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

Contaminants in fish section

This section should be read in conjunction with Annex 3 of paper FICS/03/01, which accompanies this paper.

Dioxins and Dioxin-Like PCBs

1. Table 1 shows estimates of intakes of dioxins and dioxin-like PCBs by UK consumers of oily fish based on the results of analyses made in a survey of dioxins and PCBs in marine fish, 1994-1995. The estimates include the contaminant intakes from one portion of cod per week and from the rest of the diet, and assume a portion size of 140g (70g for eels) and bodyweight of 60kg. The COT has previously noted that the effects of dioxin-like compounds are related to the body burden, rather than to daily intake, and therefore intakes have been calculated for the number of portions of fish consumed per week.

2. The estimated intakes have been compared with the Tolerable Daily Intake (TDI) of 2 pg WHO-TEQ/kg bw/day that COT identified for these substances (COT, Sept 2001, see annex 5). Consumption of one 140g portion per week of herring, kipper or eels, by a 60kg adult, would result in a 44-78% exceedance of the TDI. Consumption of 2 portions of salmon would lead to a 40% exceedance of the TDI, whereas 3 portions of trout could be consumed per week before the TDI would be exceeded. Exceedances would be smaller if a larger average bodyweight was assumed for adults.

3. The TDI is set to protect against the most sensitive effect of dioxins, which is considered to be impaired development of the fetal male reproductive system, caused by fetal exposure *in utero* and correlated with the maternal body burden. Other developmental effects have also been proposed. Taking also into account that dioxins accumulate in the body over many years, the most susceptible subgroup is considered to be females up to the time of final pregnancy, by virtue of exposure of fetuses that they might bear.

4. Males post-natally and post-reproductive age women are not at risk of the developmental effects and therefore could be considered to be at lesser risk of the effects of dioxins. Considering the other possible toxic effects of dioxins noted by COT, increased cancer risk is currently the most convincing and of most relevance for long term exposure by subgroups not at risk for the developmental effects. The Committee on Carcinogenicity (COC) has concluded that dioxins are probably weak human carcinogens, but that based on the available evidence a threshold approach to risk assessment is appropriate. Annex 3 of paper FICS/03/01 proposed that a guideline level of 8 pg WHO-TEQ/kg bw/day could be calculated from the rat carcinogenicity, using a similar body burden approach

to that used in establishing the TDI. The guideline level could be used to indicate a long term average intake that would not be expected to be associated with an appreciable increase in cancer risk (analogous to the TDI definition). Table 1 indicates that 2 portions per week of herring or kipper would not exceed the guidance level, but 3 or more portions of mackerel, salmon or trout could be consumed.

5. The above calculations are based on long term intakes. However, some women may wish to modify their oily fish consumption during pregnancy, either because of the nutritional benefits or because of concern about risks associated with contaminants. The COT has previously noted (COT, 2001):
   - there are no short-term measures that can be used to decrease the body burden of dioxins and dioxin-like PCBs in humans because of their long half-lives and widespread presence at low levels in food.
   - Similarly, short term exceedances of the TDI are not expected to result in adverse effects. Nevertheless, it is not possible to identify a duration and degree of exceedance at which adverse effects might occur.

6. Paper TOX/2004/10 (Toxicological opinion on the results of the SUREmilk project) cites a physiologically-based pharmacokinetic (PBPK) model of the effects of lactation on a woman's body burden of dioxins. This model indicates that breast-feeding a first baby would lower the mother's body burden, which suggests that the risk of exceeding a harmful body burden would be lower if oily fish consumption was increased in a subsequent pregnancy. Furthermore, a few months of modifying the diet may not have a significant impact on the total body burden (see Figures 1-3, provided by AR Renwick, unpublished).

Methylmercury

7. The COT had previously concluded (COT, 2002) that the Provisional Tolerable Weekly Intake (PTWI) for methylmercury of 3.3 µg/kg bw/week, that had been recommended by the JECFA in 2000, was sufficiently protective for the general population, not for high risk groups. The COT therefore considered that the reference dose of 0.1 µg/kg bw/day (0.7 µg/kg bw/week), that had been recommended by the US EPA, would be more applicable for high risk groups because it took account of effects on the developing fetus. The COT identified pregnant women, women who may become pregnant within the next year and breast feeding mothers as high-risk groups because of the effects of methylmercury on the developing nervous system of the fetus or newborn baby.

