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

OCCURRENCE OF MIXED HALOGENATED DIOXINS AND BIPHENYLS IN UK FOOD

1. At the meeting in September Members considered data from an FSA project looking at the occurrence of mixed halogenated (chlorine and bromine) dioxins, furans and biphenyls in some UK food. Members asked the Secretariat to draft a short statement on their conclusions.

Questions asked of the Committee

2. Members are invited to consider the following questions and to raise any other matters that arise from the data;

(i) Members are invited to comment on the draft statement at Annex A.

Secretariat
October 2010

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

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DRAFT COT STATEMENT ON OCCURRENCE OF MIXED HALOGENATED DIOXINS AND BIPHENYLS IN UK FOOD

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DRAFT STATEMENT ON OCCURRENCE OF MIXED HALOGENATED (CHLORINE AND BROMINE) DIOXINS AND BIPHENYLS IN UK FOOD

Introduction

1. The Food Standards Agency (FSA) has recently completed a survey that analysed 19 mixed halogenated (chlorine and bromine) dibenzo-*p*-dioxins (PXDDs), dibenzofurans (PXDFs) and biphenyls (PXBs) in samples of farmed and wild fish and shellfish, meat and eggs consumed in the UK. These results will be published in a Food Safety Information Sheet (FSIS) at http://www.food.gov.uk/science/surveillance/.

2. The Committee was invited to consider the data and advise prior to the writing of the FSIS on whether the levels of these PXDDs, PXDFs and PXBs were a health concern. Data on the concentrations of PXDDs, PXDFs and PXBs in food consumed in the UK have not been available for consideration previously. The Committee was provided with data on levels of polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), dioxin-like polychlorinated biphenyls (PCBs) polybrominated dibenzo-*p*-dioxins (PBDDs), polybrominated dibenzofurans (PBDFs) and dioxin-like polybrominated biphenyls (PBBs) measured in the same food samples.

Dioxins and dioxin-like organic contaminants

Polychlorinated dibenzo-p-dioxins, dibenzofurans and dioxin-like PCBs,

3. Dioxins, a group of 75 PCDD and 135 PCDF congeners, are persistent organochlorine compounds that are widely dispersed environmental contaminants and accumulate in fatty foods. Dioxins can be formed as a result of thermal reactions and as trace contaminants in the synthesis of some chemicals and some industrial processes.

4. PCBs are persistent organochlorine chemicals that are no longer manufactured, but may be released to the environment during disposal of materials and obsolete electronic equipment. Twelve non-*ortho* or mono-*ortho* PCBs, of the 209 theoretically possible PCB congeners, exhibit similar biological activity to dioxins and are, therefore, referred to as dioxin-like PCBs.

5. Exposure of the general population to dioxins and dioxin-like PCBs is primarily from food[1,2]. The estimated exposures from the UK Total Diet Study samples for all age groups have declined substantially over the past 2 decades [2]. Based on occurrence and consumption in 2000/1, the most recent estimates of dietary exposure were in the region of 0.8 and 1.6 pg WHO-TEQ/kg bw/day for average and 97.5th percentile consumers[2].

Previous COT evaluations

6. The COT has considered dioxins on a large number of occasions, the most relevant of which are noted here. In 2001, COT set a TDI of 2 pg WHO-TEQ/kg bw/day† to protect against the most sensitive effect of dioxins. This was considered to be impaired development of the fetal male reproductive system, caused by fetal exposure *in utero* and correlated with the maternal body burden of dioxins[2]. In 2006 the Committee endorsed the revised WHO-TEFs proposed following the WHO-IPCS re-evaluation of TEF values based on a recently published relative effect potency (REP) database[3,4,5]. In 2007 COT considered the results of a FSA funded developmental toxicity study which aimed to address some of the limitations identified by the Committee in setting the TDI in 2001. The Committee considered this study was valuable in clarifying some of the uncertainties in their 2001 risk assessment. In the new study, the most sensitive effect of dioxin was a delay in puberty, rather than altered sperm quality. However, this was observed at levels of dioxin exposure that were similar to those used as the basis for the 2001 risk assessment. Therefore, the Committee considered that this study provides additional evidence that the current tolerable daily intake (TDI) of 2 pg/kg bw/day is protective for the developing male fetus[6].

Polybrominated dibenzo-p-dioxins, polybrominated dibenzofurans and dioxin-like polybrominated biphenyls

7. PBDDs and PBDFs are structurally closely related to chlorinated dioxins and furans. They are not intentionally produced (except for scientific purposes) but, as with dioxins, are generated as undesired by-products in various processes. They can be formed by chemical, photochemical, or thermal reactions from precursors. In experimental animal models, exposure to PBDDs or PBDFs is reported to result in many of the effects typical for the chlorinated dioxins.

