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

COT Statement on the 2006 UK Total Diet Study of Metals and Other Elements

Issue

1. The Food Standards Agency (FSA) has completed a survey of aluminium, antimony, arsenic, barium, bismuth, cadmium, chromium, copper, germanium, indium, lead, manganese, mercury, molybdenum, nickel, palladium, platinum, rhodium, ruthenium, selenium, strontium, thallium, tin and zinc in the 2006 Total Diet Study (TDS). The results provide up to date information on the concentrations of these elements in foods and were used to estimate dietary exposures for UK consumers. The Committee was asked to comment on the survey results and assess if the levels of any of the elements in the diet posed a risk to human health. The COT last evaluated population and consumer exposures to twelve of these elements (aluminium, arsenic, cadmium, chromium, copper, lead, manganese, mercury, nickel, selenium, tin and zinc) in 2003, using data from the 2000 TDS[1]. Eleven other elements (antimony, barium, bismuth, germanium, molybdenum, palladium, platinum, rhodium, ruthenium, strontium and thallium) were last analysed in the 1994 TDS and evaluated by the COT in 1998[2]; and indium was included for the first time in the 2006 TDS.

The survey

2. The TDS is an important part of the UK Government's surveillance programme for chemicals in food and has been carried out on a continuous annual basis since 1966. Results from the TDS are used, together with food consumption data from the National Diet and Nutrition Survey (NDNS), to estimate dietary exposures of the general UK population to chemicals in food, such as nutrients and contaminants, to identify changes or trends in exposure, and to make assessments on the safety and quality of the food supply. Such data can then be used as background information when considering issues such as the possible health impact of incidents of high-level contamination, and regulatory levels for nutrients and contaminants in various foodstuffs. Results from the TDS also indicate where there is a need for more targeted surveys, such as of arsenic levels in food, metals in infant food, and mercury levels in fish, all of which have been the subject of previous statements[3,4,5]. Analysis for metals and other elements in the TDS is carried out every 3 years.

3. The design of the UK TDS has been described in detail elsewhere[6] and involves 119 categories of foods combined into 20 groups of similar foods for analysis. The relative proportion of each food category within a group reflects its importance in the average UK household diet and is largely based on an average of three previous years of food purchase data from the National Food Survey (now the Expenditure and Food Survey, EFS). Foods are grouped so that commodities known to be susceptible to contamination (e.g. offal, fish) are kept separate, as are foods that are consumed in large quantities (e.g. bread, potatoes, milk)[6,7].

4. The survey data provided to the Committee related only to food prepared as for consumption. Information on exposure from other sources, such as drinking water and dietary supplements, is not captured by the TDS methodology. The Committee was informed on exposures from drinking water and dietary supplements using data from the Drinking Water Inspectorate (DWI) and the Expert Group on Vitamins and Minerals (EVM), respectively[8,9].

5. At present there are no specific limits on the levels of trace elements, minerals or other micronutrients that may be contained in supplements sold under food law, although the EU is currently in the process of setting maximum permitted levels for vitamins and minerals in dietary supplements. Industry guidance on upper levels of vitamins and minerals is available for manufacturers of supplements to ensure levels are not excessive. However, the supplements industry is not obliged to follow this guidance and is only bound by the provisions of the Food Safety Act, which make it an offence to offer for sale a food product that is injurious to health. The use of dietary supplements has increased during the last decade[10-12]. Vitamin and mineral supplements surveys suggest that between 20 and 40% of the UK adult population take supplements, with use most common among women aged 50-65 years[13-16]. The EVM has advised on supplemental amounts of minerals that even in conjunction with high exposure from food and drinking water would not result in safe upper levels of intake being exceeded[9]. Where supplements on the UK market exceed these amounts, the FSA has made recommendations for reformulation or labelling with advisory statements in advance of the EU regulations on maximum permitted levels[i].

6. Consideration of speciation of an element is an important component of risk assessment as it focuses the toxicological evaluation on the most relevant species, and allows a better understanding of the mechanisms of toxicity. Despite advances in speciation analysis in the past 20 years and the availability of methods for determination for some elements[17], in general, the TDS only determines the total concentration of elements. Elemental toxicity may vary according to the oxidation state, the formation of complexes, and the biotransformation of the element[17]. The relevance of speciation to health effects in humans has been demonstrated for a number of endpoints - for example, acute toxicity (lead), sensitisation (nickel), neurotoxicity (manganese), nephrotoxicity (cadmium), reproductive toxicity (mercury), genotoxicity (chromium), and carcinogenicity (arsenic)[17]. Where the 2006 TDS provided information on the chemical forms in which an element occurred in foods, the COT took this into account in its evaluation of potential risks to health. However, there were uncertainties in the risk assessment where this information was

[i] http://www.food.gov.uk/foodindustry/guidancenotes/labelregsguidance/supplementreformguidance

unavailable or published toxicological data did not relate to the same chemical forms of the element as occurred in food.

Concentrations of the elements in the foods surveyed

7. The full results of the 2006 TDS are published in a Food Survey Information Sheet[18]. In general, the concentrations of each of the elements in the food groups were lower than or similar to those reported in the 1994 and 2000 total diet studies, with the exception of aluminium, barium and manganese.

8. Most of the food groups had aluminium concentrations lower than or similar to those reported in the 2000 TDS, the exceptions being bread, meat products, and other vegetables groups. The miscellaneous cereals group had the highest mean concentration of aluminium (17.5 mg/kg), although this was lower than the concentration in the 2000 TDS (19 mg/kg). The miscellaneous cereals group was the main contributor to the population dietary exposure (42%) to aluminium. Possible sources of aluminium in this food group include aluminium compounds present naturally, aluminium-containing additives, and contamination from processing and storage of food in aluminium-containing utensils.

9. Barium concentrations were similar to or lower than those reported in the 1994 TDS except for the nuts group, in which the mean concentration was 131 mg/kg compared to 56 mg/kg in 1994.

10. Manganese concentrations were similar to or lower than those reported in the 2000 TDS except for the bread, miscellaneous cereals and meat products groups. The largest increase (nearly 2-fold) was seen in the meat products group.

Dietary exposure assessment

11. The exposure assessments reported for the 2006 TDS were made by combining concentration data for the food groups with corresponding consumption data. The main source of data used by the FSA to estimate food consumption is the NDNS[15,19-22]. The NDNS was carried out as a series of cross-sectional surveys of diet and nutritional status; data from each of four age groups were collected over the years 1992-1993 (pre-school children aged 1.5-4.5 years, commonly referred to as toddlers), 1994-1995 (elderly), 1997 (young people), and 2000-2001 (adults). The Committee noted that these food consumption data used to estimate exposures might not reflect current dietary habits and did not include children under 18 months or sufficient data to estimate the intake of sub-groups such as ethnic minorities. The respondents in the surveys were asked to complete diaries of foods and beverages consumed over a 4 or 7 day period (depending on the survey), inside and outside the home. Quantities of foods consumed at home were assessed by weighing them with digital scales. Quantities of foods eaten outside the home were estimated from descriptions referenced to household measures. The dietary information was recorded "as consumed" so recipes were required to identify the food components. These recipes were obtained from the respondent's diaries, food manufacturers or published sources (e.g. recipe books and websites). The fieldwork covered a 12-

month period to account for possible seasonal variations in eating habits. Other surveys such as the Expenditure and Food Survey[23] and the Dietary Survey of Vegetarians[24] provided supporting information. The EFS is carried out annually and provides data on food purchases at a household level. This information is used to inform the quantities and relative proportions of each food that contributes to the total diet. The fieldwork for the Dietary Survey of Vegetarians was carried out during 1994-1995[24].

12. The vast majority of FSA dietary exposure assessments for chemicals are carried out using a bespoke in-house software package known as the Intake Programme. This programme estimates exposure by combining data on the concentration of a chemical in each food group with information on the distribution of individuals' food consumption patterns. Participants in the NDNS keep a diary of their food consumption, from which calculations are made of the total amount of each food group that each individual consumed. With the assumption that each food group contained an element at the concentration at which it was measured in the TDS, an estimate was made of the total daily amount of the element that each participant consumed. From the distribution of estimated exposures across all participants, values for mean- and high-level (97.5th percentile) exposure were then derived, which represent estimated exposures for individuals who consume average amounts of the element from food (mean-level consumers) and those who are among the highest consumers (high-level consumers). Where a chemical could not be detected in one or more food groups, two alternative calculations were made. In the first, all undetectable concentrations were assumed to be zero (lower bound), and in the second, they were all assumed to be at the limit of detection for the method of assay (upper bound)[ii]. Mean- and high-level exposures were then each expressed as a range, with the lower bound derived under the first assumption and the upper bound under the second.

13. Table 1 compares the estimated dietary intakes of each element that was measured in the 2006 TDS for the consumer groups for which consumption data were available, and also summarises relevant tolerable intakes or other health based guidance values where they exist.

14. Estimates of dietary exposure for the different consumer groups were compared with available tolerable intakes, such as Provisional Tolerable Weekly Intakes (PTWIs) set by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), taking into account previous COT evaluations. The COT evaluation was also informed by a summary of toxicological data on the elements[25]. The PTWI is used by JECFA to define tolerable intakes of food contaminants with the potential to accumulate in the body. In this statement, the PTWI has been divided by 7 to provide a tolerable daily intake (TDI) for comparison with the estimated daily dietary exposures (Table 1).

15. Exposure estimates were also carried out at the population level in order to assess trends in average exposure for the UK population as a whole. Such trends

[ii] In the calculation of upper bound exposures for inorganic arsenic, the concentration in the food groups was assumed to be equal to the concentration of total arsenic (since this was lower than the LOD for inorganic arsenic) except in the case of the poultry food group where it was considered to be equal to the LOD.

may reflect changes in food consumption patterns, changes in the concentrations of elements in foods, or both. Population dietary exposures were estimated by multiplying the average amount of each food group consumed (based on consumption data from the EFS survey and expressed in mg/day) by the corresponding elemental concentration in the food group from the TDS study, and then summing across all food groups. The EFS covers the total number of people in a household regardless of whether they ate specific foods or not, and so the EFS consumption data are averaged for the whole population. Tables 2a and 2b compare mean population dietary exposures to the 24 elements in the UK total diet studies dating back to 1976.

