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

COT STATEMENT ON BROMINATED FLAME RETARDANTS IN FISH FROM THE SKERNE-TEES RIVERS SYSTEM

Introduction

1. The Food Standards Agency (FSA) has recently completed a survey to determine the concentrations of brominated flame-retardants (BFRs) in brown trout and eels from the Skerne-Tees river system. The Committee was asked to assess the toxicological properties of selected BFRs in order to advise on any health implications of the estimates of dietary exposure.

Background

2. Brominated flame-retardants (BFRs) are structurally diverse chemicals used in plastics, textiles and other materials to enhance their flame-retardant properties. Some BFRs, including polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCD) are mixed into polymers rather than being chemically bound to them and can leach out of the products/materials in which they are used and into the environment.

3. PBDEs are produced by direct bromination of diphenyl ether. There are 209 individual PBDE congeners, each of which is identifiable by a unique congener number. Three commercial PBDE flame-retardants, pentabromodiphenyl ether (pentaBDE), octabromodiphenyl ether (octaBDE) and decabromodiphenyl ether (decaBDE) have been available in the UK. The commercial PBDEs are not pure products but a mixture of various diphenyl ethers with varying degrees of bromination.

4. The actual composition of the commercial products varies with supplier and is considered to be commercially sensitive information. However, example compositions of PBDEs have been published (see Table 1). These figures are broadly representative of the commercial products currently supplied. The commercial products are usually named on the basis of the principal PBDE congener e.g. pentaBDE. Trade-name nomenclature may also incorporate a number, which is related to the performance characteristics (e.g. flame retardant properties) of the commercial mixture rather than the constituent congeners[1].

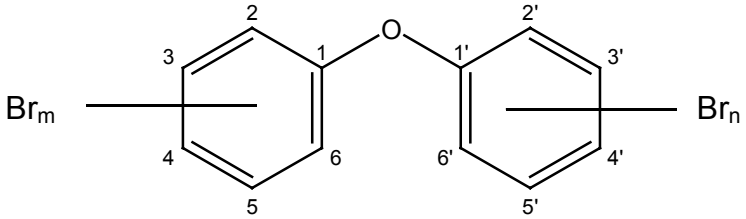
Table 1. Relative congener distribution for penta- and octaBDE

Commercial product	% congeners in commercial product						
	tetra	penta	hexa	hepta	octa	nona	deca
PentaBDE[1]	24-38	50-62	4-12	-	-	-	-
OctaBDE[2]	-	-	≤12	≤45	≤33	≤10	-
DecaBDE[3]	-	-	-	-	-	≤3	≤97

5. The commercial PBDEs have recently been evaluated under the EU Existing Substances Regulations. As a result of their potential to bioaccumulate in the environment, the EU has agreed to ban the marketing and use of penta- and octaBDE from 1 July 2004. However, for some time after this date there will still be existing PBDE-containing products in use.

6. There are limited data available on the potential of decaBDE to bioaccumulate in the environment and it is not currently included in the EU prohibition. In addition, it was not measured in the Skerne Tees survey. However, information on decaBDE has been included in this statement for completeness and as a basis for future evaluations because decaBDE will be the only PBDE product commercially available when the ban on penta- and octaBDE comes into force. The chemical structure of PBDEs is given in Figure 1.

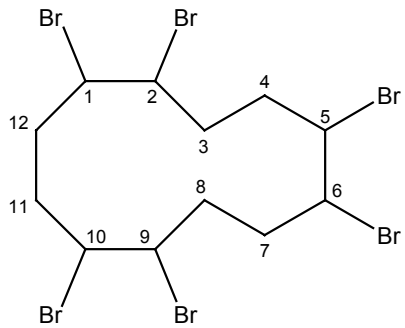
Figure 1. Chemical structure of PBDEs



Where (m) plus (n) equal between 1 and 10 bromine atoms.

7. HBCD is synthesised through bromination of cyclododecatriene. It is commercially available in the UK as a mixture of three stereoisomers α, β and γ. There is currently no proposal to ban HBCD in the EU[4]. The chemical structure of HBCD is given in Figure 2.

Figure 2. Chemical structure of HBCD



Toxicology of PBDEs and HBCD

8. Completed EU risk assessments are available for pentaBDE[1] and octaBDE[2], and draft risk assessments are available for decaBDE[3] and HBCD[4]. Unless otherwise indicated, the following summary is based on the information provided in these risk assessments. The COT also considered new studies published subsequent to the final literature searches for the EU risk assessments. A more detailed summary of the toxicological data is available at http://www.food.gov.uk/multimedia/pdfs/tox14.pdf. Throughout this statement the terms pentaBDE, octaBDE, decaBDE and HBCD refer to the commercial mixtures of brominated flame-retardants whereas individual congeners are denoted by inclusion of the specific congener number e.g. PBDE-99.