8. Theoretically, 75 PBDDs and 135 PBDF congeners are possible, and as with the chlorinated analogues the most toxic congeners are reported to be those substituted at the 2, 3, 7, and 8 positions[7].

† Toxicity Equivalency Factors (TEFs) allow concentrations of the less toxic dioxin-like compounds (16 PCDDs/PCDFs and 12 PCBs) to be expressed as a concentration equivalent to the most toxic dioxin 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD). These toxicity-weighted concentrations are then summed to give a single value, which is expressed as a Toxic Equivalent (TEQ). The system of TEFs used in the UK and a number of other countries is that set by the World Health Organisation (WHO), and the resulting overall concentrations are referred to as WHO-TEQs.

9. Polybrominated biphenyls (PBBs) are brominated hydrocarbons formerly used as additive flame retardants. As such these substances were added, rather than chemically bound, to plastics used in a variety of consumer products, such as computer monitors, television, textiles and plastic foams, and were able to leave the plastic and enter the environment. They are structurally similar compounds in which 2-10 bromine atoms are attached to the biphenyl molecular structure. In total, as with the PCBs, 209 different PBB congeners are possible.

10. Individual PBB congeners vary in their pattern of toxicity. PBBs have been categorised on a similar structural basis as the PCBs, with category I comprising congeners lacking *ortho* substituents (coplanar PBBs). Coplanar PCBs are dioxin-like with regards to their toxicity and are included in the toxicity equivalency factor (TEF) concept.

Previous evaluations of brominated dioxins, furans and biphenyls by COT

11. In December 2005 COT discussed the key toxicological data for the PBDDs/PBDFs and dioxin-like PBBs. The limited data available supported the conclusion that these compounds share a common mechanism of action with their chlorinated analogues.

12. On the basis of the available data COT concluded that TEFs developed for the chlorinated dioxins could be used as an indication of the dioxin-like activity of the PBDDs, PBDFs and dioxin-like PBBs. The TEQs for the brominated contaminants could be combined with the TEQs for the chlorinated dioxins to provide an indication of the total intake of chemicals with dioxin-like properties as this would be more protective of public health than to view the chemicals separately. However, the Committee highlighted that this was tentative advice. The uncertainties in the available data with regards to the comparative toxicokinetics in rodents and humans, and lack of chronic dosing studies with these compounds indicated the need for maintaining a watching brief. It was acknowledged that the use of TEFs assigned to chlorinated congeners for the brominated analogues was likely to be over-conservative. However, further data were require to support the use of the TEF concept for the brominated compounds[7].

13. The Committee agreed that in light of this evidence, and the absence of an alternative approach, it would be prudent to apply the TEFs assigned to the chlorinated dioxins to the brominated congeners. The TEQs for the brominated contaminants should be combined with the WHO-TEQs for the chlorinated dioxins to provide an indication of the total intake of chemicals with dioxin-like properties.

14. The Committee noted that estimated exposures to the chlorinated dioxins and dioxin-like compounds had declined substantially over the previous two decades. Including the brominated congeners in the TEQs for intake from fish and the rest of the diet did not raise additional toxicological concerns. As there were no new toxicity data giving rise to new concerns, it was considered unnecessary to alter the COT's previous advice on oily fish consumption[7].

Mixed halogenated dioxins, furans and biphenyls

15. Theoretically there are 4600 individual mixed halogenated (bromine and chlorine) dioxins and furans and 9180 mixed halogenated biphenyls. Mixed halogenated biphenyls have never been produced commercially except for research purposes. As with the chlorinated and brominated dioxins, furans and biphenyls, these compounds are likely to show a range of toxicities with only a small subset being potent. The mixed halogenated (bromine and chlorine) dioxins and furans are believed to share a common mechanism of action with PCDDs/PCDFs and PBDDs/PBDFs.

Selection of mixed halogenated (bromine and chlorine) dioxins, furans and biphenyls for analysis.

16. The mixed halogenated (bromine and chlorine) dioxins, furans and biphenyls were selected for analysis based on chemical configuration, type and degree of halogenation, and the limited knowledge on toxicological properties and environmental occurrence levels. In particular compounds containing 2,3,7,8 substitutions were targeted as chlorinated and brominated congener with these substitutions generally have higher TEFs. However the final selection of 19 compounds for analysis in food (6 dioxins, 7 furans and 6 biphenyls (table 1)) was also determined by practical considerations such as the availability of standards or ability to synthesize such standards in the project time frame.