16. Exposures from drinking water were estimated for those elements included in The Water Supply (Water Quality) Regulations 2000[26]. Results from monitoring undertaken by each water company in 2007 provided a 1st percentile and a 99th percentile at consumers' taps, except where fewer than 100 samples were taken, when the figures are the actual maximum and minimum results[8]. The 99th percentile or maximum concentration was used to calculate exposure estimates from drinking water, based on UK data for chronic tap water consumption (mL/kg body weight/day, 97.5th percentile) of 158 pre-school children, 60 young people, 39 adults, and 28 elderly[15,19,21,22]. For those elements not included in The Water Supply (Water Quality) Regulations 2000, WHO Guidelines for Drinking-water Quality were used to estimate potential exposure from drinking water[27]. Exposure estimates from drinking water represent a worse case scenario because they are based on chronic water consumption at the maximum concentration of the element. Concentrations of elements in drinking water vary over time, even in the same region, and so it is highly unlikely that exposure to the maximum concentration would occur persistently over a prolonged period. Estimates of exposure from drinking water were carried out for aluminium, antimony, arsenic, barium, cadmium, chromium, copper, lead, manganese, mercury, molybdenum, nickel, and selenium (see Table 3).

COT evaluation

17. Health based guidance values were available for aluminium, antimony, barium, cadmium, chromium, copper, lead, manganese, mercury, nickel, selenium, tin, and zinc. There were no relevant tolerable intakes or reference doses by which to assess the safety of exposure to total or inorganic arsenic, bismuth, germanium, indium, molybdenum, palladium, platinum, rhodium, ruthenium, strontium or thallium.

Aluminium

18. Aluminium occurs naturally in the environment where it is present in its 3+ oxidation state and not in the metallic elemental state. Natural processes such as soil erosion and weathering of rocks, as well as human activities, result in the release and redistribution of aluminium compounds to other environmental compartments. Aluminium may form organic and inorganic compounds and is naturally present in varying amounts in most foodstuffs. The use of aluminium and aluminium compounds in processing, packaging and storage of foods, and as flocculating agents in the treatment of drinking water, all contribute to its presence in foods and

drinking water. Medicinal antacid preparations can provide much larger aluminium doses, of up to 5 g per day.

19. Speciation is an important factor when considering the absorption of aluminium and it is widely assumed that soluble aluminium compounds are more bioavailable than insoluble compounds[28]. Absorption is also influenced by the presence or absence of particular foods and beverages (dietary ligands) in the intestines, and by acid digestion in the stomach. Citrate, which could be present in foods consumed at the same time as aluminium-containing foods, increases the absorption of aluminium[29]. The net absorption of aluminium from food is approximately 1%, although this varies based on the chemical forms present in the intestinal tract[28,29]. This low bioavailability is due to the formation of aluminium complexes as the pH increases from the stomach to the intestines.

20. The JECFA recently revised the PTWI for aluminium because of emerging evidence that aluminium compounds have the potential to affect the reproductive system and developing nervous system at doses lower than the NOAEL used in establishing the previous PTWI[28]. The PTWI was reduced from 7 mg/kg body weight to 1 mg/kg body weight, and applies to all aluminium compounds, including additives[28]. The PTWI incorporated a total uncertainty factor of 300 applied to the lower end of the range of LOAELs (50 mg Al/kg body weight/day) to allow for inter- and intra-species differences and deficiencies in the the database, notably the absence of NOAELs in the majority of the studies evaluated and the absence of long-term studies on the relevant toxicological end-points. The deficiencies were counterbalanced by the probable lower bioavailability of the less soluble aluminium species present in food. Overall, an additional uncertainty factor of three was considered to be appropriate. The JECFA noted that dietary exposure through foods containing aluminium compounds used as food additives represented the major route of aluminium exposure for the general population, but that further data were required on the bioavailability of different aluminium-containing food additives[28]. The EFSA also recently evaluated the safety of aluminium from dietary intake, basing its evaluation on the combined evidence from several studies showing adverse effects on testes, embryos and the developing and mature nervous system following dietary administration[29]. The EFSA derived the same TWI of 1 mg/kg body weight, noting that it was not possible to draw conclusions on the specific sources contributing to the aluminium content of a particular food[29]. Limitations of the studies evaluated by the JECFA and the EFSA included lack of information on dose-response relationships, and on specific individual aluminium compounds or species present in food, and a failure in some studies to consider the basal aluminium content of the animals' feed.

21. Estimates of dietary exposure to aluminium (high-level intake for adults, pre-school children, young people, institutionalised elderly and vegetarian groups; and mean-level intake for pre-school children) exceeded the PTWI set by the JECFA and the EFSA (equivalent to 143 µg/kg body weight/day) by up to 2.4-fold. The current average population exposure to aluminium (5.4 mg/day) was increased compared to that reported in the 2000 and 1997 total diet studies (4.7 mg/day and 3.4 mg/day, respectively) but lower than previous estimates (10 mg/day and 11 mg/day in 1991 and 1994, respectively). In previously discussing the 2000 TDS, the Committee noted that the aluminium concentrations in the miscellaneous cereals, sugars and

preserves, and nuts groups were higher than those reported for the 1997 TDS. The largest increase was seen in the miscellaneous cereals group and this was considered possibly to be due to increases in the use of aluminium-containing preservatives in these foods, or the different proportions of products sampled in this group compared to previous total diet studies[1].

22. In the 2006 TDS most of the food groups had aluminium concentrations lower than or similar to those reported in the 2000 TDS, the exceptions being the bread, meat products, poultry, other vegetables, canned vegetables and fresh fruits groups, all of which had higher concentrations of aluminium compared to those reported in the 2000 TDS. The miscellaneous cereals group had the highest mean concentration of aluminium (17.5 mg/kg). This was lower than the concentration in the 2000 TDS (19 mg/kg) but three times greater than the concentration from the 1997 TDS (5.2 mg/kg). The levels of aluminium in this food group have varied from 4.8 mg/kg (1988 TDS) to 78 mg/kg (1994 TDS).

23. The miscellaneous cereals group, which comprises cakes, scones, biscuits, breakfast cereals, flour and rice, was the principal dietary contributor to the population dietary aluminium exposure (42%). Possible contributors to the relatively high aluminium concentration found in this group include naturally present aluminium compounds, aluminium-containing additives which are permitted for use in some bakery products[30,31], and contamination from processing and storage of food in aluminium-containing utensils.

24. The results of the 2006 TDS show an apparent increase in dietary exposure to aluminium, although this is within the estimated mean dietary exposure of European adults (1.6-13 mg/day)[29]. Variations in dietary exposure may be accounted for by differences in soil composition in the regions where food is produced, in individual dietary patterns and in consumption of foods with aluminium-containing food additives. It is acknowledged throughout Europe, that for certain groups of the population, exposure to aluminium will exceed the PTWI. This includes infants and young children, who have a higher food intake than adults when expressed relative to body weight[29]. Consumption of tap water has the potential to increase high-level exposure to aluminium by 3-7%, such that the worst case high level intake of pre-school children could exceed the PTWI by 2.7-fold.

25. The Committee noted that whilst the estimates of dietary exposure to aluminium were not markedly higher than previous estimates, they present uncertainty with regard to the safety of aluminium in food in the light of the recent reduction in the PTWI, which is exceeded by some population subgroups. There is a need for further information on possible sources and forms of aluminium in the diet and their bioavailability.

Antimony

26. Antimony was detected in most of the food groups except the oils and fats, eggs, and milk groups. The meat products group had the highest concentration of antimony (0.0099 mg/kg). The estimates of dietary exposure to antimony for all population subgroups were well below the TDI of 6 µg/kg body weight/day set by the

WHO in 2003. The TDI was based on a NOAEL of 6 mg/kg body weight/day for decreased body weight gain and reduced food and water intake in a 90-day drinking water study in rats; and an uncertainty factor of 1000 (100 for inter- and intra-species variation and 10 for the short duration of the study)[27]. The toxicity of antimony is a function of the water solubility and the oxidation state of the species, with antimony (III) being more toxic than antimony (V) and inorganic compounds being more toxic than organic compounds[27]. No information was provided on how this TDI was set in relation to speciation, although, the WHO noted that antimony leached from antimony-containing materials would be in the form of the antimony(V) oxo-anion, which is the less toxic form. Intake of antimony from drinking water could be up to about twice that from high-level intake from food, but estimated worst case total intake is below the TDI.

27. The Committee concluded that the estimated dietary exposures to antimony were not of toxicological concern.

Arsenic

28. The toxicity of arsenic is dependent on the form (inorganic or organic) and the oxidation state of arsenical compounds. It is generally accepted that inorganic arsenic compounds are more toxic than organic arsenic compounds, with the toxicity being linked to the soluble inorganic trivalent forms[27].

29. In 2003 the Committee recommended that future surveys should measure both total and inorganic arsenic and include consideration of other sources of exposure such as water[1]. The 2006 TDS surveyed both total and inorganic arsenic but this information was not available for the arsenic content of water. Food is generally the principal contributor to the daily intake of total arsenic in non-occupationally exposed individuals[32], but water can contribute more to the intake of inorganic arsenic. The levels of arsenic reported in drinking water in England & Wales for 2007 ranged between 0.3 and 7.9 µg/L[8]; and high-level intake from this source could be up to 1.2 µg/kg body weight/day for pre-school children, or 0.3 µg/kg body weight/day for adults. Since this is likely to be all in the inorganic form, it exceeds the intake from food. There is potential for significant exposure from work in some industries, although in the UK, arsenic and its compounds have been assigned a maximum airborne exposure limit of 0.1 mg/m^3 (averaged over an 8-hour period)[33]. For people who are not occupationally exposed, inhalation exposure can contribute up to approximately 10 µg/day in a smoker and about 1 µg/day in a non-smoker[32]. Other potential sources of exposure include contaminated soils and polluted atmospheres[32].

30. The Committee has concluded previously, when considering the 1999 TDS of total and inorganic arsenic, that there are no relevant tolerable intakes or reference doses by which to assess the safety of either inorganic or organic arsenic in the diet. The COT considered that the approach used to establish the JECFA PTWI for inorganic arsenic (15 µg/kg body weight) in 1989 would now not be considered appropriate, in view of the evidence of genotoxicity and carcinogenicity[3]. When establishing the PTWI, the JECFA noted the epidemiological evidence of an association between overexposure of humans to inorganic arsenic from drinking

water and an increased cancer risk, and also noted that skin cancer did not occur in the absence of other toxic effects of arsenic[34]. The COT concluded that inorganic arsenic is genotoxic and a known human carcinogen and therefore exposure should be as low as reasonably practicable (ALARP)[3]. The European Commission has requested that the EFSA evaluate the risks to human health related to the presence of arsenic in foodstuffs (including drinking water), covering the ratios between inorganic and organic arsenic forms, the contribution of different foodstuffs to exposure, and the exposures of specific population groups. There is currently an open call for relevant data with the objective to collect all available data analysed during the time period from January 2003 to November 2008[35]. These data will then be used by the EFSA in its risk assessment of arsenic in food.