PBDEs

9. There is limited information on the toxicokinetics of penta-, octa- and decaBDE. Studies in laboratory animals have indicated that penta- and octaBDE are absorbed following oral administration however, the extent of absorption is unknown[1,2]. DecaBDE is not well absorbed after oral administration (<10%)[3].

10. The primary route of excretion for all PBDEs is considered to be the faeces, although it is unclear how much of the PBDE present in the faeces represents unabsorbed material. In rats, following oral administration, the majority of pentaBDE was detected unchanged in the faeces[1]. Limited information indicates that decaBDE is metabolised to lesser brominated phenolic products[3]. There is no information on the metabolism of octaBDE. Elimination of pentaBDE from rat adipose tissue is slow ($t_{1/2}$ = 25-47 days) indicating that it has the potential for bioaccumulation[1]. There is no information on the elimination of octa- or decaBDE in animals, or on the bioaccumulation or the route of elimination of PBDEs in humans.

11. There is no information on PBDE levels in adipose tissue from the UK. However, PBDE-47 (2,2',4,4'-tetraBDE), PBDE-99 (2,2',4,4',5-pentaBDE), PBDE-100 (2,2',4,4',6-pentaBDE), PBDE-153 (2,2',4,4',5,5'-hexaBDE) and PBDE-154 (2,2',4,4',5,6'-hexaBDE) have been detected in human breast adipose tissue in the US. The sum of total PBDEs detected was 86 ng/g fat[5]. PBDE-47 has also been detected in adipose tissue in Sweden (1.0-98.2 ng/g lipid)[6].

12. In Sweden, there has been an increase in total PBDE levels in samples of human milk over a 25 year period from 1972-1997. The predominant congener was PDBE-47 (2,2',4,4'-tetraBDE) which accounted for 62% of the total (2.28 ng/g lipid). PBDE-99 (2,2',4,4',5-pentaBDE) accounted for 13% (0.48 ng/g lipid) and PBDE-153 (2,2',4,4',5,5'-hexaBDE) accounted for a further 8% of the total (0.46 ng/g lipid). The remaining 17% was accounted for by other tri-, tetra-, penta- and hexa congeners[7]. Data from North America also indicate an increase in total PBDE levels in breast milk. In 1992, samples of breast milk from the Canadian milk bank contained less than 50 ng PBDE/g fat. In 1997, concentrations of approximately 150 ng PBDE/g fat were detected in

samples from women in New York State and 200 ng PBDE/g fat was detected in samples from Austin and Denver in 2000[8]. A recent abstract reported a mean concentration of total PBDE of 6.6 ng/g lipid in breast milk sampled from women in the UK in 2001-3[9].

13. Repeat dose studies of commercial pentaBBDE in rodents have identified the liver as a key target organ, with effects seen at doses of 2 mg/kg bw/day and greater. Based on a study in which a commercial pentaBDE product was administered to rats in the diet for 30-days (0-1 mg/kg bw/day) with no treatment related changes, the EU risk assessment concluded, the no observable adverse effect level (NOAEL) for pentaBDE was 0.45 mg/kg bw/day[1]. This value was derived based on the content of 50-62% pentaBDE in the commercial product and assuming a maximum oral absorption of 90%, by analogy with other polyhalogenated diaromatic compounds. Applying similar correction factors to the doses at which liver toxicity has been observed indicates a LOAEL of 0.9 mg/kg bw/day.

14. For octaBDE, a LOAEL of 7.2 mg/kg bw/day was identified for histopathological liver changes in the rat[2]. A NOAEL for liver changes following administration of octaBDE has not been established. The repeat dose toxicity of decaBDE is low. The EU risk assessment reported a NOAEL of 1,120 mg/kg bw/day for liver changes seen in the carcinogenicity study in rats (paragraph 19)[3].

