} and the lower 90% confidence limit for the BMD_{01} calculated by JECFA, and corresponds to a dietary exposure of 0.5 µg/kg bw/day.

Sources of lead exposure

Environmental

41. People may be exposed to lead and lead compounds via air and drinking water, and through eating foods or swallowing dust or dirt that contains lead. Ingestion of contaminated soil and dust as a result of “hand-to-mouth” activities, can be an important source of lead intake in some infants and young children. In the past, lead was an ingredient in some pigments and paints, which among other things, were used in toys, and these may be a further source of exposure. (EFSA, 2010). In addition, traces of lead are commonly found in coal, leading to diffuse release when it is burned domestically or industrially. Historically, the most important source of diffuse lead pollution in the general environment was from the use of alkyl lead as an additive in petrol. (Ander *et al.*, 2011). However, since 1998, leaded fuel has been unavailable in the UK other than for a few specialist applications.

Soils and dust

42. Lead concentrations in soil are influenced both by underlying lithological lead concentrations and by anthropogenic release of lead (Ander *et al.*, 2011). Lead was

measured in topsoils[3] from England as part of a DEFRA-commissioned project (Ander *et al.*, 2011), and the median concentration was 47 mg/kg with a range from 2 to >10196 mg/kg. Median concentrations of lead were 35, 57 and 166 mg/kg respectively in rural, semi-urban and urban areas. In urban areas, the minimum level of lead was 2.1 mg/kg and the 75th percentile was 322 mg/kg.

43. Lead-contaminated floor dust and soil contribute to lead intake during the first two years of life (Lanphear *et al*., 2002). In a pooled analysis of 12 epidemiological studies the loads of lead in floor dust (all less than 10 µg/ft^2 (107.6 µg/m^2)) were significantly associated with blood lead levels in children aged 6 – 24 months (Lanphear *et al*., 1998).

Air

44. Long-term monitoring has demonstrated a substantial reduction in environmental concentrations of airborne lead in many countries following the phase-out of leaded petrol. According to the National Atmospheric Emissions Inventory, the main sources of lead emissions to the atmosphere in the UK in 2008 were metal production (mainly iron and steel) (63%), industrial combustion (9%), and residential, commercial, institutional and agricultural combustion (7%). Atmospheric lead concentrations vary widely, but usually decline with increasing distance from emission sources. In the atmosphere, lead particles/aerosols are transformed by chemical and physical processes, and are ultimately removed by dry and wet deposition to terrestrial or aquatic ecosystems. (EFSA, 2010). The EU limit value for lead in outdoor air (0.5 µg/m^3) is met throughout the UK. Recently, typical annual mean concentrations of lead have ranged from less than 0.005 µg/m^3 at rural monitoring sites, to 0.05-0.09 µg/m^3 at urban industrial sites. (Defra, 2012). Values for median lead concentrations were 0.001 (Scotland), 0.004 (Northern Ireland) and 0.006 µg/m^3 (both England and Wales), with a range from 0.0003 (Scotland 1st percentile) to 0.09 µg/m^3 (England 99th percentile).

Drinking water

45. The most common sources of lead in tap water are lead pipework installed before the 1970s, and non-approved solder used inappropriately in cold water systems. Lead may also leach from brass fittings. (DWI, 2012). Currently the maximum permitted level of lead in drinking water is 25 µg/L. A new EU value of 10 µg/L was set in 1998 and Member States have until 25th December 2013 to ensure that the new standard is met (Directive 98/83/EC, 1998).

46. Data on lead concentrations in public drinking water sampled in 2011 were obtained from the Scottish government, Northern Ireland Water, and the Drinking Water Inspectorate (DWI) (measurements made by 29 water companies in England and Wales). Lead concentrations ranged from <1 to 18 µg/L, with median values by country between 0.03 and 0.6 µg/L (Table 2). The concentrations of lead in samples of water that were tested, may be higher than those in water as consumed, if samples were taken before water was flushed through the tap.