31. The estimates of average population dietary exposures to total arsenic in the 2006 TDS were comparable to those reported in the 1999 TDS of total and inorganic arsenic (0.061 - 0.064 mg/day and 0.055 mg/day, respectively[3]). The current population exposure to total arsenic was also similar to that reported in total diet studies since 1991 (see Table 2a). In discussing the 1999 and 2000 total diet studies, the Committee previously noted that fish was the major contributor to dietary exposure to arsenic and that the predominant form of arsenic in fish is organic[1,3]. Inorganic arsenic contributed less than 10% of the total dietary exposure to arsenic in 1999. Similarly, the results of the 2006 TDS indicate that fish was the major contributor to dietary arsenic exposure and that inorganic arsenic contributed less than 12% of the total dietary exposure.

32. With regard to population dietary exposures to total arsenic, since 1976 intakes have fluctuated but the general trend appears to be downwards. Therefore, the previous COT conclusion that the organic arsenic component is unlikely to constitute a hazard to health appears still valid. The average population dietary exposure to inorganic arsenic was 0.0014 - 0.007 mg/day and was comparable to the range reported in 1999 (0.0009 - 0.005 mg/day)[3] and therefore does not raise any new concern. Furthermore, although there is uncertainty about whether the JECFA PTWI for inorganic arsenic is sufficiently protective, estimated dietary exposures in all of the population groups examined were less than 20% of the PTWI (Table 1), and possibly less than 10% of the PTWI, taking into account the large number (18/20) of food groups with inorganic arsenic levels below the limit of detection.

33. The Committee concluded that the data on arsenic appear consistent with previous surveys of total and inorganic arsenic in food. Current dietary exposure to organic arsenic is unlikely to constitute a risk to health. The advice on inorganic arsenic continues to be that exposures should be ALARP.

Barium

34. Barium occurs in nature as a divalent cation in combination with other elements. The two most prevalent naturally occurring barium ores are barium sulphate and barium carbonate[36]. Barium sulphate is present in soils but only a limited amount accumulates in plants. The main route of exposure to barium compounds for the general population is oral intake via drinking water and food, with food being the primary source[36]. Where barium levels in water are high, associated

with groundwater of low pH, drinking water may contribute significantly to barium intake[27]. No data are available on levels of barium in drinking water in the UK.

35. Case reports indicated that in humans, intentional or accidental ingestion of barium can cause gastroenteritis, hypokalaemia and hypertension. The WHO considered that the critical end-points for deriving a TDI for barium are hypertension and impaired renal function[36]. Hypertensive effects have been observed in humans who ingested acute high doses of barium compounds and in workers who inhaled barium carbonate and dusts of barium ores. Hypertension has also been reported in rats exposed to barium chloride in drinking-water for 1 month at an estimated daily dose of 7.1 mg barium/kg body weight. Drinking water studies in rats and mice also indicated the kidney to be a sensitive target organ, with a lowest identified NOAEL of 45 mg/kg body weight in female rats given barium chloride in drinking water for 2 years. The WHO identified a NOAEL of 0.21 mg barium/kg body weight/day from a 10-week experimental study in humans (barium chloride in drinking water up to 10 mg/L) and an epidemiological study in populations living in communities with mean drinking water barium concentrations of 0.1 and 7.3 mg/L. Blood pressures were not significantly affected by barium exposure in either study. Applying an uncertainty factor of 10 to the NOAEL to allow for database deficiencies and differences between adults and children resulted in derivation of a TDI of 20 µg/kg body weight[36]. The WHO assigned medium confidence to this tolerable intake because neither study identified a LOAEL, and noted that there were uncertainties about the most sensitive toxic end-point in humans, and about whether there were differences in toxicity or toxicokinetics between adults and children.

36. In its Guidelines for Drinking Water, the WHO used the NOAEL of 7.3 mg/L from the epidemiological study described above in which a population with drinking water containing a mean barium concentration of 7.3 mg/L were compared with a population whose water contained a barium concentration of 0.1 mg/L. Subjects were selected randomly from a pool that included every person 18 years of age or older that had lived in the community for more than 10 years. There were no significant differences between the two populations in the mean systolic or diastolic blood pressures, or in history of hypertension, cardiovascular disease, or kidney disease, and thus no LOAEL was identified. An uncertainty factor of 10 was applied to the NOAEL to allow for intra-individual variation, resulting in a guideline value of 0.7 mg/L[37]. Assuming a 60 kg adult drinking 2 litres of water per day, this guideline value is equivalent to 23 µg/kg body weight/day which is comparable to the TDI established by the WHO in 2001, as described in paragraph 35. Both of these reference doses apply to barium as an element, and were derived from studies with barium chloride.

37. As with the results from 1994, the highest levels of barium in the 2006 survey were reported in nuts (131 mg/kg) and bread (0.81 mg/kg). All other foodstuffs contained lower levels than in bread. Levels of barium in nuts were double those reported in 1994 (131 mg/kg and 56 mg/kg, respectively). Estimated average population dietary exposures to barium have increased by approximately 46% since the last TDS in 1994. The estimates of dietary exposure to barium for pre-school children (mean- and high-level dietary intakes) and of high-level intakes by adults, young people, free living elderly, and vegetarians, exceeded the WHO TDI of 20 µg/kg body weight/day by up to 4.3-fold. Consumption of tap water has the potential to increase high-level exposure to barium by 60-130%, which could result in a total

dietary exposure for high-level intake in pre-school children of 980% of the WHO TDI. However, because barium levels in water vary over time and given that the drinking water estimated exposure was based on the WHO guideline value and not a measured concentration, it is highly unlikely that this worst case scenario would occur over a prolonged period.

38. The population exposures that most exceeded the TDI were the high-level intakes for adults (~220% of the TDI), young people and vegetarians (~320% of the TDI), and pre-school children (~420% of the TDI). The mean population group exposures were below or in the region of the WHO TDI. Since the TDI is derived from studies in which no statistically significant effects were observed, the LOAEL could have been very much higher than the dose identified as a NOAEL, and hence the TDI may be over-precautionary. Therefore, the Committee concluded, that the estimated exposures, which exceeded the TDI by up to 4-fold, were not necessarily a toxicological concern. The Committee noted the uncertainty regarding the lack of information on effect levels and on the bioavailability of barium in the principal food group (nuts).

Bismuth

39. Bismuth was analysed previously in the 1994 TDS. Since 1994, estimated population dietary exposures have increased by 5-fold from 0.4 µg/day to 2 µg/day. There are no health based guidance values for bismuth. Bismuth is widely used in many medical applications, such as in compounds used in the treatment of diarrhoea, nausea and other gastrointestinal disturbances, and suppressants of lupus erythmatosus. Insoluble bismuth salts have also been used in cosmetics. No data are available on levels of bismuth in drinking water in the UK, and a WHO drinking water guideline value has not been set.

40. In 9 patients being treated with tripotassium dicitratobismuthate for 6 weeks, Gavey *et al.*[38] found that a daily oral dose of 432 mg/day was without adverse effect. This dose is equivalent to approximately 7000 µg/kg body weight/day for a 60kg adult. The margin of exposure between this human therapeutic dose and the highest estimated dietary exposure (0.217 µg/kg body weight/day; high-level intake by pre-school children) is 32300 (rounded to the nearest 100). This margin of exposure indicates a low concern for human health at the highest high-level dietary exposure. The Committee noted that doses used in medicines are very much larger than the estimated dietary exposure. The Committee concluded that dietary exposures to bismuth were unlikely to be of toxicological concern.

Cadmium

41. The major route of exposure to cadmium for the non-smoking population is via food, due to contamination of soil and water. Gastrointestinal absorption is influenced by the type of diet and nutritional status. For example, low iron status increases the uptake of cadmium. Cadmium was present at low concentrations in ten of the food groups, with the highest concentrations in the offal (0.084 mg/kg) and nuts (0.065 mg/kg) groups. The estimates of dietary exposure to cadmium for all population

subgroups were below the PTWI of 7 µg/kg body weight (equivalent to 1 µg/kg body weight/day) set by the JECFA in 1989[34]. The PTWI was based on the risk of kidney damage at levels of cadmium in excess of 50 µg/g in the renal cortex. Assuming an absorption rate of 5% and a daily excretion of 0.005% of body burden, the JECFA concluded that total intake should not exceed 1 µg/kg body weight/day continuously for 50 years; the PTWI was maintained in 2003[74]. No information was provided on how the PTWI was set in relation to speciation. Cadmium toxicity arises only when the chelation capability of metallothionein in the critical organs or tissues is used up[17]. Consumption of tap water has the potential to increase high level dietary exposure to cadmium by about 10-25%, but estimated worst case total intake is below the TDI.

42. The Committee concluded that the estimated dietary exposures to cadmium were not of toxicological concern. This conclusion might need to be reviewed after completion of a risk assessment by the EFSA.

Chromium

43. The toxicity of chromium varies depending on the valency state, with hexavalent chromium being more toxic than trivalent chromium, which is an essential trace element. Ingested trivalent chromium has a low level of toxicity, due partly to its poor absorption. Hexavalent chromium and its compounds are oxidizing agents capable of directly inducing tissue damage, and epidemiological studies have found an association between exposure to hexavalent chromium and lung cancer[39]. The EVM considered that for guidance purposes, an intake of 150 µg/kg body weight/day trivalent chromium would be expected to be without adverse health effects[9].

44. Almost all of the sources of chromium in the earth's crust are in the trivalent state, and chromium compounds in the hexavalent state are almost always derived from human activities[39]. Hexavalent chromium in the soil tends to be reduced to trivalent chromium by organic matter; and studies with gastric juices have demonstrated that hexavalent chromium is reduced to the trivalent form in the gastrointestinal tract[40]. It was noted that chromium in food is likely to be largely, if not entirely, in the trivalent form. Analysis of hexavalent chromium in a range of infant foodstuffs did not detect any hexavalent chromium, although these observations were limited by the relatively high limit of detection (300 ng/g)[41].

45. The estimates of dietary exposure to chromium (mean- and high-level intakes) for all consumer groups were within the EVM guidance level for trivalent chromium of 150 µg/kg body weight/day. Results from total diet studies indicate that average dietary exposures to chromium have been steadily declining since 1991. The estimated population dietary exposure to chromium from the 2006 TDS was 0.022-0.029 mg/day, reduced from 0.046 mg/day in 2000. The Committee on Medical Aspects of Food and Nutritional Policy (COMA) did not set reference nutrient intakes (RNIs) for chromium but suggested that an adequate level of intake lies above 0.025 mg/day for adults (equivalent to 0.4 µg/kg body weight/day for a 60 kg adult) and between 0.1 and 1 µg/kg body weight/day for children and adolescents[42]. The current population dietary exposure was comparable to the COMA suggested adequate level of intake for adults. Consumption of tap water has the potential to increase high-level

dietary exposure to chromium by 50-120%. In addition dietary supplements could provide up to 0.6 mg/day (10 µg/kg body weight/day for a 60kg adult)[9]. Worst case total intake from food, water and supplements is well below the EVM guidance level.

