TOX/2008/29

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

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). Estimates of dietary exposure have been calculated for each of the twenty four elements using food consumption data taken from the National Food Survey and the National Diet and Nutrition Surveys (NDNS).

2. The Committee is invited to comment on the results of this survey (attached at Annex A). To aid the discussions, the Committee is referred to the brief summary of toxicology for each of the elements surveyed (Annex B). 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 the 2000 TDS in 2003 and published a Statement (COT, 2003a).

Current survey

3. 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 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 make assessments on the safety and quality of the food supply. Analysis for metals and other elements in the TDS is carried out every 3 years.

4. The design of the UK TDS has been described in detail elsewhere (Peattie *et al.*, 1983) 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 consumption data from the National Food Survey. Foods are grouped so that commodities known to be susceptible to contamination (e.g. offal, fish) are kept separate, as are foods which are consumed in large quantities (e.g. bread, potatoes, milk) (MAFF, 1994; Peattie *et al.*, 1983).

5. Twenty four elements were measured in the 2006 TDS. Foods representing the average UK diet are purchased from different towns, prepared and combined into groups of similar foods for subsequent analysis. Each food group obtained from each town was analysed for the twenty four elements of interest. The results of the TDS are used to estimate dietary exposures of the general UK population to chemicals in food. Annex A contains the draft Food Survey Information Sheet (FSIS) of the 2006 TDS, which gives the background to the TDS (pages 2-3), the methods used (pages 3-4) and the results (pages 4-21, Tables 2-8).

6. Table 1 in this cover paper gives a comparison of the estimated dietary intakes of each element for each age group for which consumption data are available and for vegetarians (taken from Tables 4a – 4d in Annex A) with the relevant safety guidelines for each element (where they exist, taken from the toxicity summary provided in Annex B). Tables 2a and 2b in this paper give a comparison of the population dietary exposures to the twenty four elements from the UK total diet studies dating back to 1976 (taken from Tables 6a and 6b in Annex A). Annex B is an updated review of the toxicity summaries previously included in papers TOX/2003/39 and TOX/98/4 for the COT discussions on the results of the 2000 and 1994 total diet studies, respectively.

Previous surveys

7. The COT has considered the results for metals and other elements for two previous total diet studies, conducted in 1994 and 2000.

8. In 1998 the COT considered estimates of intakes by adults in the UK of antimony, barium, bismuth, germanium, gold, iridium, palladium, platinum, rhodium, ruthenium, strontium and thallium in the diet, from the 1994 TDS. Acknowledging a number of limitations, the Committee concluded that there was no evidence to suggest that any of the estimated intakes should be a cause for concern (COT, 1998). The limitations noted by the Committee were:

a) *The chemical forms of the elements in food are not known. The relevance of the available toxicity data is therefore uncertain.*
b) *The estimates of intake assume that, where an element has not been detected, it is present at the limit of detection. Intakes in these cases are therefore dependent on the limit of detection (or other limit) assigned and can be regarded as overestimates, possibly by a considerable margin.*
c) *The toxicity data available to us are inadequate for complete evaluation of any of these elements in the diet, particularly germanium, gold, iridium, palladium, rhodium and ruthenium.*
d) *The data are insufficient to allow the identification of groups of individuals who might be particularly susceptible to any adverse health effects from dietary intakes of these elements. Consequently, our evaluation applies to healthy adults.*

9. In 2003, the COT commented on the results of the 2000 TDS and assessed whether the levels of each element surveyed in the diet posed a risk to human health. The 2000 TDS surveyed twelve metals and other elements in the diet (aluminium, arsenic, cadmium, chromium, copper, lead, manganese, mercury, nickel, selenium, tin and zinc). Having considered the results of the survey the COT produced a statement (COT, 2003a). The conclusions of this statement were:

i) *We conclude that current dietary exposures to aluminium, cadmium, chromium, copper, mercury, nickel, selenium, tin and zinc are unlikely to be of any toxicological concern for consumers.*

ii) *We note that the current survey measured total arsenic only, but that the data appear consistent with a survey of total and inorganic arsenic in food, which we reviewed recently. We reaffirm our previous conclusions that current dietary exposure to organic arsenic is unlikely to constitute a hazard to health, and exposure to inorganic arsenic should be as low as reasonably practicable (ALARP).*

iii) *We note that estimates of total exposure to lead, including that from the diet, do not exceed the PTWI. We conclude that current dietary intakes are unlikely to result in adverse effects, but that efforts should continue to reduce exposure to lead from all sources.*

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

v) *We recommend that in future surveys of elements in food, priority should be given to those of greatest toxicological concern, such as arsenic, mercury and lead. Speciation of metals such as mercury, arsenic and chromium would be helpful for the risk assessment.*