[3] From a depth of 0-15 cm

Table 2. Lead concentrations (µg/L) in tap water from public supplies

	England and Wales	Northern Ireland¶	Scotland**
1st percentile	0* – 0.02**	0.05	0.2
25th percentile	0* – 0.3**	0.3	0.2
Mean	0.9* – 1.0**	1.6	1.1
Median	0.03* – 0.5**	0.6	0.2
75th percentile	0.6* – 0.8**	1.0	0.5
99th percentile	9.8	17.7	18.1
Number of samples	12851	408	1549

Water from England and Wales is analysed by 29 water companies. The limits of detection (LODs) are not the same for each company, which explains the difference between the upper bound values for the 1st and 25th percentiles.
*Assuming results lower than the LOD are equal to zero.
**Assuming results lower than the LOD are equal to the LOD.
¶Results lower than the LOD are reported as half of the LOD value

Human breast milk

47. Lactation requires a substantial redistribution of maternal calcium with mobilisation from bone stores. It is estimated that up to 5% of bone mass is mobilised during lactation, and lead that has accumulated in this bone from past exposures may be released into the blood and excreted in breast milk. Generally, when current maternal exposure levels are low, there is little potential for transfer of lead to milk. However, because more than 90% of lead in the adult human body is located in the bone, there can be substantial redistribution of accumulated lead from bone into plasma and subsequently into breast milk, during periods of heightened bone turnover such as pregnancy and lactation (Ettinger *et al*., 2004a). Tellez-Rojo *et al.* suggested that women with higher bone lead levels may mobilise more lead to the bloodstream during pregnancy and lactation than those with lower lead burdens (Tellez-Rojo *et al.*, 2002).

48. In a study of the effect of breast milk lead on infant blood lead levels at one month of age, infant blood lead was significantly correlated with levels of lead in breast milk, and the latter accounted for 12% of the variance of infant blood lead levels. (Ettinger *et al.*, 2004b).

49. As part of the SUREmilk study (2004), levels of lead were measured in breast milk from women in the UK, the highest concentration in an individual sample being 2.6 µg/kg (Woolridge *et al.*, 2004). The COT[4] noted that the SUREmilk samples were collected primarily to explore the viability of breast milk collection methods, and not as part of a rigorous survey.

[4] http://cot.food.gov.uk/pdfs/cotsuremilk.pdf

Infant formulae

50. The Food Standards Agency (FSA) has reported a survey of metals in complementary foods and formulae for infants, which were sampled during 2004 and 2005 (FSA, 2006). Table 3 shows the lead concentrations in samples of 46 different types of infant formulae (powdered and ready-to-consume infant formulae, follow-on formulae and growing-up milks) in the survey. All formulae sampled had lead levels lower than the 20 µg/kg limit set by the European Commission (EC 1881/2006). Powdered formulae showed higher lead levels (µg/kg as sold) than ready-to-consume infant formulae.

Table 3. Average lead concentrations (µg/kg as sold) in infant formulae calculated from data from the FSA survey (2006).

Formula type	Number of samples	Average lead (µg/kg as sold)	Standard deviation** (SD)	Range* (µg/kg as sold)
Powdered				
All formulae	32	4.6**	3.0	2 - 16
Cows' milk-based	27	4.0**	2.9	2 - 16
Goats milk-based	3	8.0*	2.6	5 - 10
Soya-based	2	6.5*	2.1	5 - 8
Ready-to-consume Cows' milk-based	14	0.7**	0.3	0.4 – 1.1

*Data published in FSA (2006)
**Calculated from data published in FSA (2006)

Complementary foods[5]

51. As part of the FSA survey of metals in foods and formulae for infants, lead concentrations were measured in 153 samples of commercial infant foods sampled in November 2004 and February 2005. Values were approximately two-fold higher in breakfast foods, biscuits, cereal bars/rice cakes and rusk products than in the other foods tested (FSA, 2006). Table 4 shows the means and ranges of lead concentrations measured.

[5] Solid foods introduced into the infant diet complement the milk feed, which remains the predominant part of the infant diet for most of the first year of life.