15. In short term gavage studies in rats commercial mixtures of pentaBDE (10-300 mg/kg bw/day), PBDE-47 (2,2',4,4'-tetraBDE; 18 mg/kg bw/day) and a commercial mixture of octaBDE (10-100 mg/kg bw/day) have been shown to increase the metabolism of model substrates for drug metabolising enzymes, in a manner consistent with induction of cytochrome P450 isozymes of the CYP1A and CYP2B subfamilies and UDP-glucuronosyl transferase. This induction was associated with perturbation of thyroid hormones, liver enlargement and histopathological changes in the thyroid[1,10,11,12]. DecaBDE was not found to induce a similar spectrum of changes in CYP subfamilies and thyroid hormones[10,13]. In this study the effect of decaBDE was investigated in rats at doses up 100 mg/kg/day for 4 consecutive days. This dose is an order of magnitude below the LOAEL for lesions in the liver and thyroid in the carcinogenicity studies and as such, may have been insufficient to produce an effect in short-term studies.

16. Penta-BDE has not been shown to be mutagenic in four studies in *S. typhimurium* and one study in *S. cerevisiae*. A cytogenetic study in human peripheral blood lymphocytes also gave negative results. In a single study in *S. typhimurium*, a commercial pentaBDE referred to as Tardex 50 (10-10000 μg/plate) was shown to increase point mutations by 3-fold at the highest concentration in the absence, but not in the presence, of metabolic activation. This single positive result was considered in the EU risk assessment to be a chance finding[1]. PentaBDE has not been tested for genotoxicity *in vivo*.

17. Commercial octaBDE preparations were not mutagenic in four studies in *S. typhimurium* and one in *S. cerevisiae* in the presence and absence of

metabolic activation. One preparation referred to as Muster 82 showed weak mutagenic activity in *S. typhimurium* without activation. No information is available on the composition of this preparation. Commercial octaBDE did not induce unscheduled DNA synthesis in human fibroblasts, sister chromatid exchange (SCE) in Chinese hamster ovary (CHO) cells or chromosomal aberrations in human peripheral blood lymphocytes. OctaBDE has not been tested for genotoxicity *in vivo*[2].

18. Commercial decaBDE preparations of known purity (97-98%) were not mutagenic in *S. typhimurium* or *E. coli* in the presence and absence of rat metabolic activation. Two preparations referred to as Muster 83 and Muster 88 had positive effects in strains TA 98, 100 and 1535 with and without activation, but not in strains TA 1537 or 1538. No information is available on the composition of these preparations. In studies reported by the NTP, decaBDE was not mutagenic in the mouse lymphoma assay and did not induce SCE or chromosomal aberrations in CHO cells. In a reproductive study with dietary administration of decaBDE (3-100 mg/kg/day), there was no increase in chromosomal aberrations in the bone marrow cells of parent rats or of the offspring at weaning[3].

19. There are no carcinogenicity data for pentaBDE and octaBDE. The EU risk assessment noted that the evidence for carcinogenicity of decaBDE was considered to be equivocal. In a 103-week feeding study in mice there was an increase in hepatocellular adenomas or carcinomas at the lowest dose (3200 mg/kg bw/day), but not at the higher dose (6650 mg/kg bw/day). Thyroid gland follicular cell adenomas were reported in male mice at both doses. There was no evidence of carcinogenicity in female mice. In a 103-week feeding study in rats there was a dose dependant increase in neoplastic liver nodules, which was significantly greater than control in low dose males (1120 mg/kg bw/day) and in both sexes at the high dose (2240 mg/kg bw/day)[3].

20. In a developmental study in rats, oral administration of commercial pentaBDE on days 6-15 of gestation resulted in no adverse fetal effects at the doses up to 200 mg/kg bw/day[1]. Commercial preparations of octaBDE have been shown to cause fetal toxicity and malformations at doses below those causing maternal toxicity in rats and rabbits. The EU risk assessment identified 2 mg/kg bw/day as the lowest NOAEL for octaBDE, from a study in rabbits in which slight fetotoxicity was observed at 5 mg/kg bw/day[2]. A commercial preparation of decaBDE did not show developmental effects following dietary administration in the diet to rats at doses up to 100 mg/kg bw/day for 60 days prior to mating until weaning[3].

21. The PBDE congeners PBDE-47 (2,2',4,4'-tetraBDE) and PBDE-99 (2,2',4,4',5-pentaBDE) have been reported to cause neurobehavioural changes in NMRI mice following a single oral dose administered on post natal day (PND) 3, 10 or 19. Neurobehavioural effects were detected at 60 and 120 days of age[14,15,16]. In addition, perinatal exposure of CD1 mice to PBDE-99 resulted in neurobehavioural effects detected at 60 days[17]. The main neurobehavioural effect of PBDE-99 was delayed habituation behaviour, which

was found to occur at the lowest doses tested (0.6 mg/kg[17]; and 0.8 mg/kg[15,16]).