46. The Committee concluded that current dietary exposures to chromium were unlikely to be of toxicological concern.

Copper

47. Copper is an essential trace element that has two valency states, copper (I) and copper (II). Copper was present in all of the food groups analysed in the 2006 TDS. The offal (52.5 mg/kg) and nuts (9.15 mg/kg) groups contained the highest concentrations of copper. Although copper is an essential trace element, high levels can cause acute gastrointestinal effects. This may be a direct irritant effect of copper in water and is not so apparent when copper is present in the food matrix[9]. The estimates of dietary exposure for all population subgroups were well within the PMTDI of 50-500 µg/kg body weight/day set by the JECFA in 1982[43] and the safe upper level of 160 µg/kg body weight/day set by the EVM[9]. The JECFA PMTDI was initially proposed in 1973 on the basis of human epidemiological and nutritional data related to background exposure to copper. The EVM safe upper level was based on a 13-week feeding study of copper sulphate in rats in which the NOAEL was 16 mg/kg body weight/day, with effects on the liver, kidney and forestomach seen at higher doses. Reported minimum and maximum tap water concentrations for 2007 were 0.015 and 4.25 mg copper/L, respectively[8]. Consumption of tap water has the potential to increase high-level dietary exposure to copper by up to three-fold in pre-school children, which could result in a total dietary exposure of 190% of the EVM safe upper level. However because levels of copper in water vary over time, even in the same region, it is highly unlikely that this worst case scenario would occur over a prolonged period. In addition dietary supplements could provide up to 2 mg/day (33 µg/kg body weight/day for a 60kg adult)[9].

48. The Committee concluded that the estimated mean- and high-level dietary intakes of copper were unlikely to be of any toxicological concern.

Germanium

49. Germanium can exist in valency states of 2 and 4, and was last analysed in a TDS in 1994. Since 1994, average population dietary exposures have decreased from 4 µg/day to 0.1-1.5 µg/day. Based on population dietary exposures estimated from the 1994 TDS, the COT previously concluded that the estimated dietary intakes of germanium in adults did not give cause for concern[2]. There are no health based guidance values for germanium but the EVM concluded that naturally occurring germanium present in food does not appear to be associated with any adverse effect, though there were insufficient data to define a NOAEL for chronic exposure[9]. No information was available on what forms of germanium are naturally present in foods or on potential intake from drinking water.

50. The Committee noted that population dietary exposures have decreased significantly since 1994 and given that germanium was not detected in most (18/20) of the food groups analysed in the 2006 TDS, the current dietary exposures to germanium were unlikely to be of toxicological concern.

Indium

51. Indium has not previously been included in a TDS. A food survey conducted in 1979 found concentrations in nine food groups to be low, with only fats and green vegetables showing concentrations of indium above the limit of detection. The mean daily dietary intake of indium was estimated as between 5 and 27 µg[44]. In the 2006 TDS, the average population dietary exposure to indium was comparable at 5 - 19 µg/day. With the exception of the canned vegetables and fruit products groups, indium concentrations were below the limit of detection of 0.003 – 0.02 mg/kg. For these two food groups, indium concentrations were 0.096 mg/kg (canned vegetables) and 0.031 mg/kg (fruit products). In 1998 the COT evaluated the results from a multi-element survey of cows' milk and vegetables produced near industrial sites, concluding that the intakes of indium in adults were very low[45]. There are no health based guidance values for indium. No information is available on indium in drinking water in the UK and a drinking water guideline has not been set by the WHO.

52. There are no data or reports of human toxicity from oral exposure to indium. Developmental toxicity was reported following oral gavage administration of indium chloride to rats at doses of 100 mg/kg body weight/day on days 6-15 of gestation[46] and 300 mg/kg body weight on day 9 of gestation[47]. Indium was found to cross the placenta resulting in a direct cytotoxic action on the embryo[46]. A lifetime drinking water study in mice conducted with indium chloride suggested a LOAEL of 250 µg/kg body weight/day for growth suppression[48]. The margin of exposure between this chronic mouse LOAEL and the highest estimated dietary exposure (0.93-1.48 µg/kg body weight/day; lower-bound to upper-bound estimate for high-level intake in pre-school children) is 170 - 270 (rounded to the nearest 10). There are no data on indium toxicity from food and the implications of the estimated dietary exposures to indium and margins of exposure are uncertain.

53. The Committee concluded that, although there is uncertainty, the sparse data available did not suggest that the estimated dietary exposures to indium give cause for toxicological concern.

Lead

54. Lead is dispersed throughout the environment as a result of human activities and food is one of the major sources of exposure[27,49,50]. Lead in foods may be derived from the environment in which the food is grown (air pollution from nearby industrial sources) or from preparation of foods with lead-contaminated water and/or utensils[27]. The most critical effect of lead at low concentrations is impaired cognitive development and intellectual performance in children, and studies have shown an association between blood lead concentrations and reduced intelligence quotient (IQ) in children exposed pre- and post-natally[51]. Young children are especially vulnerable

to the effects of lead, because they absorb a higher percentage of ingested lead and are more susceptible to its neurotoxicity. The Committee noted that there could be subgroups of children with increased susceptibility to lead, such as those with calcium deficiencies or living in areas of high social deprivation.

55. The concentration of lead in blood is the most widely used biomarker of exposure and is typically reported in micrograms per decilitre (µg/dL). No threshold for intellectual deficits has been identified but there is evidence of an association at blood lead concentrations below 10 µg/dL[51]. Surveys of blood lead concentrations have indicated reductions in mean blood lead concentrations since the late 1970s[49,51-53]. Current mean levels in children in developed countries are in the region of 3 µg/dL[52]. This reduction has been attributed to the reduced use of lead in petrol and to programmes aimed at reducing exposure from other sources (such as phasing out the use of lead-based paints, eliminating the use of lead in food containers, and the replacement of lead water pipes with non-lead alternatives).

56. In 1999 the JECFA performed a quantitative risk assessment of the effects of dietary lead intakes on IQ in children. In order to correlate dietary intake with blood lead levels, the JECFA assumed that a dietary intake of 1 µg/kg body weight/day would result in an increase in blood lead concentration of 1 µg/dL (this being the upper estimate for infants), and that this relationship was valid over the long-term (in utero and for the first 10 years of life)[51]. There have been a number of epidemiological studies published since the 1999 JECFA assessment. Taken together, the available epidemiological data suggest that an IQ deficit of between 1 and 5 points occurs for each 10 µg/dL increase in blood lead level[49]. Recent studies have suggested that the dose-effect relationship is steeper than this at blood lead levels below 10 µg/dL, but the precise shape of the dose-effect relationship at lower blood lead levels remains uncertain[49,54,55]. There therefore remains no identified threshold for toxicity.

57. Using the JECFA correlation of dietary intake to increase in blood lead level, and assuming an IQ deficit of between 1 and 5 IQ points per 10 µg/dL increase in blood lead level, it is possible to quantify approximately the IQ deficit resulting from exposure to lead in infants and young children at the level of the PTWI. Dietary lead intake at the PTWI may be expected to increase the blood lead level in a young child by 3.6 µg/dL, with a resulting indicative mean IQ deficit of between 0.36 and 1.8 IQ points. Because of the uncertainties, this can only be regarded as an approximation of the degree of effect. Uncertainties include the true steepness of the dose-effect relationship at blood lead levels of <10 µg/dL; the nature of the dose-effect relationship below the lowest blood lead levels which have been studied in epidemiological studies (<1 µg/dL); variation between individual children; and those that arise because studies have assessed different aspects of cognitive and motor performance (such as distractibility, poor organisational skills, impulsivity, inability to follow sequences of directions, and short attention span). Limits to the precision of analytical and psychometric measurements further increase uncertainty in estimates of the effect of blood lead concentrations below 10 µg/dL.

58. The highest estimate of dietary exposure to lead was 0.42 µg/kg body weight/day (for high-level intake by pre-school children). This is comparable to the estimate from the 2000 TDS (0.47 µg/kg body weight/day) and is approximately 12%

of the JECFA PTWI (equivalent to 3.6 µg/kg body weight/day). The JECFA PTWI of 25 µg/kg body weight for infants and children was originally set in 1986[50]. At the time of that evaluation, the PTWI was considered to be a level of exposure from all sources that was not expected to cause an increase in blood lead concentration in young children (the historical background being blood lead levels in UK infants at birth in the early 1980s). The JECFA again evaluated lead in 1993 when the Committee estimated what blood lead level the PTWI would lead to. As this was below levels known to be associated with intellectual deficits in children at the time, the PTWI of 25 µg/kg body weight for infants and children was re-confirmed and extended to all age groups[56]. The review of the health effects of lead in 1993 was based on an assessment of lead that had been performed by an International Programme on Chemical Safety Task Group, which was subsequently published[57]. In the most recent evaluation by the JECFA, the Committee assessed the risk of dietary exposure of infants and children, with special emphasis on the most critical effect, which was considered to be impaired neurobehavioural development. The PTWI was not re-considered[51].

59. A UK study of lead intake in children aged 2 years showed that dietary exposure to lead contributed approximately 30% of total lead exposure, with the remainder coming mainly from sources such as house dust, water and the air[58]. Thus, if dietary exposure to pre-school children is less than 30% of the JECFA PTWI (i.e. less than 1.08 µg/kg body weight/day), total intake is unlikely to exceed the PTWI. Reported minimum and maximum tap water concentrations for 2007 were 0.44 and 102 µg lead/L, respectively[8]. Consumption of tap water has the potential to increase high-level dietary exposure to lead by up to 10-fold in pre-school children. In 2003 the COT commented on a survey of metals in infant food[4]. The maximum estimated intake of lead was lower than for the previous survey and approximately 17% of the JECFA PTWI. The COT welcomed the apparent decline in lead exposure since the previous survey and concluded that efforts should continue to reduce lead exposure from all sources[4].

60. Table 2a illustrates that average population dietary exposures have declined considerably since 1976, with the current population exposure at its lowest level (7 µg/day compared to 26 µg/day in 1997). Although the JECFA PTWI for lead cannot be considered to be fully protective (i.e. there is an indicative minimal effect at the PTWI), all population groups' dietary exposures were well below the PTWI (Table 1). However, drinking water has the potential to increase exposure further in some areas, with high-level total intake by pre-school children exceeding the PTWI by up to 23%. Lead levels in water vary over time, even in the same region, and therefore it is highly unlikely that this worst case scenario would occur over a prolonged period. Estimated worst case total intakes for all other population groups were below the PTWI.