Table 4. Mean and range of lead concentrations (µg/kg as sold) in commercial infant foods

Food type	Number of samples	Mean lead concentration* (µg/kg as sold)	SD**	Range of lead concentrations* (µg/kg as sold)
Baby rice	8	4	3	<2 - 8
Biscuits	8	13	13	3 - 39
Breakfast foods	27	10	16	0.7 – 75
Cereal bars/rice cakes	9	11	9	5 - 28
Desserts	12	5	7	1 - 21
Fish	7	4	5	0.5 – 14
Fruit puree	7	5	3	2.7 – 11.9
Meat	45	5	3	0.5 – 16
Pasta/dairy	16	5	5	0.9 - 20
Rusks	7	12	11	2 - 33
Vegetables	7	5	2	1.8 - 8

*Data published in FSA (2006)
**Standard deviation calculated from data published in FSA (2006)

Exposure to lead

52. Exposure assessments for air, soils and dust and the diet are based on external exposure, assuming that absorption of lead by the different routes is similar. In its dietary exposure estimations, the COT has previously used bodyweight data from a relatively old survey (DH, 1994). Bodyweight data are now available from the recently published UK Dietary and Nutrition Survey of Infants and Young Children (DNSIYC) (DH, 2013), with average bodyweights of 7.8, 8.7 and 9.6 kg for infants aged >4.0-6.0, >6.0-9.0 and >9.0-12.0 months old, respectively. Since DNSIYC did not include infants younger than 4 months, in this statement a value of 5.9 kg for infants aged 0-3 months from an earlier survey (DH, 1994), is assumed for infants aged 0-4.0 months.

Environmental exposure to lead

Soils and dust

53. Potential exposures of infants to lead through ingestion of soil were calculated assuming ingestion of 100 mg soil/day (WHO, 2007) that contained lead at the median measured concentrations in rural, semi-urban and urban areas (35, 57 and 166 mg/kg respectively), the minimum measured level of lead in urban areas (2.1 mg/kg) and the 75th percentile value for urban areas (322 mg/kg) (paragraph 42). Calculations were for an infant aged >9.0-12.0 months (with an assumed bodyweight of 9.6 kg (DH, 2013)) since infants are likely to consume more soil at this age than when they are younger and less able to move around and come into contact with soil. The estimated levels of exposure from soil ingestion based on the median soil concentrations in rural, semi-urban and urban areas were 0.36, 0.59 and 1.7 µg/kg bw/day, while those for the minimum and 75th percentile urban concentrations were 0.022 µg/kg bw/day and 3.4 µg/kg bw/day.

54. No recent data were available for levels of lead measured in dust in the UK.

Air

55. Potential exposures of UK infants to lead in air were calculated assuming a ventilation rate of 3 m^3/day (US EPA, 1989), median airborne lead concentrations of 0.001 (Scotland), 0.004 (Northern Ireland), and 0.006 (England and Wales) µg/m^3, the 1st percentile for Scotland (0.0003 µg/m^3) and the 99th percentile for England (0.09 µg/m^3), and infant bodyweights as in paragraph 52.

56. Based on the median airborne concentrations, the calculated exposures to lead were lower in Scotland than in Northern Ireland and England and Wales (Table 5). The lowest calculated exposure was 0.000094 µg/kg bw/day in infants aged >9-12.0 months (based on the 1st percentile concentration in Scotland), and the highest was 0.046 µg/kg bw/day in infants aged 0-4.0 months (based on the 99th percentile concentration in England).

Table 5. Estimated UK infant exposure to lead (µg/kg bw/day) from the air

Lead concentration (µg/m^3)	Age (months)			
	0-4.0	>4.0-6.0	>6.0-9.0	>9.0-12.0
Scotland median (0.001)	0.00051	0.00038	0.00034	0.00031
Northern Ireland median (0.004)	0.0020	0.0015	0.0014	0.0013
England and Wales median (0.006)	0.0031	0.0023	0.0021	0.0019
1st percentile Scotland (0.0003)	0.00015	0.00012	0.00010	0.000094
99th percentile England (0.09)	0.046	0.035	0.031	0.028

Dietary exposure to lead

57. The EFSA has concluded that 800 mL and 1200 mL are reasonable estimates of average and high-level daily consumption of breast milk or infant formula before weaning (e.g., EFSA, 2012a).

