Committee on TOXICITY

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

COT STATEMENT ON TWELVE METALS AND OTHER ELEMENTS IN THE 2000 TOTAL DIET STUDY

Introduction

1. The Food Standards Agency has completed a survey of aluminium, arsenic, cadmium, chromium, copper, lead, manganese, mercury, nickel, selenium, tin and zinc in the 2000 UK 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 each element in the diet posed a risk to human health. The COT last evaluated population and consumer exposures to the twelve elements in the TDS in 1995.

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 to estimate dietary exposures of the general UK population to chemicals in food, such as nutrients and contaminants, to identify 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.

3. The design of the UK TDS has been described in detail elsewhere [1] 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).[1, 2]

4. The foods making up the 20 groups of the TDS were obtained from retail outlets in 24 towns throughout the UK. Each food group obtained from each town was analysed for the twelve elements of interest. The mean element concentrations for each food group were used together with data on the consumption of these food groups [3, 4, 5, 6, 7, 8, 9, 10] to estimate dietary

exposure for the average UK population and mean and high level (97.5th percentile) consumers.

Concentrations of the elements in the foods surveyed

5. The full results of this TDS will be published in a Food Surveillance Information Sheet [11]. The concentrations of each of the elements in the food groups were lower than or similar to those reported in the previous TDS, conducted in 1997[12], with the exception of aluminium and mercury.

6. 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 (approximately 3 fold) seen in the miscellaneous cereals group may 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.

7. Mercury concentrations were similar to or lower than those reported in the 1997 TDS except for the fish group, in which the mean concentration was 0.071 mg/kg compared to 0.043 mg/kg in 1997.

Dietary exposures

8. Estimates of dietary exposure 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 the toxicological data on these metals.[13] The PTWI is used by JECFA in identifying tolerable intakes of food contaminants with cumulative properties. Within this statement, the PTWI has been divided by 7 to provide a tolerable daily intake for comparison with the estimated daily dietary exposures (Table 1).

9. Population dietary exposures have also been estimated, using the amounts of food consumed (based on consumption data from the National Food Survey from 1996 to 1998)[8, 9, 10]. These are shown in Table 2 with the population dietary exposures for each element from the UK TDS from 1976 to 2000.

COT evaluation

10. The estimated mean and high-level dietary exposures to aluminium, cadmium, chromium, copper and selenium for each consumer group were within the relevant safety guidelines and therefore are unlikely to be of any toxicological concern. Population exposures to these elements have generally declined over the course of the TDS programme, with exposures to most of these elements now at the lowest level.

Arsenic

11. The Committee has concluded previously, when considering 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. Inorganic arsenic is genotoxic and a known human carcinogen and therefore exposure should be as low as reasonably practicable (ALARP). [14]

12. The estimates of consumer dietary exposures to total arsenic in the 2000 TDS were similar to those reported in the 1999 TDS of Total and Inorganic Arsenic [14]. The current population exposure to total arsenic was also similar to that reported in the 1999 TDS (0.055 mg/day and 0.05 mg/day, respectively) and lower than previous estimates (0.065 mg/day in 1997). In discussing the 1999 TDS, 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. The Committee noted that the data on inorganic arsenic appeared to be consistent with dietary exposure being ALARP, that the dietary exposure to organic arsenic identified in the survey was unlikely to constitute a hazard to health, and that the downward trend for total arsenic was reassuring. Although different forms of arsenic were not measured in the 2000 TDS, it is likely that there was a similar distribution of inorganic to organic arsenic to that reported for the 1999 TDS, and that the previous COT conclusions are still valid.

13. The Committee recommended that future surveys should measure both total and inorganic arsenic and include consideration of other sources of exposure such as water.

Lead

14. The highest estimate of dietary exposure to lead was 0.47 μg/kg bw/day (for toddlers at the 97.5 percentile of consumption). This is approximately 13% of the JECFA PTWI for lead[15] (equivalent to 3.6 μg/kg bw/day) which is a level of exposure from all sources that is not expected to cause an increase in blood lead concentration in young children. 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. 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 [16]. Thus dietary exposure to toddlers that is within 30% of the JECFA PTWI (i.e. less than 1.2 μg/kg bw/day) is not expected to result in an increase in the blood lead concentration above background levels. Therefore the dietary exposures to lead identified from the 2000 TDS are unlikely to represent a toxicological concern. However, the COT confirmed its previous opinion, from when they

considered a survey of metals in infant foods, that because it has not been possible to identify a threshold for the effects of lead, efforts should continue to reduce exposure from all sources[17].