61. The Committee concluded that adverse effects, if any, are likely to be small at the estimated dietary exposures to lead. However, since it is not possible to identify a threshold for the association between lead exposure and decrements in intelligence quotient, efforts should continue to reduce lead exposure from all sources.

Manganese

62. Manganese is an essential trace element that can exist in a variety of oxidation states. It is neurotoxic at high levels of occupational inhalation exposure, but there is limited evidence of neurological effects at lower doses. The extent of neurotoxicity is determined by the oxidation state, with Mn (III) being more toxic than Mn (II)[17]. The dose response relationship in experimental animals has not been adequately clarified and the effects observed in animals may not reflect the subtle neurological effects reported in humans[9]. Children might be particularly susceptible to the neurotoxicity of manganese. There is insufficient information to determine whether there are risks associated with dietary exposure to manganese and no available health based guidance value.

63. The EVM considered that, based on the results of epidemiological studies of neurological effects associated with concentrations of manganese in drinking water, total manganese intakes of 12.2 mg/day for the general population (equivalent to 200 µg/kg body weight/day for a 60kg adult) and 8.7 mg/day for older people (equivalent to 150 µg/kg body weight/day) would not result in adverse health effects[9]. This conclusion was based on a number of assumptions since neither of the two studies used to establish these guidance values recorded water consumption or dietary manganese intake. The WHO derived a TDI of 60 µg/kg body weight/day in the Guidelines for Drinking Water Quality[59]. This was based on the upper range value of manganese intake of 11 mg/day, identified using dietary surveys, at which there were considered to be no observed adverse effects. An uncertainty factor of 3 was applied to take into consideration the possible increased bioavailability of manganese from water. No information was provided on how these reference doses were set in relation to speciation.

64. The estimated high-level dietary exposure of pre-school children exceeded the EVM guidance value by approximately 50%. All other estimated dietary exposures were within the EVM guideline values. In the UK, intake from drinking water would have a minimal effect on total exposure to manganese. Dietary supplements provide up to 10 mg/day[9], which if added to the high level dietary exposure results in a total intake of 290 µg/kg body weight/day in a 60kg adult, representing 145% of the EVM guidance value.

65. The Committee concluded that there was insufficient information to determine whether there are risks associated with dietary exposures to manganese. However, the population dietary exposures to manganese (Table 2b) have remained fairly constant from the time manganese was first included in a TDS in 1983 (4.6 mg/day) to the 2006 TDS (5.24 mg/day), and there is no basis for assuming any concern for health.

Mercury

66. Mercury exists in multiple forms and in three oxidation states (elemental mercury, mercurous mercury, and mercuric mercury). The properties and chemical behaviour of mercury strongly depend on its oxidation state and its chemical form. Mercurous and mercuric mercury form numerous inorganic and organic chemical

compounds. Organic forms of mercury are the most toxic following ingestion as they are absorbed more effectively in the gastrointestinal tract than elemental mercury or inorganic mercury compounds[17]. Food is the major source of exposure to mercury in the general population, particularly methylmercury in fish. There have been no reports of methylmercury being detected in drinking water[27].

67. Estimates of average population exposure to mercury have decreased since 1976 (0.005 mg/day), with the 2006 TDS population dietary exposure (0.001-0.003 mg/day) comparable to that in 2000, when levels were at their lowest (0.0012-0.0015 mg/day). Mercury concentrations were similar to those reported in the 2000 TDS except for the fish group, in which the concentration had decreased to 0.056 mg/kg from 0.071 mg/kg in 2000.

68. The estimates of dietary exposure to mercury (mean- and high-level intakes) for all consumer groups were within or in the region of the PTWI for methylmercury set by the JECFA in 2003 to protect against neurodevelopmental effects (equivalent to 0.23 μg/kg body weight/day), and endorsed by the COT[5]. The estimate for high-level consumption by pre-school children exceeded the JECFA PTWI for methylmercury by 13%. It is unlikely that all the mercury in the diet is in the form of methylmercury. Inorganic mercury is less well-absorbed than methylmercury by the oral route, and therefore comparing dietary exposure to total mercury to the PTWI for methylmercury is a worst case scenario. The Committee concluded that current dietary exposures to mercury were unlikely to be of toxicological concern.

Molybdenum

69. Molybdenum is an essential trace element. It does not exist naturally in the metallic state, but occurs in association with other elements. The predominant form of molybdenum occurring in soil and natural waters is the molybdate anion, MoO_4^{-2}[9]. Estimated average population dietary exposures to molybdenum were comparable to previous estimates (0.123-0.125 mg/day vs. 0.11 mg/day in 1985, 1991 and 1994). There are no health based guidance values for molybdenum and there are few reliable data on its oral toxicity. The EVM noted that intakes of >1 mg/day could be associated with an increased incidence of gout-like symptoms but concluded that the maximum molybdenum intake from the UK diet and drinking water, estimated to be 0.23 mg/day (approximately 4 µg/kg body weight/day for a 60 kg adult), was not expected to present any risk to health[9]. There were insufficient data on the safety of molybdenum intakes in excess of those naturally occurring in the diet for the EVM to provide further guidance on supplementary intake. Dietary supplements can provide up to 333 µg/day (about 5 µg/kg body weight/day for a 60 kg adult)[9]. No data were available for molybdenum in drinking water in the UK, but the WHO noted that levels are usually less than 0.01 mg/L, which was the value used by EVM in reaching its conclusions.

70. The Committee concluded that the sparse data on the oral toxicity of molybdenum do not suggest that the estimated dietary exposures, excluding supplements, give cause for toxicological concern.

Nickel

71. Nickel is an abundant metallic element that can exist in valency states of 0, +1, +2, and +3. Nickel is usually analysed in food as total nickel. Therefore the chemical form is unknown, although nickel in food is normally considered to be in the form of complex bound organic nickel, which may be less bioavailable than other forms[27]. The estimates of dietary exposures to nickel for mean- and high-level intake by pre-school children and high-level intake by young people exceeded (by up to about 2-fold) the total nickel intake level of 4.3 µg/kg body weight/day, considered by the EVM as a dose that would not result in effects in non-sensitised individuals[9]. However, these estimated exposures were within the WHO TDI of 12 µg/kg body weight/day. Nickel in drinking water could increase high-level dietary exposure by 20-30%, with a potential total high-level intake of 11.1 µg/kg body weight/day for pre-school children. Dietary supplements can provide up to 5 µg/day (0.08 µg/kg body weight/day for a 60 kg adult)[9].

72. The value identified by EVM was based on the LOAEL of 1.3 mg/kg body weight/day from a multigeneration study in rats given nickel chloride in drinking water, and incorporated an uncertainty factor of 300. However, the EVM also noted that UK dietary intake of nickel in food was not expected to result in harmful effects. The WHO TDI was established on the basis of a study in which 20 nickel-sensitised patients ingested a single dose of 12 µg/kg body weight ^{61}Ni in solution on a fasted stomach with abstinence from food maintained for a further 4 hours. Nine out of the 20 patients developed flare-up of symptoms after 12 hours. This dose was considered to be the acute LOAEL and a dose much higher than would normally be possible through drinking-water and/or with the presence of food in the stomach. Deriving the total acceptable intake for oral challenge from studies using drinking water on an empty stomach in fasted patients was, therefore, considered a worst-case scenario[27].

73. Previously the COT concluded that the estimated dietary exposure to nickel from the 2000 TDS was unlikely to be of any toxicological concern for consumers[1]. Population dietary exposures to nickel have decreased since 1976 (0.33 mg/day), with the current average dietary exposure at its lowest level (0.127-0.129 mg/day) and comparable to results from the 2000 TDS (0.13 mg/day). Nickel may exacerbate contact dermatitis/eczema in pre-sensitised individuals but the COT has concluded previously that pre-school children are less likely than adults to be sensitised and would therefore not be considered to be a sensitive sub-group[1]. The Committee therefore concluded that dietary exposures to nickel were unlikely to be of toxicological concern.

Palladium

74. The platinum group of metals, which includes palladium, rhodium, and ruthenium, are used in catalytic converters, which have been fitted to the engines of all new vehicles since 1993. Research has shown an increase in the concentration of these metals in roadside dust[60]. There is little information about the biological effects of platinum group metals in food and at present there is no evidence in relation to possible adverse health effects from these metals in the general environment[61].

75. Palladium was last analysed in a TDS in 1994. Since 1994, estimated average population dietary exposures have decreased slightly from 1 µg/day to 0.7 µg/day. Based on the estimated population dietary exposures from the 1994 TDS, the COT previously concluded that from the available data, there was no reason to believe that intakes of palladium from the diet posed a risk to health[2]. However, the COT did note that the toxicological database on palladium metal and its compounds was extremely limited[2]. There are no health based guidance values for palladium. No data are available on levels of palladium in drinking water in the UK.

76. The WHO concluded that the main source of concern regarding palladium is the sensitisation risk; and that the available data did not allow identification of a NOAEL for sensitisation in humans[62]. The WHO noted that in an unpublished 28-day gavage study in which rats were dosed with tetraamine palladium hydrogen carbonate at 1.5, 5 or 150 mg/kg body weight/day[63], treatment-related abnormalities, confined to histopathological changes in the spleen and glandular region of the stomach, were observed at 5 and 150 mg/kg body weight/day. The study authors considered 1.5 mg/kg body weight/day to be the NOAEL, but significant increases in absolute brain and ovary weights were observed in females of this dose group. The margin of exposure between this sub-chronic rat NOAEL/LOAEL and the highest estimated dietary exposure (0.056 µg/kg body weight/day; high-level intake by pre-school children) is about 9700.

77. The Committee concluded, based on the limited database and the evidence that exposure had not increased since 1994, that there was no reason to believe that current intakes of palladium from the diet pose a risk to health. Analysis of dietary palladium was no longer considered to be a high priority for future study.

Platinum

78. Platinum was last analysed in a TDS in 1994, when the estimated population dietary exposure was 0.2 µg/day. Platinum was not detected in any of the food groups analysed in the 2006 TDS, resulting in an estimated average population exposure of 0-2.3 µg/day based on the lower-bound to upper-bound approach, which is not clearly different from 1994. There are no health based guidance values for platinum and it is not known what form of platinum, if any, is present in foods. No data are available on levels of platinum in drinking water in the UK.