Dietary exposure assessment

10. The exposure assessments reported for the 2006 TDS are based on combining concentration data following analysis of the food groups with corresponding consumption data. The main source of data used by the FSA for estimating food consumption is the NDNS (Henderson *et al.*, 2002; Gregory *et al.*, 1990). The NDNS has been conducted as a series of cross-sectional surveys of diet and nutritional status covering the population from age 18 months upwards; data from approximately 2000 individuals in each of four age groups have been collected. 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 consumed were estimated by weighing foods eaten at home using

digital scales. Quantities of foods eaten outside the home are estimated from descriptions and household measures. The dietary information was recorded "as consumed" so recipes are required to consider 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 covers a 12-month period to account for possible seasonal variations in eating habits. Other surveys such as the Expenditure and Food Survey (EFS; DEFRA, 2003/04) and the Dietary Survey of Vegetarians are also used for providing 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 makes up the total diet.

11. In general the FSA adopts a hierarchical or tiered approach to select the best method to carry out exposure assessment. The assessment is consistent with the approach adopted by the European Food Safety Authority (EFSA, 2005) and the World Health Organization (WHO, 2000a). Current policy on exposure assessment of chemicals has been to use deterministic and distributional methods.

12. The vast majority of FSA exposure assessments are carried out using an in-house software known as the Intake Programme. The Intake Programme is a bespoke statistical software which allows the estimation of dietary exposure to food chemicals. The software estimates exposure values by using the levels of chemicals measured in food and combines this information with the amount of that food that is consumed. The food consumption diaries from the NDNS are uploaded onto the Intakes Programme using recipe information and the data are used to derive lists of foods mirroring the TDS samples; the concentrations of the metals analysed in the TDS are also uploaded onto the Intake Programme. The full distribution of exposure is then calculated by the software and plotted for deriving summary statistics for average and high-level (i.e. 97.5^{th} percentile) consumers. The exposures reported for consumers in the 2006 TDS study are presented in Tables 4a - 4d in Annex A. Exposure values are estimated from a range (lower - upper bound) of mean concentrations; that is, where individual sample analyses were less than the limit of detection, the concentration is expressed as zero (lower bound), or as equal to the limit of detection (upper bound) and the exposure calculated accordingly.

13. Exposure estimates were also carried out at the population level in order to follow trends in exposure for the UK population as a whole, as this provides an indication of changes in both consumption of the various foods making up the UK diet and the concentrations of elements in these foods. Population dietary exposures have been estimated by multiplying the amounts of food consumed (based on consumption data from the EFS survey), by the corresponding upper and lower bound mean elemental concentrations in each food group from the TDS study. Comparisons of population dietary exposure for each element from the UK TDS from 1976 to 2000 are given in Tables 5a and 5b in Annex A.

14. Estimates of dietary exposure were compared with available tolerable intakes, such as Provisional Tolerable Weekly intakes (PTWIs) where they exist,, taking into account previous COT evaluations (Table 1). The PTWI is used by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in identifying tolerable intakes of food contaminants with cumulative properties. Within this paper, the PTWI has been by divided by 7 to provide a tolerable daily intake (TDI) for comparison with the estimated daily dietary exposures.

Concentrations of the elements in the foods surveyed

15. Members are referred to pages 4-21 of Annex A for a summary of the population exposures to each element, and the dietary exposures of each age group and vegetarians to each element. Where possible, comparisons have been made to previous surveys to illustrate trends in population dietary exposure. The FSIS in Annex A will be finalised and published after incorporation of the COT views of the results.

16. 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, inorganic arsenic, barium and manganese.

Evaluation

17. As shown in Table 1, estimated mean and high-level intakes of antimony, cadmium, copper and selenium were within the relevant safety guidelines.

18. The COT is invited to consider the following draft conclusion:

> *We conclude that current dietary exposures to antimony, cadmium, copper and selenium are not of toxicological concern.*

19. There are no relevant tolerable intakes or reference doses by which to assess the safety of total or inorganic arsenic, bismuth, germanium, indium, molybdenum, palladium, platinum, rhodium, ruthenium, strontium or thallium.

Aluminium

20. 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 (WHO, 2007a). The PTWI was reduced from 7 mg/kg body weight to 1 mg/kg body weight, and applies to all aluminium compounds, including additives (equivalent to 143 µg/kg body weight/day; WHO, 2007a). 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 (EFSA, 2008a). The EFSA derived the same TWI of 1 mg/kg body weight.

21. The estimates of dietary exposure to aluminium (high-level for adults, toddlers, young people, institutionalised elderly and vegetarian groups; and mean for toddlers) exceeded the PTWI set by JECFA and EFSA (equivalent to 143 µg/kg body weight/day) by up to 2.4-fold. The current population exposure to aluminium (5.4 mg/day) is 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 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 to be possibly 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 (COT, 2003a).