15. Table 2 illustrates that population dietary exposures have declined considerably since 1976, with the current population exposure at its lowest level (7.4 µg/day compared to 26 µg/day in 1997), which is in accordance with the COT opinion on reducing lead exposure.

Manganese

16. Manganese is an essential trace element but is neurotoxic at high occupational levels of inhalation exposure and 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. [18] There is insufficient information to determine whether there are toxicological risks associated with dietary exposure to manganese and no available safety guideline. The population exposures to manganese have remained fairly constant since manganese was first included in a TDS in 1983 (4.6 mg/day) and there is no basis for assuming that the current dietary exposure to manganese (4.9 mg/day) is a concern for health to consumers.

Mercury

17. With the exception of high-level consumption by children aged 1.5-4.5 years, the estimates of dietary exposure to mercury (mean and high-level) for all consumer groups were within the PTWI for methylmercury set by JECFA in 2003 to protect against neurodevelopmental effects[19] (equivalent to 0.23 µg/kg bw/day). The estimate for high-level consumption by children aged 1.5-4.5 years exceeded the JECFA PTWI for methylmercury by 17%. 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. Furthermore, the COT has previously noted that toddlers are likely to be less sensitive to the neurodevelopmental effects of methylmercury than the fetus or infant [20]. Therefore the dietary exposures to mercury do not give rise to toxicological concerns for consumers. The Committee also noted that the population exposures to mercury have decreased since 1976 (0.005 mg/day), with the current dietary exposure at its lowest level (0.0015 mg/day).

Nickel

18. The estimates of dietary exposures to nickel for high-level consumers aged 1.5-4.5 years and 4-18 years exceeded the WHO TDI (5 µg/kg bw/day)[21] for nickel by 44% and 6%, respectively. The TDI was set as a basis for establishing a WHO guideline for drinking water quality. It was derived from an animal study showing general toxicity in a 2 year dietary study and incorporated an uncertainty factor of 1000 to allow for inadequacies in the

data and a higher absorption of nickel from drinking water than from food. The EVM noted that ingested nickel may exacerbate contact dermatitis/eczema in pre-sensitised individuals[18], however toddlers are less likely than adults to be sensitised and would not therefore be considered to be a sensitive group. Population exposures to nickel have decreased since 1976 (0.33 mg/day), with the current dietary exposure at its lowest level (0.13 mg/day). Overall the Committee concluded that the estimated nickel intakes were unlikely to result in any adverse health effects.

Tin

19. The estimates of dietary exposures to tin for high-level consumers aged 1.5 - 4.5 years were lower than the PTWI of 2000 μg/kg bw/day [22], but exceeded the EVM guidance level of 220 μg/kg bw/day by approximately 29%. The PTWI is not directly applicable to long term dietary exposures since it is based on intakes associated with acute toxicity (the threshold concentration for manifestation of gastric irritation). The EVM guidance level was based on a no observed adverse effect level (NOAEL) of 22-33 mg tin/kg bw/day from a sub-chronic study in rats, in which anaemia and changes to liver cells were observed at higher doses [23]. The EVM used the lower NOAEL (22 mg/kg bw) and an uncertainty factor of 100 to derived the guidance level of 0.22 mg/kg bw/day. The small exceedance of this guidance level is therefore within an area of uncertainty, but is not expected to result in adverse effects.

Zinc

20. The estimated dietary exposure for the high level consumers aged 1.5-4.5 years exceeded the EVM safe upper level (700 μg/kg bw/day)[18] by approximately 8%, but did not exceed the JECFA Provisional Maximum Tolerable Daily Intake (PMTDI) of 1000 μg/kg bw/day [24]. Estimated intakes for other consumer groups were within the EVM safe upper level. The EVM safe upper level was derived from studies of zinc supplementation in adults, taking into account adult dietary intake of zinc, and cannot be directly extrapolated for assessing safety of dietary intake by children. Overall, the Committee concluded that the estimated zinc intakes were unlikely to result in any adverse health effects.