79. In 1996, the COT reviewed organometallic platinum compounds in the context of their use as diesel fuel catalysts. The Committee considered the proposed usage and the projected emissions and noted that, if the majority of the emissions were in the form of the metal, there would be no risk to health; and that the platinum emissions from the catalyst were unlikely to be in an allergenic form[64]. The most significant health effect from exposure to soluble platinum salts is sensitisation, though there are no studies of sensitisation by the oral route in humans[65]. Hypersensitivity reactions to platinum-based chemotherapy are frequently encountered, including anaphylactic shock[66-68]. Reactions usually occur after several courses of treatment, although the pathogenic mechanisms are not fully understood. From the limited available data from experimental animals, a NOAEL of 13 mg

platinum/kg body weight/day can be tentatively identified from a study in which rats were given $PtCl_4$ in drinking water for 30 days. The margin of exposure between this subchronic rat NOAEL and the highest estimated dietary exposure (0.130 µg/kg body weight/day; upper bound estimate for high-level intake in pre-school children) is 100000. This margin of exposure indicates a low concern for human health at the highest high-level dietary intake.

80. The Committee concluded that the very low dietary exposures to platinum did not suggest a reason for concern.

Rhodium

81. Rhodium was last analysed in a TDS in 1994, when the average estimated population dietary exposure was 0.3 µg/day. The chemical nature of rhodium in the diet is unknown. Rhodium was not detected in any of the food groups analysed in the 2006 TDS, resulting in an estimated population exposure of 0-2.3 µg/day (lower-bound to upper-bound range), which is not clearly different from 1994. There are no health based guidance values for rhodium. No data are available on levels of rhodium in drinking water in the UK.

82. There are no data in the literature relating to the acute or chronic health effects of rhodium or its compounds in man and few data from studies in experimental animals. When considering the results of the 1994 TDS, the COT concluded that there were insufficient experimental and human toxicological data to be able to make an appraisal of the toxicity of rhodium and its compounds, although, rhodium compounds would appear to be less potent than their platinum counterparts[2]. The Committee concluded that the very low dietary exposures to rhodium did not suggest a reason for concern.

Ruthenium

83. Ruthenium was last analysed in a TDS in 1994. Since 1994, the estimated average population dietary exposure has decreased from 4 µg/day to 0.03-0.81 µg/day (lower bound to upper bound range). Based on the estimated population dietary exposures from the 1994 TDS, the COT previously concluded that from the available data, there was no reason to believe that intakes of ruthenium from the diet posed a risk to health[2]. However, the COT did note that there were insufficient data for a full evaluation[2]. There are no health based guidance values for ruthenium. No data are available on levels of ruthenium in drinking water in the UK.

84. There are no data on the human toxicity of ruthenium compounds and limited experimental toxicological data, although there is some clinical usage as a candidate chemotherapeutic agent. Ruthenium compounds such as NAMI-A and KP1019 have displayed antitumour activity in Phase I clinical trials, with data indicating ruthenium compounds to be less potent in toxicity than their platinum counterparts[69-71]. The Committee concluded that the very low dietary exposures to ruthenium did not suggest a reason for concern.

Selenium

85. Selenium is an abundant element that can exist in 4 oxidation states (-2, +1, +2, and +6). In foods, selenium is generally present as the amino acid derivatives selenomethionine and selenocysteine[9]. Selenium was present in 14 of the 20 food groups analysed in the 2006 TDS. The offal (0.77 mg/kg) and fish (0.42 mg/kg) groups contained the highest concentrations of selenium. Selenium is an essential trace element. Selenium in drinking water has the potential to increase dietary exposure by approximately 20-30%. Adding potential intake from drinking water to the highest estimated dietary exposure (for pre-school children) indicates a possible highest total exposure of 5.3-5.6 µg/kg body weight/day (lower bound to upper bound range), which is below the safe upper level of 7.5 µg/kg body weight/day set by the EVM in 2003[9]. This safe upper level was based on a LOAEL of 0.91 mg/day, derived from an epidemiological dietary study in which signs of selenosis (prolonged prothombin time, morphological changes in the nails, and increased white blood cell count) were observed in individuals with selenium blood levels of 1.054 to 1.854 mg/L, which were calculated to represent a selenium intake of 0.91 mg/day. An uncertainty factor of 2 was applied to extrapolate from the LOAEL to a NOAEL. A larger uncertainty factor was not considered necessary because the intake of 0.91 mg/day produced only slight effects and was close to a NOAEL. Dietary supplements can provide up to 0.3 mg/day (5 µg/kg body weight/day for a 60 kg adult), which together with intake from food and water would not result in the safe upper level being exceeded in adults.

86. The Committee concluded that the estimated dietary exposures to selenium were not of toxicological concern.

Strontium

87. Strontium occurs in nature chiefly as the minerals celestite ($SrSO_4$) and strontianite ($SrCO_3$), which are widespread in rocks and waters. Strontium is present in small quantities in most plants. Strontium was last analysed in a TDS in 1994, when the estimated average population dietary exposure was 1.3 mg/day, which the COT concluded to be of no health concern[2]. The population dietary exposure estimate for 2006 was comparable (1.2 mg/day). There are no health based guidance values for strontium. No data are available on levels of strontium in drinking water in the UK.

88. There are no epidemiological data concerning the health effects of strontium, although there is a long history of clinical use of strontium in the treatment and prevention of osteoporosis, and relatively high levels of strontium (1700 mg/day) have been given without any clear evidence of toxicity. This dose is equivalent to 28 mg/kg body weight/day for a 60kg adult. The Medicines and Healthcare products Regulatory Agency (MHRA) issued a warning in November 2007 related to hypersensitivity reactions to the molecule, strontium ranelate (also known as protelos), a drug used to treat postmenopausal osteoporosis[72]. The mechanism of this hypersensitivity is unknown and therefore it is uncertain whether it is related to the strontium ion, the molecule as a whole or a specific component. In rat studies, NOAELs of 190 mg/kg body weight/day (bone changes, 20-day study) and 15 mg/kg

body weight/day (increased thyroid and pituitary weights, and increased thyroid activity, 90-day study) have been reported. The margin of exposure between the human therapeutic dose and the highest estimated dietary exposure (71.1 µg/kg body weight/day; high-level intake by pre-school children) is 400 (rounded to the nearest 10). The Committee concluded that current dietary exposures to strontium were unlikely to be of toxicological concern.

Thallium

89. Thallium is ubiquitous in nature and occurs in sulphide ores of various heavy metals (zinc, copper, iron and lead) at low concentration (<2 mg/kg)[73]. Thallium has two oxidation states, 1+ and 3+, both of which can have effects on the central and peripheral nervous systems, the skin, the gastrointestinal tract, the cardiovascular system, and the kidney. The more water-soluble salts are considered to have greater toxicity than the salts of lower water solubility[17]. In areas with a naturally high concentration of thallium in soil (such as Macedonia), the majority of vegetables, fruits and meat contain less than 1 mg/kg[73].

90. Thallium was last analysed in a TDS in 1994. Since 1994, estimated population dietary exposures have decreased from 2 µg/day to 0.7-0.8 µg/day. The COT previously concluded that there was no evidence that dietary intake of thallium by the UK population was harmful to health[2]. There are no health based guidance values for thallium. No data are available on levels of thallium in drinking water in the UK.

91. The WHO considered that exposures causing urinary thallium concentrations below 5 µg/L were unlikely to cause adverse health effects in humans[73]. In the range of 5-500 µg/L the magnitude of the risk and severity of adverse effects were uncertain, while exposures giving values over 500 µg/L had been associated with clinical poisoning[73]. The estimated daily oral intake corresponding to a urinary thallium concentration of 5 µg/L was determined to be approximately 10 µg/day as a soluble form of thallium, or 0.17 µg/kg body weight/day for a 60kg adult. The margin of exposure between this daily oral human intake and the highest estimated dietary exposure (0.046 µg/kg body weight/day; high-level intake by pre-school children) is approximately 4. The Committee concluded that current dietary exposures to thallium were unlikely to be of toxicological concern.

Tin

92. Tin is rarely found as the metallic element in nature but is more usually found combined with other substances, most commonly as the dioxide[9]. It has oxidation states of II and IV. Inorganic tin is of low toxicity, whereas some organotin compounds are potent neurotoxicants, though these are not normally present in food, beverages or food supplements[9,17]. No data are available on levels of tin in drinking water in the UK.

93. The estimates of dietary exposures to tin for high-level intake by pre-school children were lower than the JECFA PTWI of 2000 µg/kg body weight/day, but

exceeded the EVM guidance level of 220 μg/kg body weight/day by approximately 55%. All other estimated subgroup dietary exposures (mean- and high-level intakes) were within the EVM guidance level. Dietary supplements can provide up to 10 μg/day (0.17 μg/kg body weight/day for a 60 kg adult), which would not lead to the guidance level being exceeded by adults. The PTWI, originally set as a provisional maximum tolerable daily intake in 1982, is not directly applicable to long term dietary exposures since it appears to be based on intakes associated with acute toxicity (the threshold concentration for manifestation of gastric irritation). The EVM guidance level was based on a NOAEL of 1000 mg/kg diet of stannous chloride (corresponding to an intake in the range of 22-33 mg tin/kg body weight/day) from a sub-chronic study in rats, in which anaemia and changes to liver cells were observed at higher doses. The EVM used the lower end of the NOAEL range (22 mg/kg body weight/day) and an uncertainty factor of 100 to derive the guidance level of 220 μg/kg body weight/day[9]. The Committee concluded that the small exceedance of this guidance level is within an area of uncertainty, but that current dietary exposures were unlikely to be of toxicological concern.

Zinc

94. Zinc is an essential trace element, occurring in nature as the sulphide, the silicate, and the oxide[9]. It is found in virtually all food and potable water. Zinc concentrations in tap water can be much higher than those of surface and ground waters as a result of the leaching of zinc from piping and fittings[27]. The WHO noted that drinking water makes a negligible contribution to zinc intake unless high concentrations of zinc occur as a result of corrosion of piping and fittings. The WHO did not derive a guideline value for drinking water quality but noted that drinking water containing zinc at levels above 3 mg/L may not be acceptable to consumers[27]. Excessive zinc intake interferes with copper absorption, potentially leading to copper deficiency, which can result in conditions such as anaemia and bone abnormalities. The current estimated dietary exposures to zinc for all subgroups were below or in the region of the EVM safe upper level (700 μg/kg body weight/day) and within the JECFA PMTDI of 1000 μg/kg body weight/day. Dietary supplements can provide up to 50 mg/day (833 μg/kg body weight/day for a 60 kg adult), which exceeds the safe upper level before taking into account the diet. The Committee concluded that current dietary exposures to zinc, excluding supplements, were unlikely to be of toxicological concern.

Conclusions

95. We *conclude* that current dietary exposures to antimony, cadmium, copper and selenium are not of toxicological concern. We *note* that this conclusion with respect to cadmium might need to be reviewed after the current risk assessment by the European Food Safety Authority (EFSA) is published.