22. In the 20 food groups of the TDS, most groups have aluminium concentrations lower than or similar to those reported in the 2000 TDS, the exceptions being bread, meat products, poultry, other vegetables, canned vegetables and fresh fruits groups. The miscellaneous cereals group has the highest mean concentration of aluminium (17.5 mg per kilogram). This is lower than the concentration in the 2000 TDS (19 mg per kilogram) but is three times more than the value from the 1997 TDS (5.2 mg per kilogram). The levels of aluminium in this group have varied from 4.8 mg per kilogram (1988 TDS) to 78 mg per kilogram (1994 TDS).

23. In the current TDS the miscellaneous cereals group, which comprises cakes, scones, biscuits, breakfast cereals, flour and rice, is the principal dietary contributor to the population dietary 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 (SI, 1995a and b), or a result of processing and storage of food in aluminium containing utensils.

24. It is widely assumed that soluble aluminium compounds are more bioavailable than insoluble compounds (WHO, 2007a). However, the net absorption of aluminium from food is approximately 1%, although this varies based on the chemical forms present in the intestinal tract (EFSA, 2008a; WHO, 2007a). This low bioavailability is due to the formation of aluminium complexes as the pH increases from the stomach to the intestines The bioavailability of aluminium is also influenced by the presence or absence of particular foods and beverages (dietary ligands) in the intestines (EFSA, 2008a).

25. 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; EFSA, 2008a). Variations in dietary exposure may be accounted for by differences in soil composition in the region food is produced, individual dietary patterns and 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, including infants and young children, who have a higher food intake than adults when expressed on a body weight basis (EFSA, 2008a).

26. The COT is invited to consider the following draft conclusion:

> *We note that whilst the estimates of dietary exposure to aluminium are not markedly higher than previous estimates, they lead to uncertainty with regard to the safety of aluminium in food, indicating a need for further information on possible sources and forms of aluminium in the diet.*

Arsenic

27. 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 (COT, 2003a). The current TDS surveyed both total and inorganic arsenic but did not consider other sources of exposure.

28. 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 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 (0.015 mg/kg body weight) in 1989 would now not be considered appropriate, in view of the evidence of genotoxicity and carcinogenicity (COT, 2003b). 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 (WHO, 1989). The COT concluded that inorganic arsenic is genotoxic and a known human carcinogen and therefore exposure should be as low as reasonably practicable (ALARP) (COT, 2003b). 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), including the ratios between inorganic and organic arsenic forms, the contribution of different foodstuffs to exposure, and the exposure of specific population groups. There is currently an open call for data with the objective to collect all available data analysed during the time period from January 2003 to November 2008 (EFSA, 2008b). These data will then be used to produce the EFSA opinion on arsenic in food.

29. The estimates of population dietary exposures to total arsenic in the 2006 TDS are 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;

COT, 2003b). The current population exposure to total arsenic is 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 noted that fish was the major contributor to dietary exposure to arsenic and the predominant form of arsenic in fish is organic. Inorganic arsenic contributed less than 10% of the total dietary exposure to arsenic in 1999. Similarly, the results of the most recent TDS indicate that fish is the major contributor to dietary arsenic exposure and that inorganic arsenic contributes approximately less than 11% of the total dietary exposure.

30. When considering the population dietary exposures to total arsenic since 1976, intakes have fluctuated but the general trend appears to be downwards. Therefore, the previous COT conclusions appear still valid, that is, the organic arsenic component is unlikely to constitute a hazard to health. The population dietary exposure to inorganic arsenic is 0.0014 - 0.007 mg/day and is comparable to the range reported in 1999 (0.0009 - 0.005 mg/day; COT, 2003b) and therefore does not raise concern. Furthermore, although there is uncertainty regarding whether the JECFA PTWI for inorganic arsenic is sufficiently protective, all population groups' dietary exposures were less than 20% of the PTWI, 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 (Table 1)..

31. In the estimation of lower bound consumer dietary exposures, the contribution from the miscellaneous cereals and fish groups alone were considered. In the calculation of upper bound exposures, the concentration of inorganic arsenic in the rest of the food groups was assumed to be equal to the concentration of total arsenic (since this was lower than the limit of detection for inorganic arsenic) except in the case of the poultry food group where it was considered to be equal to the limit of detection for inorganic arsenic.

32. The COT is invited to consider the following draft conclusions:

> *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 hazard to health. The evidence that exposure to inorganic arsenic has not increased from the previous survey indicates that the exposure is as low as reasonably practicable (ALARP).*
>
> *We note that the risks to human health from the presence of arsenic in foodstuffs might need to be reviewed after the EFSA opinion is published.*

Barium

33. Population dietary exposures to barium have increased by approximately 46%, since the last TDS in 1994. The WHO derived a TDI of 20

µg/kg body weight/day in 2001 (WHO, 2001). The estimates of dietary exposure to barium for toddlers (mean and high-level) and high level adults, young people, free living elderly, and vegetarians, all exceed the WHO TDI of 20 µg/kg body weight/day by up to 4.3-fold. As with the results from 1994, the highest levels of barium in the current survey were reported in nuts (131 mg/kg) and bread (0.81 mg/kg); and all other foodstuffs contained lower levels than for breads. Levels of barium in nuts are double those reported in 1994 (131 mg/kg and 56 mg/kg, respectively).