Table 1. Congeners measured

Analyte	**Configuration**	**Degree of halogenation**	**Equivalent chlorinated congener**	**2005-WHO TEF of chlorinated congener**
Dioxins	2-Br-7,8-Cl-DD	Tri		
	2-Br-3,7,8-Cl-DD	Tetra	2,3,7,8-TCDD	1
	2,3-Br-7,8-Cl-DD	**Tetra**	2,3,7,8-TCDD	1
	1-Br-2,3,7,8-Cl-DD	**Penta**	1,2,3,7,8-PCDD	1
	2-Br-1,3,7,8-Cl-DD	Penta	1,2,3,7,8-PCDD	1
	2-Br-3,6,7,8,9-Cl-DD	Hexa	1,2,3,4,7,8-HCDD	0.1
Furans	**2-Br-7,8-Cl-DF**	**Tri**	2,7,8-TCDF	-
	2-Br-6,7,8-Cl-DF	Tetra	2,6,7,8-TCDF	-
	3-Br-2,7,8-Cl-DF	**Tetra**	2,3,7,8-TCDF	0.1
	2,3-Br-7,8-Cl-DF	Tetra	2,3,7,8-TCDF	0.1
	1-Br-2,3,7,8-Cl-DF	Penta	1,2,3,7,8-PCDF	0.03
	4-Br-2,3,7,8-Cl-DF	**Penta**	2,3,4,7,8-PCDF	0.3
	1,3-Br-2,7,8-Cl-DF	Penta	1,2,3,7,8-PCDF	0.03
Biphenyls	**4'-Br-3,3',4,5-Cl-B**	**Penta**	PCB 126	0.1
	3,4-Br-3',4',5'-Cl-B	Penta	PCB 126	0.1
	3',4',5-Br-3,4-Cl-B	Penta	PCB 126	0.1
	4'-B-2,3,3',4-C	**Penta**	PCB 105	0.00003
	4'-B-2,3',4,5-CB	Penta	PCB 118	0.00003

	4'-B-2,3,3',4,5-CB	Penta	PCB 156	0.00003

Bold type indicates ^{13}C-labelled standards

Analytical methodology and levels in food.

17. Analytical methodology for the measurement of these mixed halogenated compounds was developed based on high resolution mass spectrometry. The method was validated and used to measure concentrations of these mixed halogenated compounds in around 100 foods. The limits of detection achieved were similar to those used for chlorinated dioxin and biphenyl analysis and ranged from 0.005 to 0.02 ng/kg fat depending on the congener and food type.

18. Mixed halogenated (bromine and chlorine) dioxins, furans and biphenyls in common items of retail food. Whilst the frequency and magnitude of detection varied depending on the food type, levels generally followed the order – biphenyls > furans > dioxins. The mono-brominated mixed halogenated compounds were observed in food samples more frequently than di- or tri-brominated mixed halogenated compounds. Most of the foods analysed showed the presence of at least some of these mixed halogenated compounds but a higher frequency of detection and relatively higher values of these contaminants were observed for samples of shellfish, fish and liver.

Applicability of the TEFs for chlorinated congeners to the mixed halogenated (bromine and chlorine) dioxins, furans and biphenyls.

19. As noted above, in 1997, a WHO working group concluded that 'at present, insufficient environmental and toxicological data are available to establish a TEF value' for brominated compounds. However, the WHO discussed the concept of using TEFs for the assessment of these chemicals and WHO suggested that the preliminary use of the same TEF values for the brominated congeners as described for the chlorinated analogues appears to be justified..

20. The Committee concluded that the same arguments and uncertainties described above for the brominated dioxin-like compounds would also apply to mixed halogenated (bromine and chlorine) dioxins, furans and biphenyls. Therefore to assess the contribution of mixed halogenated congeners to the combined intake of chemicals with dioxin-like properties TEFs assigned to the chlorinated dioxins could be applied to the mixed halogenated (bromine and chlorine) dioxins, furans and biphenyls.

Estimated exposures to mixed halogenated, chlorinated and brominated dioxins, furans and biphenyls in fish, meat, offal and eggs.