Conclusions

21. 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.

22. 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).

23. 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.

24. 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.

25. 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.

COT statement 2003/07
December 2003

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

Element	Estimated Dietary exposure (μgkg bw/day) [a, b, c]												Safety Guidelines
	Adults		Toddlers (1.5-4.5 years)		Young People (4-18 years)		Elderly (free living)		Elderly (institutional)		"Vegetarians" [d]		
	Mean	High level	Mean	High level	Mean	High level	Mean	High level	Mean	High level	Mean	High level	
Aluminium	67-68	134-135	165	327	120-121	244-245	59	126-127	81-82	162-163	71-72	133-134	JECFA PTWI equivalent to 1000 μg/kg bw/day[25]
Arsenic	1.5-1.6	5.8	2.7	12	1.7	7.0	1.7	5.6	1.6	4.9	1.4	7.4	JECFA PTWI for inorganic arsenic equivalent to 2.14 μg/kg bw/day[26] COT has concluded there are no appropriate safety guidelines.[14]
Cadmium	0.12	0.21	0.31-0.32	0.56	0.22	0.42	0.12	0.21	0.14	0.24	0.13	0.23	JECFA PTWI equivalent to 1 μg/kg bw/day[27]
Chromium	0.66-0.67	1.0-1.11	1.7	2.7-2.8	1.14-1.15	2.1	0.60-0.61	0.98-0.99	0.72	1.1	0.55	0.92-0.93	EVM Guidance Level = of 150 μg/kg bw/day for total dietary intake of trivalent chromium [18]
Copper	18	33	46	81	30	56	18	40	20	41	16	29	JECFA PMTDI = 500 μg/kg bw/day[28] EVM Safe Upper Level = 160 μg/kg bw/day for total dietary intake[18]
Lead	0.1	0.18	0.25	0.47	0.17	0.32	0.094-0.095	0.17	0.12	0.19	0.1	0.18-0.19	JECFA PTWI equivalent to 3.6 μg/kg bw/day.[15] COT considered it is not possible to establish a threshold for lead[17]
Manganese	67	118	132	235	101	195	57	100	67	113	65	123	None available
Mercury	0.03-0.04	0.12-0.13	0.06-0.07	0.26-0.27	0.04-0.05	0.15-0.16	0.04	0.12	0.03-0.04	0.11-0.12	0.03	0.16	2003 JECFA PTWI for methylmercury equivalent to 0.23 μg/kg bw/day to protect against developmental effects. [19]
Nickel	1.5	2.9	3.9	7.2	2.6	5.3	1.3	2.5	1.6	2.8	1.5	3.0	WHO TDI = 5 μg/kg bw/day[21]
Selenium	0.63-0.67	1.2-1.3	1.3-1.4	2.6-2.7	0.86-0.92	1.9-2.0	0.57-0.60	1.1	0.57-0.62	1.0-1.1	0.36-0.4	0.94-0.98	WHO upper limit of the safe range for adults only = 400 μg/day [29] EVM Safe Upper Level for total dietary intake equivalent to 7.5 μg/kg bw/day[18]
Tin	20	70	70	283	38	150	17	76	17	61	26	101	JECFA PTWI is equivalent to 2000 μg/kg bw/day[22] EVM Guidance Level = 220 μg/kg bw/day for total dietary intake[18]
Zinc	141	252	386	759	226	453	133	250	156	250	84	149	JECFA PMTDI = 1000 μg/kg bw/day. [24] EVM Safe Upper Level for total dietary intake equivalent to 700 μg/kg bw/day (for 60 kg adult)[18]

Notes

a. Exposures have been estimated from the upper and lower bound mean concentrations, which assume non-detectable concentrations were the limit of detection and zero, respectively. Where the difference between the lower bound and upper bound mean concentrations is very small, rounding of the data leads to a single value.
b. 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.
c. Consumption data taken from the relevant National Diet and Nutritional Surveys.[3,4,5,6,7]
d. Some of the respondents of the dietary survey of vegetarians were consumers of fish.