34. The most prevalent route of exposure to barium compounds for the general population is oral intake via the drinking water and food, with food generally being the primary source. In humans, ingestion of high levels of soluble barium compounds may cause gastroenteritis, hypokalaemia and hypertension. The critical end-points for toxicity in humans are hypertension and impaired renal function. The WHO identified a NOAEL for effects on blood pressure in humans of 0.21 mg barium/kg body weight/day from a study in which 11 healthy male volunteers were administered drinking water containing barium chloride (0 mg/L for 2 weeks, 5 mg/L for the next 4 weeks, and 10 mg/L for the last 4 weeks). Since there no effects were observed in this study, a LOAEL was not identified. Applying an uncertainty factor of 10 to the NOAEL to allow for database deficiencies and differences between humans resulted in a tolerable intake of 20 µg/kg body weight/day (WHO, 2001). In its Guidelines for Drinking Water, the WHO identified a NOAEL of 7.3 mg/L from an epidemiological study in which a population 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. There were no significant differences in blood pressure or in the prevalence of cardiovascular disease between the two populations, and thus no LOAEL was identified. An uncertainty factor of 10 was applied to the NOAEL to allow for intraspecies variation, resulting in a guideline value of 0.7 mg/L (WHO, 1993a). Assuming a 60 kg adult drinking 2 litres of water per day, this guideline value is equivalent to 23 µg/kg body weight/day and is comparable to the more recent TDI established by the WHO.

35. The population groups that most exceed the TDI are high-level adults (~220% of the TDI), young people and vegetarians (~320%), and level toddlers (~430%). The mean population group exposures were below or in the region of the WHO TDI. Since the TDI is derived from studies in which effects were not observed, it is possible that the NOAEL was very much lower than the LOAEL and hence that the TDI is highly conservative.

36. The COT is invited to consider the following draft conclusion:

> *We conclude that the exceedance of the TDI for barium is within an area of uncertainty but is unlikely to be a toxicological concern.*

Bismuth

37. Bismuth has been analysed previously in the 1994 TDS. Since 1994, population dietary exposures have increased by 5-fold from 0.4 µg/day to 2 µg/day. There are no safety guidelines for bismuth.

38. In 9 patients being treated with tripotassium dicitrato bismuthate for 6 weeks, Gavey *et al.* (1989) found that a daily oral dose of 432 mg/day was without adverse effect. This dose is equivalent to approximately 7 mg/kg body weight/day for a 60kg adult (or 7000 µg/kg body weight/day). The margin of exposure between this human therapeutic dose and the highest estimated dietary exposure (0.217 µg/kg body weight/day; high-level toddlers) 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.

39. The COT is invited to consider the following draft conclusion:

> *We conclude that current dietary exposures to bismuth are unlikely to be of toxicological concern.*

Chromium

40. Almost all of the sources of chromium in the earth's crust are in the trivalent state, naturally occurring chromium compounds in the hexavalent state are rare. The estimates of dietary exposure to chromium (mean and high-level) for all consumer groups were within the EVM guidance level of 150 µg/kg body weight/day. Results from total diet studies indicate that dietary exposures to chromium have been steadily declining since 1991. The current population dietary exposure to chromium is 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) has set no reference nutrient intakes (RNIs) for chromium but suggested that an adequate level of intake for trivalent chromium lies above 0.025 mg/day for adults and between 0.0001 and 0.001 mg/kg body weight/day for children and adolescents (COMA, 1991). Data are lacking for estimating average chromium requirements for adults and NDNS data are not available on chromium intakes, however, the Scientific Advisory Committee on Nutrition (SACN) Secretariat note that there is little evidence of clinical effects of inadequate chromium intake and there are no reports of effects of marginal intakes.

41. The COT is invited to consider the following draft conclusion:

> *We conclude that current dietary exposures to chromium are unlikely to be of toxicological concern.*

Germanium

42. Germanium was last analysed in a TDS in 1994. Since 1994, population dietary exposures have decreased from 4 µg/day to 0.1-1.5 µg/day. Based on the estimated population dietary exposures from the 1994 TDS, the COT concluded that the estimated dietary intakes of germanium in adults did not give cause for concern (COT, 1998). There are no safety

guidelines 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 are insufficient data to define a NOAEL for chronic exposure at levels in excess of this (EVM, 2003). As 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 are unlikely to represent a concern for health.