22. Limited data on the interaction of a range of PBDE congeners with the arylhydrocarbon (Ah) receptor suggest that those measured have much lower potency than the dioxins and co-planar PCBs[18,19]. *In vitro* studies have suggested that a range of PBDEs have endocrine disrupting activity mediated via the oestrogen receptor[19,20].

HBCD

23. All toxicological studies with HBCD were conducted using the commercial mixture. Studies in laboratory animals have shown that, following oral administration, HBCD can be detected in the adipose tissue, liver and muscle. Longer-term exposure shows HBCD has the potential to bioaccumulate. The α-isomer has been found to accumulate more than the β- and γ-isomers. The extent of metabolism of the commercial HBCD is unknown. Following oral administration, the majority of HBCD was detected unchanged in the faeces, although it is unclear how much of this was unabsorbed material. There is no information on the toxicokinetics of HBCD in humans[4].

24. Repeat dose studies of HBCD have identified the liver as a key target organ. Increased liver weights and disturbances in thyroid hormones were observed at 100 mg/kg bw/day which was the lowest dose tested[4].

25. HBCD was not mutagenic in one study using *S. typhimurium* and did not induce chromosomal aberrations in human peripheral blood lymphocytes in the presence and absence of metabolic activation. HBCD caused a slight but significant increase in somatic recombinations in a non-standard assay using two Chinese hamster cell lines containing duplication mutations in the *hprt* gene. The relevance of this is unclear. *In vivo*, there were no significant increases in the frequency of micronuclei in mouse bone marrow cells. In an 18-month lifetime study of dietary administration to mice (available to the EU rapporteur in summary form only) there were no treatment related increases in tumour incidence at HBCD doses of 13-1300 mg/kg bw/day[4].

26. Administration of HBCD to pregnant rats at dietary doses up to 750 mg/kg bw/day, or gavage doses up to 1000 mg/kg bw/day did not result in fetal toxicity or teratogenicity[4]. HBCD has also been investigated for neurodevelopmental effects[21]. A single dose of HBCD resulted in changes in spontaneous behaviour. However, this information was only available as an abstract, the doses resulting in these effects were unclear and therefore the data could not be used in the risk assessment.

COT evaluation of the toxicological properties of PBDEs and HBCDs

27. There are deficiencies in the toxicological database of the PBDEs and HBCD and these uncertainties need to be reflected in the evaluation. The

majority of studies reviewed were relatively old and, although conducted to the standards of the time would not meet current requirements for study design and reporting. In addition, the duration of the longest studies undertaken with pentaBDE were similar to the reported half-life and the resulting tissue concentrations would only reach half of their maximal value by the end of the study.

28. The limited data on the toxicokinetics of the PBDEs suggest differences in absorption and excretion of individual compounds. Data on the genotoxicity, carcinogenicity and reproductive toxicity of PBDEs and HBCD are also limited. As the EU is introducing prohibitions on the use of some PBDEs, it is unlikely that new studies will be undertaken to address the deficiencies in the toxicological databases.

29. The toxicity studies have generally been conducted using commercial mixtures of PBDEs and HBCD. The composition of the material used in many of the studies was unclear and likely to differ from the mixture of congeners measured in food and the environment. Although a similar pattern of biological effects was reported for different mixtures, extrapolation of findings between mixtures should be treated with caution.

30. Whilst some Ah receptor mediated activity could be measured with PBDEs, the potency was low and the most sensitive end-points of toxicity were unlikely to be mediated by this mechanism. It has also been suggested that PBDEs have endocrine disrupting activity mediated via the oestrogen receptor, although the current data are limited.

31. The liver is a target organ for the PBDEs, with pentaBDE being the most toxic, and decaBDE the least. OctaBDE has been found to exhibit reproductive toxicity, whereas pentaBDE and decaBDE did not produce adverse effects in routine developmental studies.

32. Non-routine studies suggest that the most sensitive endpoints are neurodevelopmental. Two of the congeners that are present in commercial pentaBDE, have been shown to cause neurobehavioural effects in adult mice following administration of a single postnatal oral dose. Octa- and decaBDE, and the congeners commonly found in them, have not been investigated using this protocol.

33. HBCD is also hepatotoxic. It has not shown evidence of developmental toxicity in routine studies. One study, available in abstract form only, indicates that it might produce neurodevelopmental effects but there is insufficient detail to use the data in risk assessment.