Table 2: Comparison of population dietary exposures to aluminium (Al), arsenic (As), cadmium (Cd), chromium (Cr), copper (Cu), lead (Pb), manganese (Mn), mercury (Hg), nickel (Ni), selenium (Se), tin (Sn) and zinc (Zn) from UK Total Diet Studies 1976 to 2000

Year	Population dietary exposure (mg/day)[1,2]											
	Al	As	Cd	Cr	Cu	Pb	Mn	Hg	Ni	Se	Sn	Zn
1976	-	0.075	0.02	0.13	1.8	0.11	-	0.005	0.33	-	4.4	10
1977	-	0.1	0.018	0.17	1.8	0.1	-	0.005	0.26	-	4.2	10
1978	-	0.081	0.02	0.1	1.6	0.11	-	0.005	0.27	-	3.6	10
1979	-	-	0.017	-	-	0.09	-	0.004	-	-	3.2	-
1980	-	-	0.026	-	-	0.12	-	0.005	0.27	-	-	-
1981	-	-	0.019	-	-	0.08	-	-	0.23	-	2.4	-
1982	-	0.09	0.018	-	1.3	0.069	-	0.003	0.15	-	3.1	10
1983	-	0.07	0.018	-	1.2	0.067	4.6	-	0.15	-	2.3	10
1984	-	-	0.019	0.073	1.4	0.065	5.3	-	0.16	-	2.7	10
1985	-	-	0.018	-	1.3	0.066	5.0	-	0.14	0.063	1.7	10
1986	-	-	0.017	-	-	0.06	-	-	0.13	-	2.2	-
1987	-	-	0.018	-	-	0.06	-	-	0.15	-	2.0	-
1988	3.9	-	0.019	-	-	0.06	-	-	-	-	-	-
1991	10	0.07	0.018	0.25	1.4	0.028	6.2	0.002	0.17	0.060	5.3	10
1994	11	0.063	0.014	0.34	1.2	0.024	4.9	0.004	0.13	0.043	2.4	8.4
1995	-	-	-	-	-	-	-	-	-	0.039 [3]	-	-
1997	3.4	0.065	0.012	0.1	1.2	0.026	-	0.003	0.13	0.039	1.8	8.4
2000	4.7	0.055	0.009	0.046	1.3	0.0074	4.9	0.0015	0.13	0.034	1.4	8.4

Notes

" – " = not included in that TDS for metals and other elements

1. The above population dietary exposures have been 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.

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 [1].

3. Dietary exposure estimates 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.

References

1 Peattie, ME., Buss, DH., Lindsay, DG. And Smart, GQ. (1983). Reorganisation of the British Total Diet Study for Monitoring Food Constituents from 1981. *Food and Chemical Toxicology* **21:** 503-507

2 Ministry of Agriculture, Fisheries and Food (1994). The British Diet: Finding the Facts. *Food Surveillance Paper,* No. **40**. The Stationary office, London.

3 Henderson, L., Gregory, J. and Swan, G. (2002), The National Diet and Nutrition Survey: adults aged 19-64 years. Volume 1: Types and quantities of foods consumed. The Stationary Office, London

4 Ministry of Agriculture, Fisheries and Food (March 1999). Vegetarians Dietary Survey: Technical Report on Weighed Intake Diary Data. Research & Development and Surveillance Report:

5 Finch, S., Doyle, W., Lowe, C., Bates, CJ., Prentice, A., Smithers, G. & Clarke PC. (1998). National Diet and Nutrition Survey: People aged 65 years and over. Volume 1 report of the diet and nutrition survey. The Stationery Office.

6 Gregory, J., Lowe, S., Bates, CJ., Prentice, A., Jackson, LV., Smithers, G., Wenlock, R. & Farron M. (2000). National Diet and Nutrition Survey: Young people aged 4 to 18 years, Volume 1: Report of the diet and nutrition survey, The Stationery Office

7 Gregory, J., Collins, D.L., Davies, P.S.W., Hughes, J.M. and Clarke, P.C. (1995). National Diet and Nutrition Survey; Children Aged 1½ - 4½ Years. Volume 1: Report of the diet and nutrition survey. HMSO.