43. The COT is invited to consider the following draft conclusion:

> *We conclude that current dietary exposures to germanium are unlikely to be of toxicological concern.*

Indium

44. Indium has not been included in a TDS since 1979 when concentrations in cows' milk were found to be low, and the mean daily dietary intake of indium was established as between 5 and 27 µg (MAFF, 1985). In the current survey, the population dietary exposure of indium is comparable at 5 - 19 µg/day. With the exception of the canned vegetables and fruit products groups, indium concentrations are below the limit of detection of 0.003 – 0.02 mg/kg. For these two food groups, indium concentrations are 0.096 mg/kg (canned vegetables) and 0.031 (fruit products).

45. There are no safety guidelines for indium. In 1998 the COT evaluated the results from a multi-element survey of cows' milk and vegetables produced near industrial sites (MAFF, 1998). The COT concluded that the intakes of indium in adults were very low, and that the data indicated the upper bound estimates of dietary intakes in the 1979 TDS were probably significantly inflated by the relatively high limit of detection (0.01 mg/kg) (MAFF, 1998).

46. There are no data or reports of human toxicity from oral indium, however, a lifetime drinking water study in mice suggested a LOAEL of 250 µg/kg body weight/day for growth suppression (Schroeder and Mitchener, 1971). 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 toddlers) is 170 - 270 (rounded to the nearest 10).

47. There are no data on indium toxicity from food and therefore the implications of the estimated dietary exposures to indium and margin of exposure are uncertain. The COT is invited to consider the following draft conclusion:

> *Population dietary exposures to indium are similar to data from 1979, and the sparse data on the oral toxicity of indium do not suggest that the estimated intakes give cause for toxicological concern.*

Lead

48. The highest estimate of dietary exposure to lead is 0.42 µg/kg body weight/day (for high-level toddlers). This is comparable to the estimation 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 (WHO, 1987). At the time of the 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 (WHO, 1993b). 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 (WHO, 1995). 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 (WHO, 2000b).

49. Young children are vulnerable to the effects of lead, because they absorb a higher percentage of ingested lead and are more susceptible to the neurotoxicity, which may result in deficits in Intelligence Quotient (IQ). A UK study of lead intake in children of 2 years of age 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 (Davies *et al.*, 1990). Thus, if dietary exposure to toddlers is within 30% of the JECFA PTWI (i.e. less than 1.08 µg/kg body weight/day), total intake is unlikely to exceed the PTWI. In 2003 the COT commented on a survey in metals in infant food (COT, 2003c). 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 (COT, 2003c).

50. Due to the high number of food groups (15/20) with analysed lead levels at or below the limit of detection, there is uncertainty in the estimation of dietary exposures. Dietary exposures are expressed as lower bound and upper bound mean concentrations; that is, where individual sample analyses were less than the limit of detection, the result is expressed as zero (lower bound), or as equal to the limit of detection (upper bound) and the exposure calculated accordingly. Table 2a illustrates that 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).

51. The concentration of lead in blood is the most widely used biomarker of

exposure and is typically reported in micrograms per decilitre (µg/dL). The most critical effect of lead at low concentrations is reduced cognitive development and intellectual performance in children, and studies have shown an association between blood lead concentrations and reduced IQ in children exposed pre- and post-natally (WHO, 2000b). No threshold for intellectual deficits has been identified but there is evidence of an association at blood lead concentrations below 10 µg/dL (WHO, 2000b). Surveys of blood lead concentrations have indicated reductions in mean blood lead concentrations since the late 1970s (ATSDR, 2007; Koller *et al.*, 2004; WHO, 2000b; WHO, 2007b). Current mean levels in children of developed countries are in the region of 3 µg/dL (Koller *et al.*, 2004). This reduction has been attributed to the reduction in the use of lead in petrol and as a result of programmes to reduce exposure.

52. 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 during the long-term (in utero and for the first 10 years of life) (WHO, 2000b). 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 (ATSDR, 2007). Recent studies have suggested that the dose-effect relationship is steeper than this at blood lead levels below 10 µg/dL, but the lack of a demonstrated convincing biological mechanism which could explain this means that the precise shape of the dose-effect relationship at lower blood lead levels remains uncertain (ATSDR, 2007; Bellinger, 2004; CDC, 2005). There therefore remains no identified threshold.

53. Using the JECFA correlation of dietary intake to blood lead level increase 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 approximately quantify the IQ deficit resulting from exposure of 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 an indicative resulting mean IQ deficit of between 0.36 and 1.8 IQ points. This can be regarded as an approximate of the degree of effect, due to the large number of uncertainties. 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; other factors (in addition to IQ measurement) that describe the neurobehavioural effects of lead. The effect of limits to the precision of analytical and psychometric measurements can further increase the uncertainty of any estimate of the effect of blood lead concentrations below 10 µg/dL.