8. In June 2003, JECFA revised its PTWI to 1.6 µg/kg bw/week, in order to be protective of the developing fetus. The COT subsequently reviewed its opinion and issued an updated statement (COT, 2003, Annex 3). The updated COT conclusions were:

   - We *note* that there has been no new information published to indicate that the 2000 PTWI of 3.3 µg/kg bw/week is not sufficiently protective of the general population. We therefore *consider* that a methylmercury intake of 3.3 µg/kg bw/week may be used as a guideline to protect against non-developmental adverse effects.

- We *conclude* that the 2003 JECFA PTWI of 1.6 µg/kg bw/week is sufficient to protect against neurodevelopmental effects in the fetus. This PTWI should be used in assessing the dietary exposure to methylmercury of women who are pregnant, and who may become pregnant within the following year.

- We *consider* that a guideline of 3.3 µg/kg bw/week is appropriate in considering intakes by breastfeeding mothers as the intake of the breast-fed infant would be within the new PTWI of 1.6 µg/kg bw/week.

9. Table 2 shows the estimated intakes of mercury from 1 to 3 portions of oily fish per week. These values are compared with the PTWI and guideline level for methylmercury. Non-fish sources of mercury are not included in this comparison, since they are likely to be inorganic forms, which are less well-absorbed and therefore less toxic via the oral route. Furthermore, not all mercury in fish is expected to be methylmercury, and therefore this comparison is precautionary.

10. These data demonstrate that, of the oily fish, it is swordfish that is a major concern. Consumption of one portion of swordfish per week would lead to a mercury intake of more than twice the PTWI, but approximately equal to the guidance level. The COT has noted that this intake could be harmful to the fetus of women who are pregnant or become pregnant within a year, but would not be expected to result in adverse effects in other adults. Consumption of 2 portions of fresh tuna per week would exceed the PTWI by 17%.

11. The COT statement in Annex 3 also considers levels of mercury in non-oily fish. The levels in shark and marlin were similar to those in swordfish and therefore a similar conclusion was reached on the risks. The concentration of mercury in canned tuna was lower than for fresh tuna, with a mean of 0.19 mg/kg. Consumption of four 140g cans per week would provide 95% of the PTWI. Considering that the contribution from the rest of the diet would be mainly inorganic mercury, the COT considered that this was unlikely to result in adverse effects to the fetus.

<u>Brominated flame retardents (BFRs)</u>

12. There is currently limited information on exposure to BFRs via the diet, or from other sources. However, there is an increasing number of reports on detection of these lipophilic contaminants in fish. In considering the concentrations of polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCD) in trout and eels from the Skerne-Tees river system, the COT concluded:

- We *conclude* that the uncertainties and deficiencies in the toxicological databases for PBDEs and HBCD prevent establishment of tolerable daily intakes. A Margin of Exposure (MoE) approach has therefore been used in this risk assessment.

- We *consider* that the most sensitive endpoint for the PBDEs appears to be neurodevelopmental effects resulting from a single oral administration to neonatal mice at a developmental stage comparable to infants up to one month of age, and limited data indicate that HBCD could also have this effect. It is reassuring that infants of this age do not eat fish and therefore are not directly exposed to PBDEs from this source.

- We *note* the uncertainty in the relevance of the neurodevelopmental effects for exposure to the fetus or breast-fed infant following maternal consumption of fish containing high levels of PBDEs or HBCD. This results from the lack of neurodevelopmental studies with exposure during pregnancy and the lack of information on concentrations in breast milk that could result from consumption of fish by the mother.

- We *note* that consumption of fish from the Skerne Tees is unlikely to be widespread since there are no commercial fisheries in the area. However given the variability in BFR levels observed in this limited survey, it is not possible to exclude higher intakes in a small number of anglers or others eating their fish.

- We *consider* that comparison of the worst case estimated intakes from consumption of a single portion of eels or trout per week from the Skerne Tees with the available toxicological data indicates that these intakes are unlikely to represent a risk to health. However, in view of the uncertainties surrounding the toxicological database and exposure assessments, this conclusion should be considered tentative.

- PentaBDE and octaBDE are being phased out in 2004, which offers some reassurance that exposure to these compounds is unlikely to increase significantly. Concentrations of deca-BDE and HBCD should continue to be monitored, particularly in fatty foods.

13. The COT statement is included in Annex 4 The Food Standards Agency is currently conducting a survey of PBDEs, HBCD and the other major BFR tetrabromobisphenol A (TBBPA) in fish. The COT will be invited to advise on the toxicological implications of the data when available.

