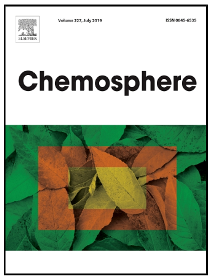
Accepted Manuscript



PBDEs in cod (*Gadus morhua*) liver products (1972 to 2017): Occurrence and human exposure

Jerzy Falandysz, Frankie Smith, Zoe Steel, Alwyn R. Fernandes

PII:	S0045-6535(19)31051-3
DOI:	10.1016/j.chemosphere.2019.05.139
Reference:	CHEM 23874
To appear in:	*Chemosphere*
Received Date:	09 March 2019
Accepted Date:	16 May 2019

Please cite this article as: Jerzy Falandysz, Frankie Smith, Zoe Steel, Alwyn R. Fernandes, PBDEs in cod (*Gadus morhua*) liver products (1972 to 2017): Occurrence and human exposure, *Chemosphere* (2019), doi: 10.1016/j.chemosphere.2019.05.139

PBDEs in cod (*Gadus morhua*) liver products (1972 to 2017): Occurrence and human exposure

[1,2]Jerzy Falandysz*, [3]Frankie Smith, [3]Zoe Steel, [4]Alwyn R Fernandes

[1]University of Gdańsk, Environ. Chemistry and Ecotoxicology, 63 Wita Stwosza Str., 80-308 Gdańsk, Poland
[2]Environmental and Computational Chemistry Group, School of Pharmaceutical Sciences, Zaragocilla Campus, University of Cartagena, 130015 Cartagena, Colombia+
[3]Fera Science Ltd, York, YO41 1LZ, UK
[4] School of Environmental Sciences, University of East Anglia, Norwich NR4 7TJ, UK

Keywords: dietary exposure, tolerable intake, brominated flame retardants, maximum limits, fish oil

***Corresponding Author:** Jerzy Falandysz - jerzy.falandysz@gmail.com (+visiting professor)

Abstract

PBDEs occur in a range of commonly consumed foods but there is very little current information on occurrence in dietary supplements such as cod liver oil or cod livers used as food. This study retrospectively investigated a number of these products, sourced from the Baltic Sea and North Atlantic, historically dating from 1972 to 2017. For the sum of 17 measured PBDEs (ΣPBDE), the concentrations ranged from 9.9 to 415 ng g^{-1} for the oils and from 10.5 to 13 ng g^{-1} for canned liver products. Concentrations in the oils were highest during the period from 1993 to 2001. For all samples, BDE-47 was the dominant congener with a maximum detected concentration of 308 ng g^{-1} in a Baltic cod liver oil from 1993. Human exposure to PBDEs from recommended doses were estimated for adults, teenagers and children. Depending on the age group, BDE-47 intakes ranged from 1.3 to 211.5 ng kg^{-1} bm day^{-1} (Baltic Sea), 2.9 to 12.7 ng kg^{-1} bm day^{-1} (Atlantic,

Norway) and 1.1 to 4.8 ng kg^{-1} bm day^{-1} (Atlantic, Iceland). Intakes for the other dominant congeners, BDE-49, BDE-99 and BDE-100, were relatively low. The intake estimates of ΣPBDE were highest for Baltic cod liver oils ranging from 2.2 to 284.8 ng kg^{-1} bm day^{-1} for adults, 2.8 to 178 ng kg^{-1} bm day^{-1} for teenagers and 2.0 to 127.8 ng kg^{-1} bm day^{-1} for a child. Estimated weekly intake of ΣPBDE from canned cod liver was highest for adults, ranging from 17.6 to 25.1 ng kg^{-1} bm.

Highlights

Individual PBDE congener occurrence of > 300 ng g^{-1} in historical medicinal grade cod liver oil

Estimated adult daily intakes of ΣPBDEs from recommended dose – max. 285 ng kg^{-1} bm day^{-1}