Breast milk

58. Based on the maximum lead level of 2.6 µg/L in breast milk that was recorded from women in the UK who took part in the SUREmilk study (paragraph 48) lead exposure levels were estimated for exclusively breastfed infants consuming average (800 mL) and high-level (1200 mL) volumes of breast milk (Table 6).

Table 6. Lead exposure (µg/kg bw/day) from exclusive breastfeeding estimated for average and high level consumption of breast milk

Lead concentration in breast milk	Age in months (consumption volume per day)			
	0-4.0 (800 mL)	0-4.0 (1200 mL)	>4.0-6.0 (800 mL)	>4.0-6.0 (1200 mL)
2.6 µg/kg	0.35	0.53	0.27	0.40

Infant exposure is based on consumption of 800 mL or 1200 mL per day, and expressed on a bodyweight (5.9 kg for infants aged 0-4.0 months and 7.8 kg for infants aged >4.0-6.0 months) basis.

Infant formulae and complementary foods

59. The FSA 2006 survey measured levels of lead in powdered and ready-to-consume infant formulae (as sold). From these data, infant lead exposure was calculated assuming average and high level consumption. The exposures range from 0.051 µg/kg bw/day for infants aged >4.0-6.0 months with average consumption of ready-to-consume formula to 0.20 µg/kg bw/day for infants aged 0-4.0 months with high consumption of powdered goats' milk-based formula. (Table 7).

Table 7. Lead exposure (µg/kg bw/day) from exclusive feeding on infant formulae estimated for average and high level consumption

Mean lead concentration in infant formula[a,b]	Age in months (consumption volume per day)			
	0-4.0 (800 mL)	0-4.0 (1200 mL)	>4.0-6.0 (800 mL)	>4.0-6.0 (1200 mL)
Powdered cows' milk 0.55 µg/L (0-6 months)	0.07	0.11	0.056	0.085
Powdered goats' milk 1.5 µg/L (0-3 months) 1.2 µg/L (4-6 months)	0.20	0.31	0.12	0.18
Powdered soya-based 0.95 µg/L (0-6 months)	0.13	0.19	0.097	0.15
Ready-to-consume (cows' milk-based) 0.5 µg/L (0-6 months)	0.07	0.10	0.051	0.077

[a] Excludes contribution of lead from water in reconstituted powdered formulae.
[b] Based on values taken from formulae targeted for the specific age ranges.
For each powdered infant formula the manufacturers' instructions provided the volume of feed to be prepared per day and the mass of powder required. From this, the mass of powder per litre was calculated in order to derive the concentration of lead in reconstituted formula. These values were averaged for the different samples of cows' milk-, goats' milk- and soya-based formulae to obtain the mean lead concentration in reconstituted formula).

60. In addition, infants will be exposed to lead through drinking water used to reconstitute infant formula. Across the UK the level of lead in drinking water varies. Exposure values from water were calculated for infants assuming consumption of an average (800 mL) or high (1200 mL) level of formula per day, and the median and 99th percentile of measured concentrations in water (Table 2). Calculated additional

exposures from lead in water ranged from 0.044 µg/kg bw/day to 3.1 µg/kg bw/day (Table 8).

Table 8. Possible additional lead exposure of exclusively formula fed infants through use of drinking water from public supplies to reconstitute the formula (µg/kg bw/day).