54. The dietary exposures to lead identified from the 2006 TDS have not

increased since the previous TDS in 2000 and although the JECFA PTWI for lead cannot be considered to be sufficiently protective (i.e. there is an indicative minimal effect at the PTWI), all population groups' dietary exposures are well below the PTWI (Table 1). Therefore, the levels of lead that are currently found in foods would be expected to have negligible effects on the intellectual development of infants and young children.

55. The COT is invited to consider the following draft conclusion:

> *We note that estimates of dietary exposure to lead have not increased since the previous survey and do not exceed the PTWI. We conclude that dietary intakes are unlikely to result in adverse effects, but 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

56. Manganese is an essential trace element that is neurotoxic at high levels of occupational inhalation exposure, but there is limited evidence of neurological effects at lower doses. 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 (EVM, 2003). There is insufficient information to determine whether there are risks associated with dietary exposure to manganese and no available safety guideline.

57. Although there is no available safety guideline for manganese, the EVM considered that, based on the results of epidemiological studies, total manganese intakes of 12.2 mg/day for the general population (equivalent to 0.2 mg/kg body weight/day for a 60kg adult) and 8.7 mg/day for older people (equivalent to 0.15 mg/kg body weight/day) would not result in adverse health effects (EVM, 2003). However, this conclusion was based on a number of assumptions since a major limitation of the two studies used to establish these guideline levels was that they both failed to provide water consumption or dietary manganese intake data. The WHO derived a TDI of 60 µg/kg body weight/day in the Guidelines for Drinking Water Quality (WHO, 2004). This was based on the upper range value of manganese intake of 11 mg/day, identified using dietary surveys at which there were no observed adverse effects. An uncertainty factor of 3 was applied to take into consideration the possible increased bioavailability of manganese from water. With the exception of high-level toddlers, all other population dietary intakes are within the EVM guideline values. High-level toddlers exceed the EVM guideline value by approximately 50%.

58. 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 current study (5.24 mg/day). When the COT commented on the 2000 TDS results with a population dietary exposure of 4.9 mg/day, they concluded that *there is insufficient information to determine*

whether there are risks associated with dietary exposure to manganese. However dietary exposures to manganese have remained fairly constant since monitoring began in 1983, and there is no basis for assuming any concern for health (COT, 2003a).

59. The COT is invited to re-consider the previous conclusions highlighted above in paragraph 58.

Mercury

60. Population exposures to mercury have decreased since 1976 (0.005 mg/day), with the current population dietary exposure (0.001-0.003 mg/day) comparable to that of 2000, when levels were at their lowest (0.0012-0.0015 mg/day). Mercury concentrations are similar to those reported in the 2000 TDS except for the fish group, in which the concentration is 0.056 mg/kg compared to 0.071 mg/kg in 2000.

61. The estimates of dietary exposure to mercury (mean and high-level) 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 (COT, 2003d). The estimate for high-level consumption by toddlers exceeds 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.

62. The COT is invited to consider the following draft conclusion:

> *We conclude that current dietary exposures to mercury are unlikely to be of toxicological concern.*

Molybdenum

63. Population dietary exposures to molybdenum are comparable to previous estimates (0.123-0.125 mg/day vs. 0.11 mg/day in 1985, 1991 and 1994). There are no safety guidelines for molybdenum and there are few reliable data on the oral toxicity of molybdenum. The EVM concluded that the maximum molybdenum intake from the UK diet, 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 (EVM, 2003). Intakes of >1 mg/day could be associated with an increased incidence in gout-like symptoms. The estimated exposure for toddlers and high-level young people exceeded this guidance level buy up to about 2-fold. For all other population groups the estimated dietary exposures are less than 4 µg/kg body weight/day.

64. The COT is invited to consider the following draft conclusion:

> *Population dietary exposures to molybdenum are similar to data from*

previous studies, and the sparse data on the oral toxicity of molybdenum do not suggest that the estimated intakes give cause for toxicological concern.

Nickel

65. The estimates of dietary exposures to nickel for mean and high-level toddlers and high-level young people exceed, 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 (EVM, 2003). However, these exposures are within the WHO TDI of 12 µg/kg body weight/day. 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 level 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 (WHO, 2003). The EVM noted that ingested nickel may exacerbate contact dermatitis/eczema in pre-sensitised individuals (EVM, 2003), however the COT has concluded that toddlers are less likely than adults to be sensitised and would therefore not be considered to be a sensitive group (COT, 2003a).

66. Population exposures to nickel have decreased since 1976 (0.33 mg/day), with the current dietary exposure at its lowest level (0.127-0.129 mg/day) and comparable to results from the 2000 TDS (0.13 mg/day). The COT concluded that the current dietary exposure to nickel from the 2000 TDS was unlikely to be of any toxicological concern for consumers (COT, 2003a).

67. The COT is invited to consider the following draft conclusion:

We conclude that current dietary exposures to nickel are unlikely to be of toxicological concern.