34. Table 2 shows the NOAELs and LOAELs for the key effects of the PBDEs and HBCD. Based on the available data, pentaBDE appears to be the most toxic of the PBDEs, with a NOAEL of 0.45 mg/kg bw/day for liver effects following repeat dosing and a LOAEL of 0.6 mg/kg bw/day for neurodevelopmental effects following a single post-natal dose. For HBCD, the LOAELs are 100 mg/kg bw/day for liver effects following repeat dosing and 0.9

mg/kg bw/day for neurodevelopmental effects following a single post-natal dose.

35. It is anticipated that the human perinatal blood-brain barrier would be as permeable to PBDE as that of the mouse neonatal blood-brain barrier. There is no single neurodevelopmental stage of the human brain that is directly comparable with the mouse, as different brain parts develop at different rates in the two species. These studies involved administration at postnatal days 3 and 10, at which age the mouse brain probably models the human brain from 1 month pre-natal to 1 month post-natal. There is a lack of data on levels in breast milk, which might be a major source at the critical time for neurodevelopmental toxicity.

Table 2. NOAELs and LOAELs for PBDEs or HBCD

BFR	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Target	Comments
Commercial pentaBDE[1]	0.45	0.9	Liver	No chronic studies available
PBDE-99 (2,2',4,4',5-pentaBDE)[15]	ND	0.6	Neurodevelopment	
Commercial octaBDE[2]	2 ND	5 7.2	Reproduction Liver	No neurodevelopmental data
Commercial decaBDE[3]	ND	1,120	Liver	No neurodevelopmental data
Commercial HBCD[4]	ND	100	Liver	Chronic data seen in summary form only

ND: NOAEL was not determined in the study identifying the LOAEL

36. In view of the inadequacies in the toxicological database and the absence of identifiable no-effect levels, it was not possible to determine a tolerable daily intake (TDI). The Committee therefore decided to take a Margin of Exposure (MoE) approach in which the estimated human exposures are compared with the relevant NOAEL or LOAEL identified from the animal studies. Had it been possible to establish a TDI from a NOAEL, uncertainty factors (UFs) would be required to allow for inter-and intraspecies differences in toxicokinetics and toxicodynamics (100) and limitations in the database such as study duration and gaps in the data (up to 10). Combining these uncertainty factors suggests a target MoE of 1000 for liver toxicity of penta-BDE, above which risks to health would not be expected. A NOAEL has not been identified for the neurodevelopmental effects of penta-BDE and therefore an additional UF of 3-10 would be required for extrapolation from a LOAEL to a NOAEL. This suggests a target MoE of 3,000-10,000. Similarly, a NOAEL has not been identified for the hepatic effects of HBCD, indicating a target MoE of 3,000-10,000. The exposure is not expected to represent a risk to health if the calculated MoE exceeds the target MoE.

PBDEs and HBCDs in fish from the Skerne Tees survey and in the 2001 Total Diet Study (TDS)

37. In 1999, a study sponsored by the Department of the Environment, Transport and Regions measured the concentration of PBDEs in rivers and estuaries downsteam of potential sources. The maximum concentrations of PBDEs were detected in the livers of fish (1294 µg/kg wet wt) and sediment (239 µg/kg dry wt) from the Skerne-Tees river system and the Tees estuary at Newton Aycliffe, which is downstream from the Great Lakes Chemical Company[22]. The Great Lakes Chemical Company is known to have manufactured both penta- and octaBDE at this site until the late 1990's, and still produces HBCD. DecaBDE was never manufactured at the site but may have been distributed via this site. The concentrations detected in the fish livers and sediment were only measured at one time-point and it is important to note that the trout in this river are restocked annually indicating these figures may not accurately represent the actual levels of contamination in the river.

38. Following these reports, the Food Standards Agency conducted a survey to determine the concentrations of congeners known to be components of commercial penta- and octaBDE in brown trout and eels from the Skerne-Tees river system. The Great Lakes Chemical Company is also known to have manufactured HBCD and thus, it was included in the survey. The chemical formula of the each congener and the BFR to which each congener corresponds is given in Table 3. A preliminary assessment of dietary exposure based on analysis of food samples from the 2001 Total Diet Study (TDS) was also conducted.