Lead concentration in drinking water (µg/L)	Age in months (consumption volume per day)			
	0-4.0 (800 mL)	0-4.0 (1200 mL)	>4.0-6.0 (800 mL)	>4.0-6.0 (1200 mL)
Median level (0.5*)	0.058	0.086	0.044	0.065
High level (18.1)	2.1	3.1	1.6	2.4

The exposure is calculated assuming that water accounts for approximately 85% of the total volume of formula preparation. The exposure volumes used in the calculations were therefore 680 and 1020 mL instead of 800 and 1200 mL, respectively.
*Assuming results lower than the LOD are equal to the LOD

61. In 2003, the COT[6] considered the results of an FSA survey of elements, including lead, in infant foods and formulae (FSA, 2003). At that time, in the absence of recent consumption data for infants aged 6-12 months old, alternative approaches were used to estimate dietary exposures. Data from the 1986 survey of British infants on intakes at ages 6-12 months (Mills and Tyler, 1991) were considered probably to underestimate consumption, but allowed direct comparison of the data with results from a previous survey (MAFF, 1999). The high level (97.5 percentile) estimated exposure at age 7-12 months was 0.22 µg/kg bw/day as compared with 0.52 µg/kg bw/day from the 1999 survey. In addition, manufacturers' feeding instructions were used[7], which indicated a mean dietary exposure in the region of 0.5 – 0.6 µg/kg bw/day (Table 9). The COT considered that these two approaches indicated a range within which the actual exposures were likely to lie.

62. Manufacturers' feeding instructions and recommendations were also used to estimate combined exposures based on the results from a later FSA survey of metals in complementary foods and formulae for infants (FSA, 2006). The estimated mean lead exposures were 0.1, 0.1, 0.3 and 0.4 µg/kg bw/day for infants aged 0-3, 4-6, 7-9 and 10-12 months, respectively (Table 9). Overall the estimates in Table 9 suggest a reduction in the dietary exposure of infants to lead between 1999 and 2006.

[6] http://cot.food.gov.uk/pdfs/statement.pdf

[7] Manufacturers' feeding guidelines, as detailed on each product label, were used as the source of consumption data for formulae. For complementary foods an average consumption level of food and drinks for each age range from weaning at 4 months of age was calculated from three different manufacturers' feeding guidelines. The mean concentration of lead was calculated from its concentration in every eligible food for a particular age group (using a dilution factor for samples of dried food). Average weights of 5.9, 7.7, 8.9 and 9.8 kg were assumed for infants of 0-3, 4-6, 7-9 and 10-12 months of age respectively.

Table 9. Estimated dietary exposure of infants to lead from infant formulae and commercial infant foods.

Year survey published	Survey dates	Diet	Mean exposures calculated using manufacturers' consumption guidelines (µg/kg bw/day)[$]				Mean (and 97.5th percentile) exposures calculated using 1986 survey (µg/kg bw/day)
			Age (months)				Age (months)
			0 - 3	4 - 6	7 - 9	10 – 12	7 – 12
1999*	1997 - 1999	Normal					0.21 (0.52)
2003*	2001 - 2002	Normal	0.08	0.37	0.51	0.52	0.08 (0.22)
		Soya	0.22	0.56	0.59	0.61	
2006**	2004 - 2005	Normal	0.1	0.1	0.3	0.4	

These estimates relate only to commercially available infant foods and do not include the contribution from water used to reconstitute formula.
*Data taken from the COT statement on a survey of metals in infant food (2003)
**Data taken from FSA (2006)
[$]Bodyweights used were 5.9, 7.7, 8.9 and 9.8 kg respectively for infants aged 0-3, 4-6, 7-9 and 10-12 months (DH, 1994).

63. The exposure estimates in Table 9 do not take into account the contribution of lead from water used in reconstitution of some complementary foods. Data are not available on the amounts of water that are used for this purpose, but exposure from water is likely to be less than in infants exclusively fed on formula reconstituted from powder.

64. The COT has previously noted that estimates of dietary exposure in infants from the United Kingdom (UK) have relied on survey data that may have been outdated, or on assumptions about feeding patterns that may have overestimated food consumption. New data from the DNSIYC will be available for use later in 2013 and may help to refine estimates of exposure from commercial infant foods and possibly other foods consumed by infants.