Palladium

68. Palladium was last analysed in a TDS in 1994. Since 1994, 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 concluded that from the available data, there was no reason to believe that current intakes of palladium from the diet posed a risk to health (COT, 1998). However, the COT did note that the toxicological database on palladium metal and its compounds was extremely limited (COT, 1998). There are no safety guidelines for palladium.

69. 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 (Farago *et al.*, 1998). 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 (Ravindra *et al.*, 2004).

70. The WHO concluded that a major source of concern regarding palladium is the sensitisation risk; and that the available data form animal and human findings do not allow identification of a NOAEL for sensitisation in humans (WHO, 2002). However, the WHO noted a 28-day gavage study in rats dosed with tetraamine palladium hydrogen carbonate/kg body weight/day (Johnson Matthey, 1997). Treatment-related abnormalities, confined to histopathological changes, were observed at 5 and 150 mg/kg body weight/day. Although the authors considered 1.5 mg/kg body weight/day to be the NOAEL, 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 and the highest estimated dietary exposure (0.056 µg/kg body weight/day; high-level toddlers) is 9700 (rounded to the nearest 100).

71. Given that population dietary exposures to palladium are comparable to those of 1994 and the large margin of exposure for the highest dietary exposure, the COT is invited to re-consider the previous conclusion and the recommendation to include palladium in future total diet studies:

> *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. However, the toxicological database on palladium metal and its compounds is extremely limited. We recommend that palladium be included in future dietary studies in order to monitor the presence of platinum group metals in the food chain and various components of the diet.*

Platinum

72. Platinum was last analysed in a TDS in 1994, when the 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 population exposure of 0-2.3 µg/day based on the lower-bound to upper-bound approach, which is not clearly different. There are no safety guidelines for platinum.

73. 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 (WHO, 1991). It is not known what form of platinum is present in foods. From the limited available data in 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 the drinking water for 30 days. 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 (COT, 1996).

74. The COT is invited to consider the following draft conclusion:

> *We conclude that current dietary exposures to platinum are unlikely to be of toxicological concern.*

Rhodium

75. Rhodium was last analysed in a TDS in 1994, resulting in an estimated population dietary exposure of 0.3 µg/day. 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, based on the lower-bound to upper-bound approach, which is not clearly different. There are no safety guidelines for rhodium.

76. 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. However, rhodium compounds appear to be less potent than their platinum counterparts.

77. The COT is invited to consider the following draft conclusion:

> *Despite a lack of information on the effects of low doses of rhodium upon man, we conclude that current dietary exposures to rhodium are unlikely to be of any toxicological concern for consumers.*

Ruthenium

78. Ruthenium was last analysed in a TDS in 1994. Since 1994, the estimated population dietary exposure has decreased from 4 µg/day to 0.03-0.81 µg/day. Based on the estimated population dietary exposures from the 1994 TDS, the COT concluded that from the available data, there was no reason to believe that current intakes of ruthenium from the diet pose a risk to health (COT, 1998). However, the COT did note that there were insufficient data upon which a full evaluation could be made (COT, 1998). There are no safety guidelines for ruthenium.

79. 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 appear to be less potent than their platinum counterparts.

80. The COT is invited to consider the following draft conclusion:

> *Despite a lack of information on the effects of low doses of ruthenium, we conclude that current dietary exposures to ruthenium are unlikely to be of toxicological concern.*

Strontium

81. Strontium was last analysed in a TDS in 1994, when the estimated population dietary exposure was 1.3 mg/day. The population dietary exposure estimate for 2006 is comparable (1.2 mg/day). Based on the estimated population dietary exposures from the 1994 TDS, the COT concluded that current dietary levels of exposure to strontium were of no health concern (COT, 1998). There are no safety guidelines for strontium.

82. There are no epidemiological data concerning the health effects of strontium, although there is a long history of use of strontium clinically in the treatment and prevention of osteoporosis, and relatively high levels of strontium have been given (1700 mg/day) without any clear evidence of toxicity. This dose is equivalent to 28 mg/kg body weight/day for a 60kg adult. 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 toddlers) is 400 (rounded to the nearest 10).

83. The COT is invited to consider the following draft conclusion:

> *We conclude that current dietary exposures to strontium are unlikely to be of toxicological concern.*

Thallium

84. Thallium was last analysed in a TDS in 1994. Since 1994, population dietary exposures have decreased from 2 µg/day to 0.7-0.8 µg/day. Based on the estimated population dietary exposures from the 1994 TDS, the COT concluded that there was no evidence that current dietary intake of thallium by the UK population was harmful to health (COT, 1998). There are no safety guidelines for thallium.