21. The limited number of foods surveyed were not adequate for assessment of total dietary exposure to mixed halogenated dioxins, furans and biphenyls. However comparative levels of mixed halogenated, brominated and chlorinated dioxin and biphenyl congeners measured in the same samples were available. In order to allow comparison of the relative contribution of mixed halogenated, brominated and

chlorinated dioxin and biphenyl congeners exposures were estimated on a pg TEQ/kg bodyweight (b.w.) basis for a single portion of fish, offal and meat or a single egg using the TEFs for chlorinated congeners for both the brominated and mixed halogenated congeners. The estimates are summarised in tables 2-5. Estimation of total dietary exposure would need to take into account the amounts of these foods consumed as well as exposure from other foods,

Table 2. Estimates of exposure to mixed halogenated, brominated and chlorinated dioxin and biphenyl congeners expressed as pg TEQ/kg b.w. from consumption of one portion of fish.

Fish	Mixed halogenated dioxins pg TEQ/kg b.w.	Polybrominated dioxins pg TEQ/kg b.w.	Polychlorinated dioxins pg TEQ/kg b.w.
Oily fish	0.0119 – 0.14	0.035 - 0.189	2.009 – 9.079
White fish	0.035	n.m.	5.46
Shellfish	0.0049 – 0.021	0.0238 – 0.217	0.0455 – 2.079
Eel	0.014 – 0.028	0.021 – 1.526	0..791 – 4.529
Smoked oily fish	0.021 – 0.049	0.07 – 2.982	1.099 – 2.982

n.m. – not measured
Portion size of 140g or 70g, depending on type of fish; based on 60kg b.w. person

Table 3. Estimates of exposure to mixed halogenated, brominated and chlorinated dioxin and biphenyl congeners expressed as pg TEQ from consumption of one portion of offal.

Offal		Mixed halogenated dioxins pg TEQ/kg b.w.	Polybrominated dioxins pg TEQ/kg b.w.	Polychlorinated dioxins pg TEQ/kg b.w.
Liver	Deer	0.0518- 0.798	0.1827	5.817 - 6.02
	Ox	0.0105	0.1183	0.182
	Lamb	0.0098 - 0.0203	0.2597	0.63 – 1.785
	Pork	0.056 – 0.063	0.1183	0.315
	Chicken	0.035 – 0.024	0.0308 – 0.0658	0.028
Kidney	Ox	0.0049	0.0196	0.105
	Lamb	0.0035	0.0462	0.119

Portion size of 100g; based on 60kg b.w. person

Table 4. Estimates of exposure to mixed halogenated, brominated and chlorinated dioxin and biphenyl congeners expressed as pg TEQ from consumption of one portion of meat.

Meat	Mixed halogenated dioxins pg TEQ/kg b.w.	Polybrominated dioxins pg TEQ/kg b.w.	Polychlorinated dioxins pg TEQ/kg b.w.
Beef joint	0.0084 – 0.0119	0.0336	0.119 – 0.42
Beef processed	0..091 – 0..0133	0.0336 – 0.0525	0.252 – 0.301
Lamb joint	0.007 – 0.0217	0.0441	0.182 – 0.63
Lamb mince	0.0126 – 0.0147	0.0441	0.581 – 0.651
Mutton	0.007	n.m.	0.266
Chicken	0.0049 – 0.0063	0.0602	0.119 – 0.147
Duck	0.0602	n.m.	2.835

n.m. – not measured
Portion size of 100g; based on 60kg b.w. person

Table 5. Estimates of exposure to mixed halogenated, brominated and chlorinated dioxin and biphenyl congeners expressed as pg TEQ from consumption of one egg

Eggs	Mixed halogenated dioxins pg TEQ/kg b.w.	Polybrominated dioxins pg TEQ/kg b.w.	Polychlorinated dioxins pg TEQ/kg b.w.
Organic free range eggs	0.0021	0.0259	0.147
Yorkshire farmhouse eggs	0.0035	0.0175	0.042
Organic eggs, Ayrshire	0.0084	0.0259	0.658
Omega 3 free range eggs	0.0021	0.0259	0.042
Duck eggs	0.0091	0.0651	0.826
Gull eggs	0.1533	n.m.	5.67

n.m. – not measured
Portion size of 100g; based on 60kg b.w. person

Combined dietary exposure to mixed halogenated, brominated and chlorinated dioxin and biphenyl congeners.

22. Upper bound high level dietary intakes of dioxins and dioxin-like PCBs in 2001 were re-calculated using 2005 WHO-TEFs for adults in the UK were estimated to be 1.4 pg WHO-TEQ/kg bw/day. Upper bound concentrations assume that all individual congeners that are present at concentrations below the reporting limit (limit of

detection) are present at the reporting limit, and therefore are likely to overestimate the true concentrations.