Table 3. PBDE and HBCD congeners measured in the FSA survey

Congener	Chemical formula	Component
PBDE 28	2, 4, 4'-TriBDE	Possible component of commercial pentaBDE
PBDE 47	2, 2', 4, 4'-TetraBDE	Known substantial component of commercial pentaBDE
PBDE 99	2, 2', 4, 4', 5-PentaBDE	Known substantial component of commercial pentaBDE
PBDE 100	2, 2', 4, 4', 6-PentaBDE	Known substantial component of commercial pentaBDE
PBDE 153	2, 2', 4, 4', 5, 5'-HexaBDE	Possible component of commercial pentaBDE and known component of commercial octaBDE
PBDE 154	2, 2', 4, 4', 5, 6'-HexaBDE	Possible component of commercial pentaBDE and commercial octaBDE
α-HBCD	1R, 2S, 5R, 6R, 9S, 10S-HBCD	Known component of commercial HBCD
β-HBCD	1R, 2R, 5R, 6S, 9R, 10S-HBCD	Known component of commercial HBCD
γ-HBCD	1S, 2S, 5S, 6S, 9S, 10S-HBCD	Known component of commercial HBCD

R & S indicate the stereo position of the bromine on the HBCD molecule

39. A survey was commenced in late 2001 to determine the concentrations of PBDE and HBCD in brown trout and eels from the Skerne-Tees river system. The samples examined included control samples of trout and eels from the Skerne and eels from the Tees. Samples were obtained from the river Skerne and river Tees at eight easily accessible locations that were

upstream and downstream of the Great Lakes Chemical Company and at the confluence of the two rivers (see Figure 3). The PBDE congeners analysed in the survey were selected as a representative sample of those produced and used in the Skerne-Tees area. The chemical formula of each congener and the commercial PBDE to which each congener corresponds is given in Table 3.

40. At the time of this survey no data were available on other sources of dietary exposure to PBDEs and HBCDs in the UK. Therefore, a survey of the concentrations of PBDE congeners in food samples from the 2001 Total Diet Study (TDS) was commissioned in 2002. Single composite food group samples were formed by homogenising individual foods groups (excluding beverages) from 24 locations. These composite samples were analysed for the same range of PBDE congeners as the fish survey. It had been planned to additionally analyse these samples for decaBDE, however since none of the congeners measured were detectable this analysis was not undertaken.

Analytical methodology

41. The analytical method involved solvent extraction of the fat component of composite samples from the TDS or a portion of flesh removed from fish or eels. The extracts contained BFRs and other compounds that were separated from the dissolved fat component by adsorption chromatography. The PBDEs were measured using gas chromatography coupled to a mass spectrometric detector (GC-MS).

42. For HBCD, a simplified clean-up stage was performed which consisted of shaking another aliquot of the crude extract with concentrated sulphuric acid. The acid destroys the fats but leaves HBCD compounds intact. The temperatures used to separate PBDEs during GC analysis can affect the structures of the isomers and result in conversion between the three HBCD isomers. Therefore HBCD was determined using a liquid chromatography mass spectrometry (LC-MS) method.

43. Due to their lipophilicity BFRs are most likely to be detected in fatty foods. The production of composite samples from the individual foods that comprise a particular food group in the TDS may result in dilution of the overall fat content and thus may reduce the ability to detect these substances.

Dietary exposure to PBDEs and HBCD from Skerne Tees trout and eels

44. Table 4 shows the concentration ranges of total PBDEs and HBCD in trout and eels taken from those test sites where the highest concentrations were found and from the control sites. The most contaminated trout were caught at the Haughton Road site, which was the closest river Skerne location downstream of the Great Lakes Chemical Company. No eels are caught at this site, and the most contaminated eels were caught from the next river Skerne downstream location at Oxenfield Bridge.The sum of the concentrations of individual PBDE congeners detected in the edible portion varied from 12 to 14 µg/kg freshweight in trout and was 53 µg/kg freshweight in the eel at control

sites. At test sites, the sum of the concentrations varied from 59 to 197 µg/kg freshweight in trout and 164 to 288 µg/kg freshweight in eels.

45. For HBCD the concentration in the edible portion of trout varied from 21-119µg/kg freshweight and was 159 µg/kg freshweight in the eel at control sites. At test sites, the sum of the concentrations was 159 to 6758 µg/kg freshweight in trout and 570 to 9432 µg/kg freshweight in eels. The trout population of the Skerne Tees River system is restocked annually and no information was available to ascertain the ages of the fish sampled and whether concentrations increased in older fish. Detailed results will be published in a Food Surveillance Information Sheet.

46. The estimated average intake from consumption of one weekly portion (120g) of trout at the maximum levels detected were 0.056 µg/kg bw/day of PBDEs and 1.9 µg/kg bw/day of HBCD. The estimated average intake from consumption of one weekly portion (70g) of eels, were 0.048 µg/kg bw/day of PBDEs and 1.57 µg/kg bw/day of HBCD.