96. We *conclude* that current dietary exposures to bismuth, chromium, germanium, mercury, nickel, strontium, thallium, tin and zinc are unlikely to be of toxicological concern.

97. We *note* that whilst the estimates of dietary exposure to aluminium are not markedly higher than previous estimates, they present uncertainty with regard to the safety of aluminium in food in light of new data that led to the recent reduction in the Provisional Tolerable Weekly Intake (PTWI), which is exceeded by some population subgroups. There is a need for further information on possible sources and forms of aluminium in the diet and their bioavailability.

98. The data on arsenic appear consistent with previous surveys of total and inorganic arsenic in food, which we reviewed in 2003. We *reaffirm* our previous conclusions that current dietary exposure to organic arsenic is unlikely to constitute a risk to health. Our advice remains that exposure to inorganic arsenic should be as low as reasonably practicable (ALARP).

99. We *note* that the tolerable daily intake (TDI) for barium is based on studies in which no effects were observed and thus may be over-precautionary. Therefore, the estimated exposures, which exceeded the TDI by up to 4-fold, are not necessarily a toxicological concern. We *recommend* that further research be carried out to allow a TDI to be set with more confidence and to investigate the bioavailability of barium; especially from foods with relatively high levels such as nuts.

100. Population dietary exposures to indium and molybdenum are similar to previous studies and although there is uncertainty, the sparse data on the oral toxicity of indium and molybdenum do not suggest that the estimated intakes give cause for toxicological concern.

101. We *note* that estimates of dietary exposure to lead have not increased since the previous survey. At these dietary intakes, adverse effects, if any, are likely to be very small. However, since it is not possible to identify a threshold for the association between lead exposure and decrements in intelligence quotient, efforts should continue to reduce lead exposure from all sources.

102. We *conclude* that there is insufficient information to determine whether there are risks associated with dietary exposure to manganese. However dietary exposures to manganese in adults have remained fairly constant since monitoring began in 1983, and there is no basis for assuming any concern for health.

103. The toxicological database on palladium metal and its compounds is extremely limited. However, we *conclude* that from the available data, there is no reason to believe that current intakes of palladium from the diet pose a risk to health.

104. Despite a dearth of information on the effects of low doses of platinum, rhodium and ruthenium, we *conclude* that current dietary exposures do not suggest a reason for concern as the levels present in the food samples tested were very low or undetectable.

105. We *recommend* that in future research and surveys of elements in food, priorities should include:

- Information on the forms of aluminium in food and their bioavailability.

- Clarification of the large variability in aluminium concentrations in food and whether these represent an increasing trend.
- Assessment of the bioavailability of barium in nuts compared to barium chloride in water.
- A long-term human study with a large number of subjects to examine the effect of barium on blood pressure and to investigate renal end-points following oral exposure to barium in drinking water, to allow a TDI to be set with more confidence.
- Information on the bioavailability of manganese, particularly from beverages that are the principal contributing food group.

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December 2008

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Table 1: Comparison of the estimated dietary intakes of each element for each population group with the relevant health based guidance values

Estimated Dietary Exposure (µg/kg bw/day)[1, 2, 3]													
Element	**Adults**		**Pre-school children (1.5 - 4.5 years)**		**Young people (4-18 years)**		**Elderly (free living)**		**Elderly (institutional)**		**Vegetarians[4]**		**Health Based Guidance Values[5]**
	Mean	High level	Mean	High level	Mean	High level	Mean	High level	Mean	High level	Mean	High level	
Aluminium	71	144	187	345	123	246	59	135	58	167	87	151	JECFA PTWI equivalent to 143 µg/kg bw /day
Antimony	0.032 - 0.033	0.059 - 0.060	0.075 - 0.077	0.13 - 0.14	0.049 - 0.050	0.096 - 0.097	0.027	0.054	0.023 - 0.024	0.062	0.035 - 0.036	0.06	TDI of 6 µg/kg bw /day derived by WHO
Arsenic (Total)	1.7	6.8 - 6.9	2.7 -2.8	12	1.9 - 2.0	8.2	1.7 - 1.8	6.4	1.20	5.02	1. 6	8.70	COT has concluded that there are no appropriate health based guidance values.
Arsenic (Inorganic)	0.028 - 0.093	0.071 - 0.165	0.075 - 0.246	0.174 - 0.402	0.055 - 0.158	0.128 - 0.291	0.024 - 0.079	0.066 - 0.149	0.025 - 0.072	0.082 - 0.173	0.035 - 0.100	0.079 - 0.163	JECFA PTWI equivalent to 2.1 µg/kg bw /day COT concluded exposure should be ALARP.
Barium	9.40	45.3	22.2	85.0	14.4	64.8	6.4	24.5	4.64	11.7	14.2	63.3	TDI of 20 µg/kg bw/day derived by WHO
Bismuth	0.015 - 0.022	0.034 - 0.044	0.086 - 0.10	0.20 - 0.22	0.034 - 0.046	0.09 - 0.11	0.016 - 0.022	0.037 - 0.046	0.018 - 0.024	0.049 - 0.061	0.020 - 0.027	0.048 - 0.056	N/A
Cadmium	0.14 - 0.17	0.25 - 0.29	0.37 - 0.45	0.65 - 0.75	0.27 - 0.31	0.50 - 0.57	0.13 - 0.15	0.26 - 0.29	0.11 - 0.13	0.30 - 0.35	0.17 - 0.20	0.30 - 0.32	JECFA PTWI equivalent to 1 µg/kg bw /day
Chromium*	0.28 - 0.37	0.50 - 0.62	0.81 - 1.03	1.38 - 1.67	0.51 - 0.65	1.03 - 1.22	0.25 - 0.32	0.48 - 0.59	0.27 - 0.28	0.56 - 0.70	0.31 - 0.40	0.54 - 0.68	EVM guidance level of 150 µg/kg bw /day

Table 1: Comparison of the estimated dietary intakes of each element for each population group with the relevant health based guidance values *continued*

Estimated Dietary Exposure (µg/kg bw/day)[1, 2, 3]													
Element	**Adults**		**Pre-school children (1.5 - 4.5 years)**		**Young people (4-18 years)**		**Elderly (free living)**		**Elderly (institutional)**		**Vegetarians[4]**		**Health Based Guidance Values[5]**
	Mean	High level	Mean	High level	Mean	High level	Mean	High level	Mean	High level	Mean	High level	
Copper*	17.23	34.47	44.71	77.82	29.41	54.92	16.09	45.70	13.38	43.36	18.34	29.96	JECFA PMTDI of 500 µg/kg bw /day EVM safe upper limit of 160 µg/kg bw /day
Germanium	0.001 - 0.018	0.002 - 0.033	0.002 - 0.053	0.006 - 0.085	0.001 - 0.032	0.004 - 0.058	0.001 - 0.016	0.002 - 0.029	0.001 - 0.015	0.002 - 0.036	0 - 0.02	0 - 0.032	N/A
Indium	0.06 - 0.24	0.22 - 0.47	0.24 - 0.75	0.93 - 1.48	0.13 - 0.44	0.51 - 0.97	0.05 - 0.21	0.25 - 0.46	0.04 - 0.18	0.19 - 0.45	0.10 - 0.29	0.36 - 0.57	N/A
Lead	0.09 - 0.10	0.17 - 0.18	0.21 - 0.25	0.38 - 0.42	0.13 - 0.15	0.26 - 0.30	0.08 - 0.09	0.16 - 0.17	0.06 - 0.07	0.17 - 0.19	0.12	0.20 - 0.21	JECFA PTWI equivalent to 3.6 µg/kg bw /day
Manganese*	67	124	168	305	106	201	56	112	50	121	78	135	EVM guidance level of 200 or 150 (elderly) µg/kg bw /day
Mercury	0.02 - 0.05	0.10 - 0.13	0.04 - 0.12	0.17 - 0.26	0.03 - 0.08	0.11 - 0.18	0.02 - 0.05	0.09 - 0.12	0.02 - 0.04	0.07 - 0.12	0.02 - 0.05	0.12 - 0.15	JECFA PTWI for methyl mercury is equivalent to 0.23 µg/kg bw /day
Molybdenum*	1.6	3.0 - 3.1	4.8 - 4.9	7.5 - 8.3	3.0	5.8	1.4 - 1.5	3.0	1.3 - 1.4	3.5	2.0	3.3 - 3.4	N/A
Nickel	1.5 - 1.6	3.0 - 3.1	4.2 - 4.9	7.5 - 8.3	2.6 - 3.1	5.3 - 5.8	1.3 - 15	2.6 - 3.0	1.1 - 1.4	2.8 - 3.5	1.9 - 2.1	3.5 - 3.4	EVM guidance level of 4.3 µg/kg bw/day; TDI of 12 µg/kg bw/day derived by WHO
Palladium	0.009	0.015 - 0.016	0.027	0.055 - 0.056	0.016	0.032	0.008	0.015	0.007	0.018	0.010	0.018	N/A

Table 1: Comparison of the estimated dietary intakes of each element for each population group with the relevant health based guidance values *continued*

Estimated Dietary Exposure (µg/kg bw/day)[1, 2, 3]													
Element	**Adults**		**Pre-school children (1.5 - 4.5 years)**		**Young people (4-18 years)**		**Elderly (free living)**		**Elderly (institutional)**		**Vegetarians[4]**		**Health Based Guidance Valuess[5]**
	Mean	High level	Mean	High level	Mean	High level	Mean	High level	Mean	High level	Mean	High level	
Platinum	0 – 0.029	0 – 0.051	0 – 0.082	0 – 0.130	0 – 0.048	0 – 0.089	0 – 0.025	0 – 0.045	0 – 0.033	0 – 0.055	0 – 0.031	0 – 0.050	N/A
Rhodium	0 - 0.029	0 - 0.051	0 - 0.082	0 - 0.13	0 - 0.048	0 - 0.089	0 - 0.025	0 - 0.045	0 - 0.023	0 - 0.055	0 - 0.031	0 - 0.050	N/A
Ruthenium	0.0004 - 0.010	0.001 - 0.018	0.0008 - 0.029	0.0022 - 0.047	0.0005 - 0.017	0.0013 - 0.032	0.0003 - 0.0087	0.0009 - 0.016	0.0002 - 0.0081	0.001 - 0.02	0.0007 - 0.011	0.0015 - 0.018	N/A
Selenium*	0.83 - 0.95	1.65 - 1.79	1.97 - 2.27	3.77 - 4.10	1.27 - 1.44	2.60 - 2.84	0.73 - 0.82	1.48 - 1.60	0.59 - 0.68	1.58 - 1.74	0.64 - 0.76	1.43 - 1.54	EVM safe upper level of 7.5 µg/kg bw/day
Strontium	15.6	30.6	42.8	71.1	25.9	51.0	14.0	26.6	12.0	29.2	20.5	35.9	N/A
Thallium	0.011 - 0.012	0.020 - 0.021	0.024 - 0.027	0.043 - 0.046	0.016 - 0.018	0.032 - 0.035	0.009 - 0.01	0.017 - 0.018	0.007 - 0.008	0.017 - 0.019	0.010 - 0.011	0.018 - 0.019	N/A
Tin	23	82	89	341	48	191	20	93	13	68	35	132	EVM guidance level of 220 µg/kg bw/day
Zinc*	141	268	387	776	232	478	122	261	104	252	93	162	JECFA PTDI of 1000 µg/kg bw/day; EVM safe upper level of 700 µg/kg bw/day