Table 1: Estimated dietary intake of dioxins and dioxin-like PCBs from oily fish and the rest of the diet for an adult of 60 kg bodyweight using average portion size from consumers in National Diet and Nutrition Survey of British adults aged 19 to 64 years 2000/01

	HERRING	KIPPER	MACKEREL	SALMON	TROUT	EEL
Mean concentration (& range)[a] (pg WHO-TEQ/g wet weight)	8.59 (0.8-13.85)	8.59[b] (0.8-13.85)	3.11 (0.48-7.49)	3.15 (2.15-3.95)	1.13 (0.30-3.09)	13.07
Intake from one portion fish per week [c] (pg WHO-TEQ/kg bw/day)	2.9	2.9	1.0	1.1	0.4	2.2
Intake from rest of the diet [d] (pg WHO-TEQ/kg bw/day)	0.7	0.7	0.7	0.7	0.7	0.7

	% TDI or guidance level											
Portions per week	**HERRING**		**KIPPER**		**MACKEREL**		**SALMON**		**TROUT**		**EEL**	
	%TDI [e]	%GL [f]	%TDI	%GL	%TDI	%GL	%TDI	%GL	%TDI	%GL	%TDI	%GL
1	178	45	178	45	87	22	88	22	54	13	144	36
2	321	80	321	80	139	35	140	35	73	18	253	63
3	465	116	465	116	191	48	193	48	92	23	362	90
4	608	152	608	152	242	61	245	61	110	28	471	118

[a] Concentrations taken from MAFF (1999), FSIS 184.
[b] No concentration data were available for kipper, so it has been assumed that the concentration is the same as for herring.
[c] Assumes 140g portion size for all fish except eels (70g).
[d] Averaged daily intake of dioxins and dioxin-like PCBs from the non-fish part of the diet (0.7 pg WHO-TEQ/kg bw/day) and from one portion of cod per week (0.04 pg WHO-TEQ/kg bw/day).
[e] TDI = 2 pg WHO-TEQ/kg bw/day
[f] Guideline level for less susceptible subgroups = 8 pg WHO-TEQ/kg bw/day

Shaded data highlight exceedance of the TDI or guidance level.

Table 2: Estimated dietary intake of mercury from oily fish and the rest of the diet for an adult of 60 kg bodyweight using average portion size from consumers in National Diet and Nutrition Survey of British adults aged 19 to 64 years 2000/01

	HERRING	MACKEREL	SALMON	TROUT	FRESH TUNA	SWORDFISH
Concentration [a] (µg /g wet weight)	0.09	0.05	0.05	0.06	0.4	1.4
Intake from one portion fish per week [b] (µg/kg bw/week)	0.21	0.12	0.12	0.14	0.93	3.27
Intake from rest of the diet [c] (µg/kg bw/week)	0.21	0.21	0.21	0.21	0.21	0.21

	% PTWI or guidance level for methylmercury											
Portions per week	**HERRING**		**MACKEREL**		**SALMON**		**TROUT**		**FRESH TUNA**		**SWORDFISH**	
	%PTWI [d]	%GL [e]	%PTWI	%GL	%PTWI	%GL	%PTWI	%GL	%PTWI	%GL	%PTWI	%GL
1	13	6	7	4	7	4	9	4	58	28	204	99
2	26	13	15	7	15	7	18	8	117	57	408	198
3	39	19	22	11	22	11	26	13	175	85	613	297
4	53	25	29	14	29	14	35	17	233	113	817	396

[a] Concentrations in oily fish species and cod taken from surveys for mercury in marine fish 1995-97 (cod, herring and mackerel) and 2002 (salmon and trout). Predominantly but not exclusively in the form of methylmercury.

[b] Assumes 140g portion size for all fish

[c] Averaged weekly intake of mercury from the non-fish part of the diet (0.06 (µg/kg bw/week) and from one portion of cod per week (0.15 µg/kg bw/week). Provided for information, but not included in the comparison with the PTWI and guidance level