47. There are no commercial fisheries in the river and consumption would be limited to fish caught by anglers.

Table 4. Estimated average dietary intake of PBDE and HBCD following consumption of trout or eels from the Skerne-Tees river system

BFR and sampling location	Species	No of samples	Concentration range (µg/kg freshweight)	Maximum intake (µg/portion) [c]	Maximum average intake (µg/kg bw/day) [d]
PBDE (Ricknall Grange)[a]	Trout	5	12-14	1.6	0.003
PDBE (Haughton Rd)[b]	Trout	7	59-197	24	0.056
PBDE (Ricknall Grange)[a]	Eels	1	53	3.7	0.0088
PBDE (Oxenfield Bridge) [b]	Eels	5	164-288	20.2	0.048
HBCD (Ricknall Grange)[a]	Trout	5	21-119	14	0.034
HBCD (Haughton Road) [b]	Trout	7	159-6758	810	1.9
HBCD (Ricknall Grange)[a]	Eels	1	159	11.1	0.027
HBCD (Oxenfield Bridge) [b]	Eels	3	570-9432	660	1.57

[a] Control site for Skerne River

[b] Test site showing the highest concentration of PBDEs or HCBD in trout or eels

[c] Portion sizes were assumed to be 120g trout or 70g eels, as cited in MAFF Food Portion Sizes[23]

[d] Average daily intake was calculated assuming consumption of one portion of trout or eels per week and an adult bodyweight of 60kg

Total dietary exposure to PBDEs and HBCD

48. None of the congeners measured was present at concentrations exceeding the limit of detection (LOD) in any of the composite TDS samples analysed. Estimated intakes were therefore calculated from the upper bound concentrations (assuming that PBDE and HBCD were present at the LOD in all foods) together with consumption data from the 2000 National Diet and Nutrition Survey[24]. Dietary exposure for mean adult consumers was estimated to be ≤0.047 μg/kg bw/day for the sum of the PBDE congeners measured and ≤0.010 μg/kg bw/day for the sum of HBCD isomers. The actual intakes might be very much lower.

COT evaluation of dietary exposure to PBDEs and HBCD

49. The concentrations of PBDEs and HBCD detected varied widely in the fish sampled from the test sites and also from those sites considered to be control sites. In the absence of information to the contrary, it is assumed that the fish will move freely around the Skerne-Tees river system and therefore concentrations in the fish taken from one site are not representative. It is therefore not possible to identify an average concentration of PBDEs or HBCD which could be used to estimate intake for an individual regularly consuming fish caught from an individual site. Therefore worst-case intake estimations have been calculated from the highest measured concentration at any site. It is unlikely that this worst case intake would be achieved on a regular basis.

50. The PBDE congeners measured in the survey were selected as major representative components of penta- and octaBDE. Toxicity data are not available for the individual congeners. Concentrations of the individual congeners have therefore been summed for comparison with the toxicity data on the commercial PBDE mixtures. Studies on the commercial PBDEs indicate that pentaBDE is the most toxic. Comparison of the estimated intakes of the sum of the measured PBDE congeners with the reported effect levels for pentaBDE provides a precautionary approach because some of the congeners are expected to be less toxic.

51. The most sensitive effect of pentaBDE and HBCD was considered to be neurodevelopmental. The LOAEL for pentaBDE (600μg/kg bw/day) for this effect was obtained from studies in which the test material was administered by a single oral dose to mice on postnatal days 3 or 10. Limited evidence suggests that HBCD also has this effect. Human infants of comparable developmental stage (up to 1 month) would not eat fish and so would not be directly exposed to PBDE or HBCD from fish. Although pentaBDE is known to pass into breast-milk, the available data are not sufficient to estimate the potential exposure to the breast-fed infant resulting from consumption of contaminated fish by the mother. There is a need for data on levels of PBDEs and HBCD in breast-milk in the UK, in order to determine whether the breast-fed infant is at risk of neurodevelopmental effects arising from consumption of contaminated fish. The available studies on reproductive toxicity have not included investigation of neurobehavioural effects, and therefore there are no data of relevance to exposure by pregnant women. Overall, it was considered

not possible to calculate a relevant MoE with respect to neurodevelopmental effects.

52. For older children and adults eating trout or eels contaminated with PBDEs and HBCD, the liver toxicity is the most relevant and sensitive effect on which to base a risk assessment.