8 Ministry of Agriculture, Fisheries and Food (1997). National Food Survey. 1996. Annual report on Food Expenditure, Consumption and Nutrient Intakes. The Stationery Office, London.

9 Ministry of Agriculture, Fisheries and Food (1998). National Food Survey. 1997. Annual report on Food Expenditure, Consumption and Nutrient Intakes. The Stationery Office, London.

10 Ministry of Agriculture, Fisheries and Food (1999). National Food Survey. 1998. Annual report on Food Expenditure, Consumption and Nutrient Intakes. The Stationery Office, London.

11 Food Standards Agency (2004). 2000 Total Diet Study of Twelve Elements. *Food Survey Information Sheet*. (to be published)

12 Ministry of Agriculture, Fisheries and Food (1999). 1997 Total Diet Study - Aluminium, Arsenic, Cadmium, Chromium, Copper, Lead, Mercury, Nickel, Selenium, Tin and Zinc. *Food Surveillance Information Sheet,* No. **191**. The Stationery Office, London.

13 Food Standards Agency (2003), COT discussion paper, TOX/2003/39 Annex B. Available at: http://www.food.gov.uk/multimedia/pdfs/TOX-2003-39.PDF

14 COT (2003). Statement on Arsenic in food: Results of the 1999 Total Diet Study. Available at: http://www.food.gov.uk/science/ouradvisors/toxicity/statements/cotstatements2003/arsenicstatement

15 WHO (2000) Safety evaluation of certain food additives and contaminants: Lead. WHO Food Additives Series 44.

16 Davies, D.J.A., Thornton, I., Watt, J.M., Culbard, E.B., Harvey, P.G., Delves, H.T., Sherlock, J.C., Smart, G.A., Thomas, J.F. and Quinn, M.J. (1990). Lead intake and blood lead in two year old UK children. *Science of the Total Environment.* **90**: 13-29

17 COT (2003). Statement on a Survey of Metals in Infant Foods. Available at: http://www.food.gov.uk/multimedia/pdfs/statement.pdf

18 EVM (2003). Safe upper levels for vitamins and minerals. Report of the Expert Group on Vitamins and Minerals. Food Standards Agency, May 2003. ISBN 1-904026-11-7. Available at: http://www.food.gov.uk/multimedia/pdfs/vitmin2003.pdf

19 WHO (2003). Summary and conclusions of the 61st meeting, Methylmercury. Available at: http://www.fao.org/es/esn/jecfa/whatisnew_en.stm

20 COT (2003) Updated Statement on a Survey of Mercury in Fish and Shellfish. Available at: http://www.food.gov.uk/science/ouradvisors/toxicity/statements/cotstatements2003.

21 WHO (1996) Guidelines for drinking-water quality, 2nd ed. Vol. 2 Health criteria and other supporting information, (pp. 940-949) and Addendum to Vol. 2 . 1998 (pp. 281-283) Geneva.

22 WHO (2001), Safety Evaluation of certain food additives and contaminants; Tin. WHO Food Additives Series No. 46. Joint FAO/WHO Expert Committee on Food Additives.

23 De Groot, A.P., Feron, V.J., Til, H.P. (1973). Subacute toxicity of inorganic tin as influenced by dietary levels of iron and copper. *Food and Cosmetics Toxicology* **11:** 955-962.

24 WHO (1982) Safety evaluation of certain food additives and contaminants: Zinc. WHO Food Additives Series 17.

25 WHO (World Health Organisation) (1989). Evaluation of Certain Food Additives and Contaminants; Aluminium. Thirty-third Report of the Joint FAO/WHO Expert Committee on Food Additives. *WHO Technical Report Series* No. **776**. World Health Organization, Geneva.

26 WHO (1989). Toxicological Evaluations of Certain Food Additives and Contaminants; Arsenic. 33rd Report of the JECFA, WHO Food Additives Series No 24.

27 WHO (2001). Safety evaluation of certain food additives and contaminants; Cadmium. WHO Food Additives Series 46.

28 WHO (1982). Toxicological evaluation of certain food additives: Copper. WHO Food Additives Series, No. 17.

29 World Health Organization. Trace Elements in human nutrition and health (1996). WHO, Geneva.