65. EFSA estimated dietary exposures of infants to lead using submitted data on occurrence from across the EU, and findings from two surveys conducted in the EU which assessed food consumption by infants. Lower and upper bound values[8] for the mean dietary exposure to lead from the survey which had the larger number of participants (from Bulgaria), were 0.73 and 1.09 µg/kg bw/day, respectively. The lower and upper bound values for the 95th percentile exposure were 1.39 and 2.22 µg/kg bw/day, respectively. The major lead-contributing food groups in the infant diet were identified as drinking water (26.0%), milk and dairy products (21.8%), foods for

[8] Where individual data on lead concentrations are less than the limit of detection, the result is expressed as zero (lower bound), or as equal to the limit of detection (upper bound).

infants and small children (12.2%) and grains and grain-based products (9.0%). (EFSA, 2012b).

66. Mean infant dietary exposure to lead as estimated from the FSA (2006) survey (Table 9) was up to 0.4 µg/kg bw/day. This is approximately 55% of the mean lead exposure values calculated by EFSA (paragraph 63).

Trends in markers of lead exposure

67. Blood lead levels in UK children decreased from 140-360 µg/L (in children aged 4 months – 14.25 years) in 1964 to approximately 37 µg/L (in children aged 5 – 14 years) in 1991-2 (Moncrieff et al, 1964; O'Donohoe et al., 1998. The Newcastle biomonitoring study carried out during 2005 to 2008 found mean and median blood levels in 3000 individuals (age not specified) from the healthy population in Northern England of 22 µg/L and 13 µg/L respectively (Jefferson et al., 2012)[9]. Estimates of average population dietary exposure to lead decreased from 110 µg/day in 1976 to 6–7 µg/day in 2006 (COT, 2008[1]). It is likely that infants' exposure to lead has similarly decreased.

Risk characterisation

68. Potential risks from infants' exposures to lead were characterised by margins of exposure (MOEs), calculated as the ratio of the BMDL of 0.5 µg/kg bw/day to estimated exposures from diet, soil and air. As the BMDL was for a small effect (a one-point difference in IQ), derived from pooled analysis of multiple cohort studies of exposures in infants and children, and is likely to be conservative (see paragraph 40), an MOE of >1 can be taken to imply that at most, any risk is likely to be small. MOEs <1 do not necessarily indicate a problem, but scientific uncertainties (e.g. because of potential inaccuracies in the assessment of exposures, failure to control completely for confounding factors, and the possibility that the samples of children studied have been unrepresentative simply by chance) mean that a material risk cannot be ruled out. This applies particularly when MOEs are substantially <1.

69. MOEs based on the estimated dietary exposures are shown in Table 10. Most are >1, but lower values (down to 0.16) were calculated for exposures from drinking water where water concentrations of lead are at the highest end of the measured range. At median concentrations of lead in water, there is no indication of a problem.

70. In addition, a marginally low MOE (0.90) was calculated for high consumers of breast milk at ages 0-3 months, when the lead concentration in breast milk was taken as the highest that was recorded in the SUREmilk study. The MOE value is less than 1, indicating that a low level of risk cannot be ruled out. However this is based on an unusually high concentration of lead in breast milk, and is for exposure to a cumulative toxicant over a relatively short period (the calculated MOE for high consumers of breast milk at older ages was >1).

[9] Jefferson *et al.* (2012). Report to Health Protection Agency, paper in submission

Table 10. Estimated dietary exposures and MOEs compared to the $BMDL_{01}$ for neurodevelopmental effects of lead.

Food	Age (months)	Range of estimated dietary exposures (µg/kg bw/day)		MOE	
		Average consumers	High level consumers	Average consumers	High level consumers
Exclusive breast milk	0 – 4.0	0.35	0.53	1.4	0.90
	>4.0 – 6.0	0.27	0.40	1.9	1.3
Exclusive infant formula[a,b]	0 – 4.0	0.070 – 0.20	0.10 – 0.31	2.5 – 7.1	1.6 – 5.0
	>4.0 – 6.0	0.051 – 0.12	0.077 – 0.18	4.2 – 9.8	2.8 - 6.5
Water used in the reconstitution of infant formula[c]	0-4.0	0.058 – 2.1	0.086 – 3.1	0.25 - 8.6	0.16 - 5.8
	>4.0 – 6.0	0.044 – 1.6	0.065 – 2.4	0.31 - 11	0.21 - 7.7
Infant formula and complementary foods[d]	0 - 3	0.10		5.0	
	4 - 6	0.10		5.0	
	7 - 9	0.30		1.7	
	10 - 12	0.40		1.3	