Canned liver foods from 2017 show ΣPBDE concentrations of 10-13 ng g^{-1}

1. Introduction

Polybrominated diphenyl ethers (PBDEs) are mass produced, synthetic brominated flame retardant (BFR) chemicals that have been used for several decades but are now recognized as wide-spread contaminants in food and the environment (de Boer, 1989; Falandysz, 1997; 1998). This recognition is confirmed by the Stockholm convention which categorizes these chemicals as persistent organic pollutants (POPs) listed for elimination of production and use (Stockholm Convention, Annex A). A number of different commercial PBDE mixtures were widely marketed, including PentaBDE (Great Lakes DE-71 and Bromkal 70-5-DE), OctaBDE (Great Lakes DE-79, Dow FR-1208 HM and Bromkal 79-8-DE), and DecaBDE (Great Lakes DE-83, Saytex 102E, Dow FR-300BA and Bromkal 82-0-DE) (Geyer et al. 2000; Hanari et al. 2006; La Guardia et al. 2006). These products were composed of a mixture of congeners but unlike other similar products classified as POPs such as the Halowax series of polychlorinated naphthalenes (PCNs) or the Aroclor series of polychlorinated biphenyls (PCBs), which contain the majority of theoretically (configurationally) possible congeners (Hanari et al. 2013; Ishikawa et al. 2007), PBDEs formulations are composed of considerably fewer numbers of congeners. Of the 209 theoretically possible configurations, thirty-nine have been identified in the mixtures, with twenty-nine at concentrations > 0.02% by weight (La Guardia et al. 2006). These technical PBDE mixtures are contaminated with polybrominated dibenzofurans (PBDFs; in the range 257 – 49,605 ng g^{-1}) and polybrominated biphenyls (PBBs; in the range 58 - 4025 ng g^{-1}), but show no detectable levels of polybrominated dibenzo-*p*-dioxins (PBDDs) (Hanari et al. 2006).

PBDEs were integral additives in a range of plastic types that were used in numerous durable products including foams, paints, furniture, television and computer casings and other electronics, etc. (Alaee et al. 2003; Rauert and Harrad, 2015). Driven by regulation, technical PBDEs mixtures were used to a greater extent in North America and Asia than in Europe, resulting in higher PBDE blood levels and body burdens in these human populations (Alaee et al., 2003; Hites, 2004). Historically however, the global trade in household goods containing these products, coupled with the global market for disposal/ recycling, and atmospheric and marine transport via ocean currents and the atmosphere, has diffused PBDEs throughout the global environment (Aznar-Alemany et al., 2019). PBDE-containing plastic products disposed in the environment degrade very slowly, leaching out the chemicals as they age and fragment, while improper thermal disposal or fires involving PBDE-containing plastics can result in the emission of many brominated compounds including PBDD/Fs (Lundstedt et al. 2015; van den Berg et al. 2013). Children's toys made from re-cycled plastics have been shown to contain BFRs as well as PBDD/Fs (Petrlik et al. 2018). PBDEs can also be unintentionally micro-synthesized in some thermal processes but there is very little available data (Wu et al. 2019) on this mode of formation. Atmospherically borne PBDEs transported by air currents, are more photo-reactive than PCBs, PCNs or PCDD/Fs with a greater ability to absorb photons and photo-transform or degrade than similar chlorinated compounds (Pan et al., 2018).

Production of PBDE formulations ceased in many countries following the recognition of adverse health effects and directives restricting their use (e.g. in the EU - RoHS Directive, REACH Annex XVII) from 2004 for PentaBDE, from 2008 for OctaDBE and from 2017 for Deca-DBE (Stockholm Convention, 2019). Similarly, following reports of persistence, bioaccumulation, and toxicity, the PentaBDE and OctaBDE mixtures were voluntarily phased out in the US from 2005 with phasing out of Deca-DBE from the end of 2013. However, some production does continue with the reported production of decabromodiphenyl ether continuing in China (Wu et al. 2019).

The toxicity of PBDEs to humans at current exposure levels is a key issue because of reported sensitive endpoints and impacts in exposed children, although effects on pet animals have also been studied (ATSDOR, 2017). Some endpoints such as disruption to thyroid hormone regulation may be attributable to some hydroxylated PBDE metabolites (OH-BDEs) (Dishaw et al. 2014). Due to their structural similarity to endogenous thyroid hormones, OH-BDEs show the ability to bind to thyroid transporter proteins while the parent PBDEs are less, or not active. After phase two metabolism, the glucuronide and sulfate conjugates of OH-BDEs are assumed to be non-toxic and readily excreted, and hence OH-PBDEs should not accumulate in humans to the same extent as the parent PBDEs (Cisneros et al. 2019). The mechanism of PBDE neurotoxic action in humans is still not clearly understood, but prenatal and postnatal exposure may have adverse impacts on externalizing behavior (e.g. hyperactivity and conduct issues) in children (Vuong et al., 2018). In a wider sense, given the current use of PBDE replacement products, there is need for deeper insight into effects from current real-world exposures to mixtures of BFRs.

Seafood is considered to be the major dietary source of PBDEs in Europe, with additional contributions from meats and eggs, while mothers milk, hand-to-mouth exposure from physical contact with BFR containing objects, and dust from indoor environments are other factors that are particularly relevant to babies and children (Bramwell et al., 2018; Drobná et al., 2019; Fernandes et al., 2018; Knutsen et al., 2008; Lyche et al., 2015).