53. The worst-case estimated intake of total PBDEs from consuming one portion of trout per week from the Skerne-Tees river system was 0.056 μg/kg bw/day indicating a MoE of approximately 10,000 compared with the NOAEL of 450 μg/kg bw/day for liver effects of pentaBDE in rats. The MoE for intake of PBDEs from consuming one portion of eels per week would also be about 10,000. Since these MoEs are larger than the target MoE of 1000 for pentaBDE, these intakes are unlikely to pose a health risk.

54. The worst case estimated intake of total HBCD from consuming one portion of trout per week was 1.9 μg/kg bw/day indicating a MoE of approximately 50,000 compared with the LOAEL of 100,000 μg/kg bw/day for liver effects of HBCD in rats. The MoE for intake of HBCD from consuming one portion of eels per week would be about 60,000. Since these MoEs are larger than the target MoE of 3,000-10,000 for HBCD, these intakes are unlikely to pose a health risk.

Conclusions

55. 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.

56. 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.

57. 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.

58. 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.

59. 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.

60. 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.

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Corrected April 2004

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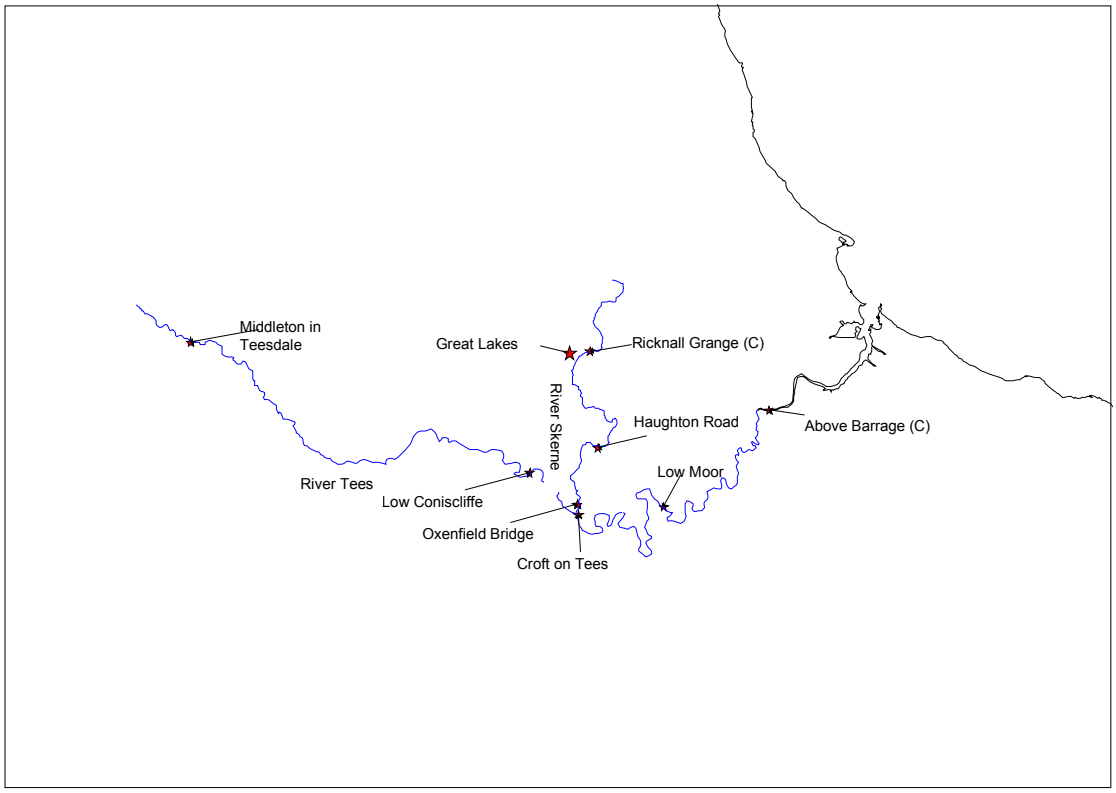
Figure 3. Sampling locations for the survey for brominated flame-retardants in fish from the Skerne-Tees River system



The sites shown on the map are the sites where samples of fish and eels were taken from. The sampling sites were upstream and downstream of the Great Lakes Chemical Company and at the confluence of the two rivers. Control samples (c) were obtained from the River Skerne at Ricknall Grange and from the River Tees at above the Tees Barrage. It was only possible to sample both trout and eels at the Oxenfield Bridge and Croft-on-Tees sampling sites.