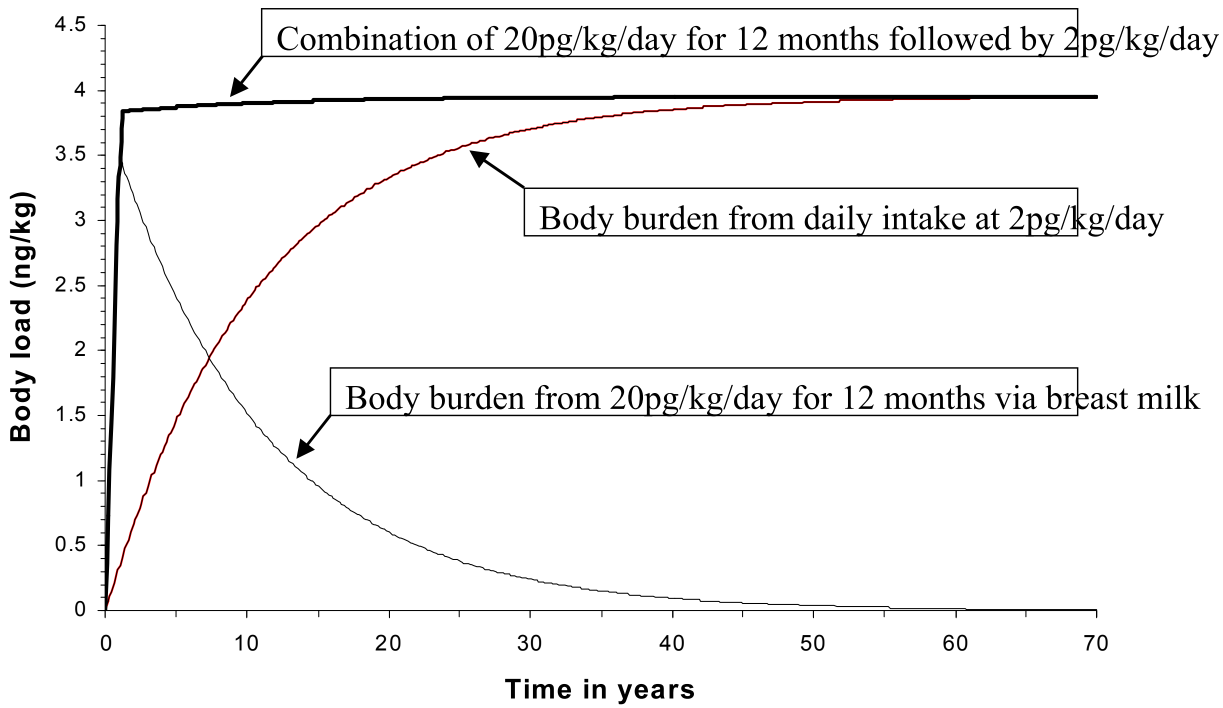
[d] PTWI = 1.6 µg/kg bw/week for methylmercury

[e] Guideline level for less susceptible subgroups = 3.3 µg/kg bw/week_for methylmercury.

Shaded data highlight exceedance of the PTWI or guidance level.

Figure 1.

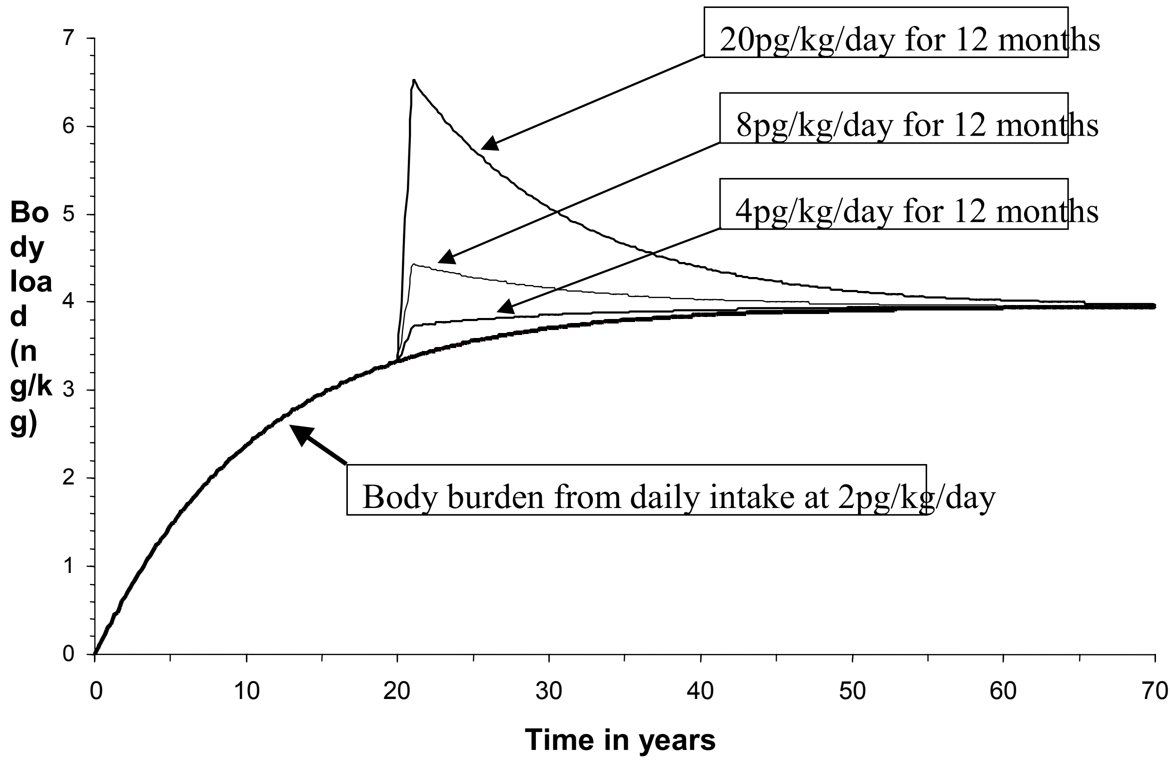
Influence of breast feeding on body burden of dioxin