The MOE is calculated by dividing the $BMDL_{01}$ of 0.50 µg/kg bw/day by the respective dietary exposure

[a]Excludes lead from water used in the reconstitution

[b]Range of estimated dietary exposures from different types of infant formulae

[c]Range of estimated dietary exposures from median and 99th percentile. Does not include additional water provided.

[d]Values based on manufacturers' feeding instructions as reported in FSA (2006).

71. Because toxicity will depend on total exposure to lead from all sources, it is important to consider combined exposures from food, water, and also non-dietary sources. Table 11 gives MOEs for median estimates of exposure from soil and air, assuming concentrations of lead in these media at the medians of measured ranges (see paragraphs 53-56). It is clear that exposures from air are negligible. However, there might be a material risk from ingestion of soil where concentrations are relatively high.

Table 11. Range of estimated median exposures to lead from air and soil and corresponding MOEs compared to the $BMDL_{01}$ for neurodevelopmental effects of lead.

Source of lead	Range of estimated median exposures (µg/kg bw/day)	Range of MOEs
Soil	0.36 – 1.7	0.30 – 1.4
Air	0.00031 – 0.0031	160 – 1600

The MOE is calculated by dividing the $BMDL_{01}$ of 0.50 µg/kg bw/day by the respective environmental exposure
These comparisons assume equivalent absorption from different sources.

72. When the MOEs in Tables 10 and 11 are considered together, they indicate that total exposure to lead is unlikely to pose a material risk to health in the large majority of UK infants. However, there remains a concern that adverse effects could occur where concentrations of lead in water or soil are unusually high.

Conclusions

73. The general population is exposed to lead through food, drinking water, air, soil and dust. Food and water are the major sources of exposure to lead, although in infants and small children, ingestion of soil and dust can also contribute importantly. Lead can be transferred to the infant from the mother in breast milk. In general, exposure to lead has decreased substantially over recent decades.

74. Recently both the European Food Safety Authority (EFSA) and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) published evaluations of lead which concluded that a provisional tolerable weekly intake (PTWI) of 25 µg/kg bodyweight (bw) previously established by JECFA could no longer be considered protective for health.

75. Lead absorption is higher in children than in adults, averaging 42% of oral intake. It is also higher in a fasting state than when people have recently eaten. Inadequate intakes of calcium, iron and zinc have been shown to increase lead absorption, and elevated levels of fat in the diet may lead to higher blood lead concentrations.

76. Absorbed lead is transported in the blood bound to proteins, predominantly in erythrocytes, but also in plasma. It is then deposited in soft tissues and bone, where it tends to accumulate with age. Maternal bone is mobilised during pregnancy and lactation to meet the demands of fetal mineralisation, and this leads to release of lead from the bone.

77. Because lead accumulates in the body, adverse effects can occur from long-term dietary exposures at levels below those which cause acute toxicity. The kidney and cardiovascular systems are adversely affected by lead exposure in adults. Neurotoxicity has been identified at lower levels of exposure, and the developing brain appears to be more vulnerable than the mature brain.

78. It has not been possible to demonstrate a threshold level of exposure below which the neurodevelopmental effects of lead do not occur.

79. The Committee concluded that a $BMDL_{01}$ of 0.5 µg/kg bw/day calculated by EFSA for a 1 point decrement in IQ should be used when evaluating potential risks from infants' exposure to lead, and that a margin of exposure (MOE) approach should be applied.

80. Calculated MOEs for dietary exposures in infants were generally >1, indicating that at most, any risk from this source of exposure is likely to be small. However, lower values (down to 0.16) were calculated for exposures from drinking water where water concentrations of lead are at the highest end of the measured range in the UK. At median concentrations of lead in water, there is no indication of a problem.