85. On the basis of acute toxicity values in animals and known lethal doses in man, it appears that humans may be more sensitive than laboratory rodents to the toxic effects of thallium. The International Programme on Chemical Safety Task Group considered that exposures causing urinary thallium concentrations below 5 µg/L were unlikely to cause adverse health effects (WHO, 1996). In the range of 5-500 µg/mL 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 (WHO, 1996). The estimated daily oral intake corresponding to a urinary thallium concentration of 5 µg/L was approximately 11 µg/day, or 0.18 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 toddlers) is 240 (rounded to the nearest 10).

86. The COT is invited to consider the following draft conclusion:

We conclude that current dietary exposures to thallium are unlikely to be of toxicological concern.

Tin

87. The estimates of dietary exposures to tin for high-level toddlers are lower than the JECFA PTWI of 2000 μg/kg body weight/day, but exceed the EVM guidance level of 220 μg/kg body weight/day by approximately 55%. All other population group dietary exposures (mean and high-level) are within the EVM guidance level. The PTWI 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 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 NOAEL (22 mg/kg body weight/day) and an uncertainty factor of 100 to derive the guidance level of 0.22 mg/kg body weight/day (EVM, 2003). The small exceedance of this guidance level is therefore within an area of uncertainty, but is not expected to result in adverse effects.

88. The COT is invited to consider the following draft conclusion:

We conclude that current dietary exposures to tin are unlikely to be of toxicological concern.

Zinc

89. The estimated dietary exposure to zinc for all subgroups are 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.

90. The COT is invited to consider the following draft conclusion:

We conclude that current dietary exposures to zinc are unlikely to be of toxicological concern.

Questions on which the views of the Committee are sought

91 The Committee is asked to comment on the information provided and consider the draft conclusions for each element, set out in paragraphs 18, 26, 32, 36, 39, 41, 43, 47, 55, 58, 62, 64, 67, 71, 74, 77, 80, 83, 86, 88, and 90.

92. The Committee is also invited to comment on priorities for future surveys and research, based on the outcome of this TDS.

Secretariat
August 2008

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Table 1: Comparison of the estimated dietary intakes of each element for each population group with the relevant safety guidelines

Estimated Dietary Exposure (µg/kg bw/day)[1, 2, 3]													
Element	**Adults**		**Toddlers (1.5 - 4.5 years)**		**Young people (4-18 years)**		**Elderly (free living)**		**Elderly (institutional)**		**Vegetarians[4]**		**Safety Guidelines[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 safety guidelines.
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 safety guidelines ***continued***

Estimated Dietary Exposure (µg/kg bw/day)[1, 2, 3]													
Element	**Adults**		**Toddlers (1.5 - 4.5 years)**		**Young people (4-18 years)**		**Elderly (free living)**		**Elderly (institutional)**		**Vegetarians[4]**		**Safety Guidelines[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

Table 1: Comparison of the estimated dietary intakes of each element for each population group with the relevant safety guidelines ***continued***

Element	Estimated Dietary Exposure (µg/kg bw/day)[1, 2, 3]												Safety Guidelines[5]
	Adults		Toddlers (1.5 - 4.5 years)		Young people (4-18 years)		Elderly (free living)		Elderly (institutional)		Vegetarians[4]		
	Mean	High level	Mean	High level	Mean	High level	Mean	High level	Mean	High level	Mean	High level	
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
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 - 0.023	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 SUL of 700 µg/kg bw/day

Table 1 Notes

1. Exposures have been estimated from a range (lower - upper bound) of mean concentrations and these have been included as ranges where they apply.
2. The dietary exposure (mean and high level) for all foods combined is not equal to the sum of the exposure from the individual food. It refers to the dietary exposure by a consumer consuming one or any combination of the foods containing the metals. These values are derived from a distribution of the individual consumer's consumption patterns with regards to the individual foods.
3. All figures have been rounded off as appropriate.
4. Some of the respondents of the dietary survey of vegetarians were consumers of fish.
5. Safety guidelines summarised from information in Annex B. N/A = none available

* Essential trace elements.

Table 2a. Comparison of 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)[1-3]											
	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[4]	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 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)[1-3]												
	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[4]	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[4]	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

Notes for tables 2a and 2b

1. 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, Ministry of Agriculture, Fisheries and Food (1998). The Stationery Office, London. 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.
2. 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 (Peattie, M.E., Buss, D.H., Lindsay, D.G. and Smart, G.Q. (1983). Reorganisation of the British Total Diet Study for Monitoring Food Constituents from 1981. *Food and Chemical Toxicology* **21**, 503-507).
3. 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.
4. 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.

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

2006 UK Total Diet Study of Metals and other Elements

Draft Food Survey Information Sheet

The contents of this Annex will be published as a Food Survey Information Sheet after incorporation of the COT views on the results.

TOX/2008/29 Annex B

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

2006 UK Total Diet Study of Metals and other Elements

The Al-Zn of element toxicity: A summary of the toxicological information on 24 elements.