23. Although it was not possible to produce reliable dietary estimates for either the mixed halogenated or the brominated dioxin and biphenyl congeners, it was possible to estimate the relative contribution of the mixed halogenated or the brominated dioxin and biphenyl congeners compared to chlorinated congeners based on the portion estimates in those foods where levels of all three had been measured. The chlorinated congeners were the major contributor followed by the brominated and the mixed halogenated. The TEQs for the brominated congeners were generally 1 or more orders of magnitude lower than the TEQs for chlorinated congeners in these samples whilst the mixed halogenated congeners were generally 2 or more orders of magnitude lower than the TEQs for chlorinated congeners. Thus based on these portion estimates the brominated congeners contributed 10% or less to the overall TEQ and the measured mixed halogenated dioxins, furans and biphenyls 1% or less to the overall TEQ.

24. The 19 mixed halogenated dioxins, furans and biphenyls measured in the samples were only a minority of possible mixed halogenated congeners. However these 19 included a higher proportion of the congeners which would be expected to have high TEFs (i.e. those with a 2,3,7,8 configuration) than congeners which would be expected to have lower or no TEFs. Provided amounts of the measured congeners are representative of the mixed halogenated, dioxin and biphenyl congeners in these samples and considering the relative representation of congeners with higher TEFs, extrapolating these results to all mixed halogenated, dioxin and biphenyl congeners would increase the overall contribution of but would probably alter the overall TEQ for combined dioxin exposure by no more than 10%.

25. Therefore, the Committee considered it unlikely that combining the mixed halogenated and brominated dioxin, furan and biphenyl congeners with the estimated dietary intake for chlorinated dioxin, furan and biphenyl congeners would lead to dietary intakes of dioxins and dioxin-like PCBs greater than the TDI.

Conclusions.

26. The new data demonstrated the presence of mixed halogenated dioxins, furans and biphenyls in a range of food samples.

27. The TEFs developed for the chlorinated dioxins could be used as an indication of the dioxin-like activity of the mixed halogenated dioxins, furans and biphenyls. This would be consistent with the Committee's previous conclusions on brominated dioxins, furans and biphenyls in 2006 and the same caveats and uncertainties would apply. The TEQs for the brominated and mixed halogenated dioxins, furans and biphenyls contaminants could be combined with the TEQs for the chlorinated dioxins, furans and biphenyls to provide an indication of the combined dietary exposure to chemicals with dioxin-like properties as this would be more protective of public health than to view the chemicals separately. However, the use of TEFs assigned to chlorinated congeners for the brominated and mixed halogenated analogues was likely to be over-conservative.

28. Based on the levels estimated per portion of the foods surveyed, the chlorinated dioxins, furans and biphenyls were the major contributors to the TEQs; the contributions from brominated and mixed halogenated dioxins, furans and biphenyls were much lower.

29. Levels of chlorinated dioxins in the environment have decreased substantially over the past two decades and it was likely the mixed halogenated compounds were generated in a similar manner to other dioxins. Therefore in the absence of intentional manufacture of mixed halogenated dioxins, furans and biphenyls, it was probable that environmental levels of mixed halogenated dioxins, furans and biphenyls would parallel those of chlorinated dioxins.

30. The most important uncertainty in the risk assessment was the lack of toxic equivalency factors for the mixed halogenated dioxins, furans and biphenyls, and the consequent reliance on toxic equivalency factors for the corresponding chlorinated dioxins, furans and biphenyls. However, based on the results presented, further research on mixed halogenated dioxins, furans and biphenyls is not a priority.

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Abbreviations.

b.w. bodyweight

FSA Food Standards Agency

FSIS Food Safety Information Sheet

PBDDs polybrominated dibenzo-*p*-dioxins

PBDFs polybrominated dibenzofurans

PBBs dioxin-like polybrominated biphenyls

PCDDs polychlorinated dibenzo-*p*-dioxins

PCDFs polychlorinated dibenzofurans

PCBs dioxin-like polychlorinated biphenyls

PXDDs mixed halogenated (chlorine and bromine) dibenzo-*p*-dioxins

PXDFs mixed halogenated (chlorine and bromine) dibenzofurans

PXBs mixed halogenated (chlorine and bromine) biphenyls

REP relative effect potency

TCDD 2,3,7,8-tetrachlorodibenzo-*p*-dioxin

TDI tolerable daily intake

TEFs Toxicity Equivalency Factors

TEQ Toxic Equivalents

WHO World Health Organisation

WHO-TEFs World Health Organisation Toxicity Equivalency Factors

WHO-TEQ World Health Organisation Toxic Equivalents