Note – assumes that 50% of the daily intake is absorbed and the elimination half-life is 7.5 years

Figure 2

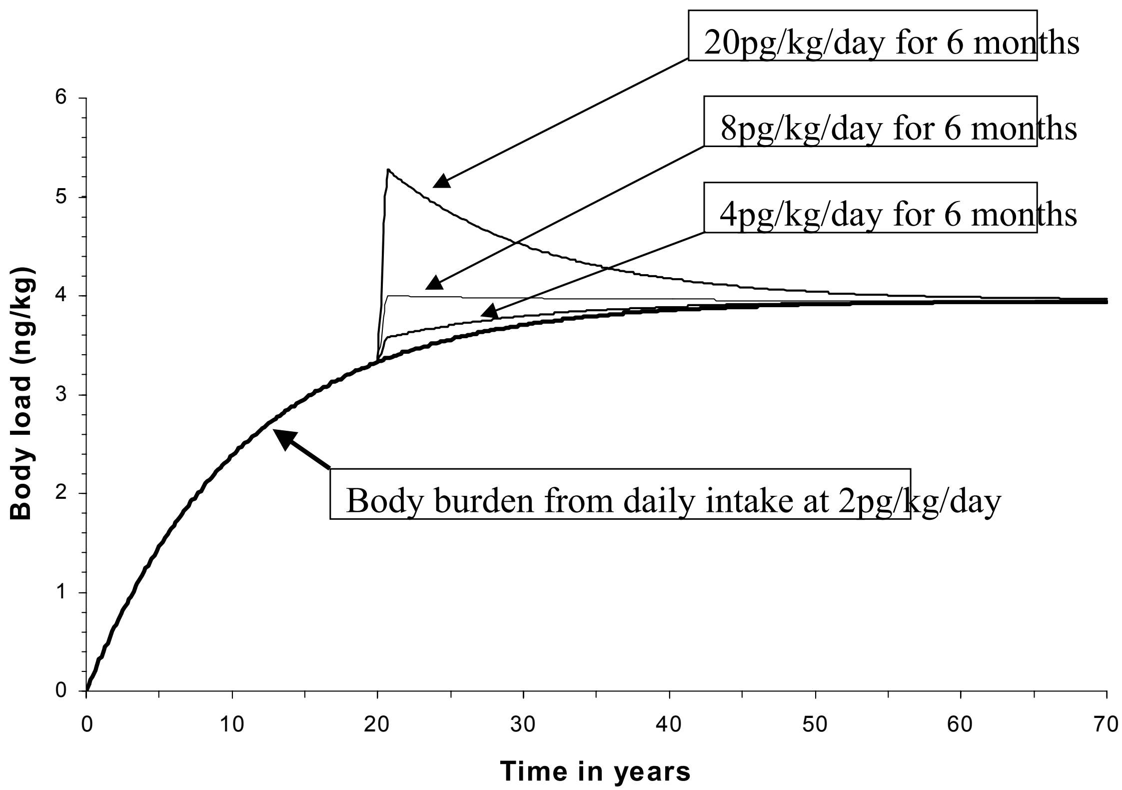
Influence of 12 months of high intake on body burden of dioxi



Note – assumes that 50% of the daily intake is absorbed and the elimination half-life is 7.5 years

Figure 3

Influence of 6 months of high intake on body burden of dioxin



Note – assumes that 50% of the daily intake is absorbed and the elimination half-life is 7.5 years