81. A marginally low MOE (0.90) was calculated for high consumers of breast milk at ages 0-3 months, when the lead concentration in breast milk was taken as the highest that was recorded in a survey of UK women reported in 2004 (the SUREmilk study). On balance, the COT does not consider that this is a cause for concern since the MOE is only a little less than one, is based on the highest concentration of lead in breast milk measured in the study, and is for exposure to a cumulative toxicant over a relatively short period.

82. Because toxicity will depend on total exposure to lead from all sources, it is important to consider combined exposures from food, water, and also non-dietary sources. Calculated MOEs indicate that exposures from air are negligible. However, there might be a material risk from ingestion of soil where concentrations are relatively high.

83. There are uncertainties in the assessment of risks to infants from exposure to lead because quantification of exposures may not always have been accurate in the epidemiological studies used to characterise hazard, confounding factors may not have been fully taken into account, and the samples of children studied may have been unrepresentative by chance. The possible contribution from foods not specifically marketed for infants is currently unknown. Further information on this may become available when full analysis of data from the DNSIYC is possible.

84. When allowance is made for these uncertainties, it appears that total exposure to lead is unlikely to pose a material risk to health in the large majority of UK infants. However, there remains a concern that adverse effects could occur where concentrations of lead in water or soil are unusually high.

COT Statement 2013/02

July 2013

Abbreviations

ALAD	δ-aminolevulinic acid dehydratase
BMD	Benchmark dose
BMDL	Benchmark dose lower confidence limit
CI	Confidence interval
CNS	Central nervous system
COT	Committee on Toxicity
DEFRA	Department for the Environment, Food and Rural Affairs
DH	Department of Health
DNA	Deoxyribose nucleic acid
DNSIYC	Diet and Nutrition Survey of Infants and Young Children
DWI	Drinking Water Inspectorate
EC	European Commission
EFSA	European Food Safety Authority
FAO	Food and Agriculture Organization
FSA	Food Standards Agency
HOME	Home observation for measurement of the environment
IARC	International Agency for Research on Cancer
IQ	Intelligence quotient
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LOD	Limit of detection
MAFF	Ministry of Agriculture, Fisheries and Food
MCV	Maximal motor nerve conduction velocity
MOE	Margin of exposure
PTWI	Provisional tolerable weekly intake
SACN	Scientific Advisory Committee on Nutrition
SD	Standard deviation
UK	United Kingdom
WHO	World Health Organization

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Search strategy

General lead exposure search

Websites interrogated –

- EFSA
- COT
- FSA
- JECFA

The following websites were interrogated for lead concentrations in soil and air

- DEFRA
- US EPA

Scientific publications literature search in PubMed

Specific search terms:

Lead AND Breast milk
Search Dates (From/To) - to 2012
Exclusion Criteria –

- Studies without lead levels in breast milk
- Non-human studies

Lead AND Iron
Search Dates (From/To) - to 2012
Exclusion Criteria –

- Non-human studies

Lead AND Calcium
Search Dates (From/To) – to 2012
Exclusion Criteria –

- Studies not looking at the effects of lead and calcium
- Non-human studies

Lead AND Absorption
Search Dates (From/To) – to 2012
Exclusion Criteria –

- Non-human studies

Lead AND Allergy
Search Dates (From/To) - to 2012
Exclusion Criteria –

- Non-human studies
- Studies with non-dietary lead

Lead AND Hypersensitivity
Search Dates (From/To) - to 2012
Exclusion Criteria –

- Non-human studies
- Studies with non-dietary lead

Lead AND Sensitization
Search Dates (From/To) - to 2012
Exclusion Criteria –

- Non-human studies
- Studies with non-dietary lead

Blood lead levels AND UK
Search Dates (From/To) - to 2012
Exclusion Criteria –

- Non-human studies
- Studies not from the UK

The above mentioned search terms were also used in Google. It identified latest government advice and opinions.