Table 1 Notes

1. The method for calculating estimated exposures is described in the text.
2. Where an element was not detected in some food groups, the estimated exposures have been expressed as a range from a lower bound (in which it was assumed that all non-detectable concentrations were zero) to an upper bound (in which all non-detectable concentrations were assumed to be at the limit of detection). Where only one value is shown, this is either because all samples contained concentrations above the limit of detection (therefore the upper and lower bound mean values are equal) or because the difference between them is negligible. In the calculation of upper bound exposures for inorganic arsenic, the concentration in the food groups was assumed to be equal to the concentration of total arsenic (since this was lower than the LOD for inorganic arsenic) except in the case of the poultry food group where it was considered to be equal to the LOD.
3. All figures have been rounded off as appropriate.
4. Some of the respondents to the dietary survey of vegetarians were consumers of fish.
5. Health based guidance values taken from: (i) the Joint FAO/WHO Expert Committee on Food Additives (JECFA) which set Provisional Tolerable Weekly Intakes (PTWI) and Provisional (Maximum) Tolerable Daily Intakes (P(M)TDI); (ii) the World Health Organization (WHO) which set Tolerable Daily Intakes (TDI); and (iii) the Expert Group on Vitamins and Minerals (EVM) which set safe upper levels and guidance levels; N/A = none available.

* Essential trace elements.

Table 2a. Comparison of average population dietary exposures of aluminium (Al), antimony (Sb), arsenic (As), barium (Ba), bismuth (Bi), cadmium (Cd), chromium (Cr), copper (Cu), Germanium (Ge), Indium (In) and lead (Pb) from UK Total Diet Studies 1976 to 2006

Year	Population dietary exposure (mg/day)[1-4]											
	Al	Sb	Total As	Inorganic As	Ba	Bi	Cd	Cr	Cu	Ge	In	Pb
1976	n.d.	n.d.	0.075	n.d.	n.d.	n.d.	0.02	0.13	1.8	n.d.	n.d.	0.11
1977	n.d.	n.d.	0.1	n.d.	n.d.	n.d.	0.018	0.17	1.8	n.d.	n.d.	0.1
1978	n.d.	n.d.	0.081	n.d.	n.d.	n.d.	0.02	0.1	1.6	n.d.	n.d.	0.11
1979	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.017	n.d.	n.d.	n.d.	n.d.	0.09
1980	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.026	n.d.	n.d.	n.d.	n.d.	0.12
1981	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.019	n.d.	n.d.	n.d.	n.d.	0.08
1982	n.d.	n.d.	0.09	n.d.	n.d.	n.d.	0.018	n.d.	1.3	n.d.	n.d.	0.069
1983	n.d.	n.d.	0.07	n.d.	n.d.	n.d.	0.018	n.d.	1.2	n.d.	n.d.	0.067
1984	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.019	0.073	1.4	n.d.	n.d.	0.065
1985	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.018	n.d.	1.3	n.d.	n.d.	0.066
1986	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.017	n.d.	n.d.	n.d.	n.d.	0.06
1987	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.018	n.d.	n.d.	n.d.	n.d.	0.06
1988	3.9	n.d.	n.d.	n.d.	n.d.	n.d.	0.019	n.d.	n.d.	n.d.	n.d.	0.06
1991	10	n.d.	0.07	n.d.	n.d.	n.d.	0.018	0.25	1.4	n.d.	n.d.	0.028
1994	11	0.003	0.063	n.d.	0.58	0.0004	0.014	0.34	1.2	0.004	n.d.	0.024
1995	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
1997	3.4	n.d.	0.065	n.d.	n.d.	n.d.	0.012	0.1	1.2	n.d.	n.d.	0.026
1999	n.d.	n.d.	0.05	0.0009 - 0.005	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
2000	4.7	n.d.	0.055	n.d.	n.d.	n.d.	0.009	0.046	1.3	n.d.	n.d.	0.0073-0.0074
2006[5]	5.4	0.0025	0.061 - 0.064	0.0014 - 0.007	0.847 - 0.848	0.002	0.011 - 0.013	0.022 - 0.029	1.24	0.0001 - 0.0015	0.005 - 0.019	0.006 - 0.007

Table 2b. Comparison of average population dietary exposures of manganese (Mn), mercury (Hg), molybdenum (Mo), nickel (Ni), palladium (Pd), platinum (Pt), rhodium (Rh), ruthenium (Ru), selenium (Se), strontium (Sr), thallium (Tl), tin (Sn) and zinc (Zn) from UK Total Diet Studies 1976 to 2006

Year	Population dietary exposure (mg/day)[1-4]												
	Mn	Hg	Mo	Ni	Pd	Pt	Rh	Ru	Se	Sr	Tl	Sn	Zn
1976	n.d.	0.005	n.d.	0.33	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	4.4	10
1977	n.d.	0.005	n.d.	0.26	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	4.2	10
1978	n.d.	0.005	n.d.	0.27	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	3.6	10
1979	n.d.	0.004	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	3.2	n.d.
1980	n.d.	0.005	n.d.	0.27	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
1981	n.d.	n.d.	n.d.	0.23	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	2.4	n.d.
1982	n.d.	0.003	n.d.	0.15	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	3.1	10
1983	4.6	n.d.	n.d.	0.15	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	2.3	10
1984	5.3	n.d.	n.d.	0.16	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	2.7	10
1985	5.0	n.d.	0.11	0.14	n.d.	n.d.	n.d.	n.d.	0.063	n.d.	n.d.	1.7	10
1986	n.d.	n.d.	n.d.	0.13	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	2.2	n.d.
1987	n.d.	n.d.	n.d.	0.15	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	2.0	n.d.
1988	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
1991	6.2	0.002	0.11	0.17	n.d.	n.d.	n.d.	n.d.	0.060	n.d.	n.d.	5.3	10
1994	4.9	0.004	0.11	0.13	0.001	0.0002	0.0003	0.004	0.043	1.3	0.002	2.4	8.4
1995	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.039[5]	n.d.	n.d.	n.d.	n.d.
1997	n.d.	0.003	n.d.	0.13	n.d.	n.d.	n.d.	n.d.	0.039	n.d.	n.d.	1.8	8.4
2000	4.9	0.0012-0.0015	n.d.	0.13	n.d.	n.d.	n.d.	n.d.	0.032-0.034	n.d.	n.d.	1.4	8.4
2006[5]	5.24	0.001 - 0.003	0.123 - 0.125	0.127 - 0.129	0.0007	0 - 0.0023	0 - 0.0023	0.00003 - 0.00081	0.048 - 0.058	1.20	0.0007 - 0.0008	1.80 - 1.81	8.8

Tables 2a and 2b Notes

1. Population dietary exposure (mg/day): the average consumption of the population, estimated by multiplying the amounts of food consumed (based on consumption data from the EFS) by the corresponding upper and lower bound mean elemental concentrations in each food group.
2. The population dietary exposures in the previous years were estimated using upper bound mean concentrations for each food group and consumption data taken from the National Food Survey 1997. The exception to this is the 2000 TDS where exposures have been estimated from the lower and upper bound mean concentrations and included as ranges where they apply.
3. Changes in the organisation of the TDS from 1981 onwards mean that exposures from TDSs before 1981 and from 1981 onwards are not directly comparable[6].
4. For those years where no values are given, these elements were not included in TDSs for metals and other elements i.e. n.d.= not determined.
5. Dietary exposure estimates for the 2006 TDS and for selenium from the 1995 TDS are not directly comparable with those from other years as they are based on analyses of composite samples of each food from all the towns in the TDS rather than the upper bound mean concentrations of analyses of each food group from each town.

Table 3: Estimated tap water intakes for those elements for which information is available

Element[6]	Concentration (µg/L)	Estimated tap water exposure (µg/kg bw/day) [5]			
		Pre-school children	Young people	Adults	Elderly
Aluminium	158 [1]	25	9.4	6.2	4.5
Antimony	1.967 [1]	0.31	0.18	0.077	0.056
Arsenic	7.871 [1]	1.2	0.47	0.31	0.22
Barium	700[4]	111	41.7	27.3	20
Cadmium	1.0418 [1]	0.17	0.062	0.041	0.030
Chromium	11.774 [1]	1.9	0.70	0.46	0.33
Copper	2000 [2]	317	119	78	57
Lead	25 [3]	4.0	1.5	0.97	0.71
Manganese	31.75 [1]	5.0	1.9	1.2	0.90
Mercury	0.3404 [1]	0.054	0.020	0.013	0.0097
Molybdenum	70[4]	11.1	4.2	2.73	2
Nickel	17.914 [1]	2.8	1.1	0.70	0.51
Selenium	9.634 [1]	1.5	0.57	0.38	0.27

Table 3 Notes

[1] Maximum (99th percentile) concentration reported for 2007. Taken from monitoring results at consumer's taps, undertaken annually by each water company[8].
[2] Maximum concentration of 4250 µg/L exceeded The Water Supply (Water Quality) Regulations 2000 for England and Wales[26]. Exposure has been calculated using the regulatory limit as it is assumed that regulatory action is taken for exceedances and that such events are a one-off occurrence.
[3] Maximum concentration of 101.659 µg/L exceeded The Water Supply (Water Quality) Regulations 2000 for England and Wales[26]. Exposure has been calculated using the regulatory limit as it is assumed that regulatory action is taken for exceedances and that such events are a one-off occurrence.
[4] World Health Organization guideline value for drinking water quality[27].
[5] Elemental intakes from tap water were calculated assuming chronic tap water (97.5th percentile) consumptions of 158.429 mL/kg bw/day (pre-school children), 59.558 mL/kg bw/day (young people), 38.943 mL/kg bw/day (adults), and 28.386 mL/kg bw/day (elderly)[15,19,21,22].
[6] There are no regulations or guideline values for bismuth, germanium, indium, palladium, platinum, rhodium, ruthenium, strontium, thallium, tin, and zinc