Recent studies from Poland show low levels of contamination with PBDEs (congeners #28, 47, 49, 99, 100, 138, 153, 154, 183 and 209) in terrestrial foods sampled in 2015 – 2017. Meat samples (n = 199) from farm animals (cattle, chicken, farm deer, horse, ostrich, pig, rabbit, sheep, turkey) contained PBDEs with median values in the range of 11.6 to 46.7 pg g^{-1} whole weight (ww), within a total range of 1.51 to 666 pg g^{-1} (Pietroń et al. 2019). The eggs from hens raised using different husbandry systems showed median PBDE levels in the range of 0.43 to 0.61 ng g^{-1} fat (total range 0.09 to 9.58 ng g^{-1} fat; n = 99) (Pajurek et al. 2019). In an earlier study in Poland, which measured the same set of PBDE congeners, in butter concentrations of 55 to 174 pg g^{-1} fat and in salmon fresh muscle meat 377 to 5,340 pg g^{-1} (1,850 to 26,700 pg g^{-1} fat basis) were recorded (Wojtalewicz et al. 2008).

The concentrations of PBDEs reported in foods are likely to reflect the extent and periods during which PBDEs were used, and the effects of restrictions on production and use, although the latter will be partly dependent on global, rather than only regional use. The same considerations are likely to apply to dietary supplements such as cod liver oil. Before the era of synthetic vitamins, cod liver oil was an important natural source of vitamins A and D with smaller amounts of vitamin E (α-tocopherol). Medicinal grade cod liver oil was widely used in the 18th, 19th and early 20th centuries as a source of vitamin D (Britannica, 2019). In Poland, cod liver oil sourced from the Baltic Sea was available in pharmacy shops until the early 1970s. Medicinal grade cod liver oil sourced from the North Atlantic and produced, e.g. in Iceland, Norway or the U.K. has been widely available in Europe up to 1980s, and from around the mid-1980s was the only product purified from environmental contaminants such as halogenated POPs. PCBs, organochlorine pesticides (DDTs and others) and PCDD/Fs were common contaminants and could occur at highly elevated concentrations in cod liver oils sourced from the northern regions of the Atlantic Ocean (Falandysz, 1981; Falandysz et al., 1994 and 2019a). Rigorous purification methods were used to reduce content of POPs in cod liver oil products (Falandysz et al. 2019b; Fernandes et al., 2006) and it can also deplete the natural vitamin D which is then substituted with synthetic Vitamin D. Varying degrees of cod liver oil decontamination efficiency from PCDD/PCDF, 76-96%; dl-PCB, 89-99%; ndl-PCB, 91-99%; PBDEs, > 86%; chlorinated pesticides, > 89% were reported (Oli et al. 2013). The aim of the present study was to investigate the historical human exposure to PBDEs resulting from the supplementary intake of historical cod liver oils produced in Iceland, Norway and Poland during 1972-2001, as well as the current potential dietary intake of PBDEs from canned liver products retailed in Poland, in 2017 of Baltic Sea origins.

2. Materials and methods

2.1. Samples

Cod liver oils produced from fish from the Baltic Sea and the North Atlantic and canned cod livers products from the Baltic Sea that were retailed in Poland were obtained as follows:

a) Cod liver oil of medicinal grade (*Oleum Jecoris Aselli* FP IV) purchased in pharmacy shops in Gdańsk, Poland (1972 – in original brown glass bottle; 100 mL),

b) Cod liver oil (1993 and 2001) obtained from a processing plant (Zakłady Rybne) in Gdynia, Poland (1993 and 2001 – in brown glass bottles, 500 mL),

c) L-Cod Liver Oil; (Czysty Świeży Tran) oleum morhuae B.P.: (Contents 1 litre - in original can), donated by Red Cross, 1980,

d) M-Tran (medicinal cod liver oil) purchased from a pharmacy shop in Norway (Contents CA 500 mL; original green glass bottle, 1982),

e) Two types of canned cod liver products: "*Cod livers in own oil*" and "*Pate – cod livers & vegetables*" produced in Łeba (Poland) in 2017; contents 150 g (Table 1).

2.2. Analysis

The method used for the extraction and analysis of cod liver products has been validated, accredited to the ISO17025 standard and documented in full in two previous reports (Fernandes et al., 2004; 2016a). The methodology is based on isotope dilution analysis and internal standardization, using $^{13}C_{12}$-labelled analogues (BDE-28, BDE-47, BDE-99, BDE-153, BDE-154, BDE-183 and BDE-209; Wellington Laboratories Inc. Ontario, Canada) and DBE-100 (Cambridge Isotope Laboratories, Inc., Tewksbury, MA, USA) of target PBDEs. The methodology has been extensively used in other studies (Fernandes et al., 2009; 2016; 2018; 2019; Garcia-Lopez et al., 2018). The following PBDEs were determined: BDE-17 (2,2´,4-Tri-BDE), BDE-28/33 (2,4,4-Tri-/2´,3,4´-Tri-BDE), BDE-47 (2,2´,4,4´-Tetra-BDE), BDE-49

(2,2´,4,5´-Tetra-BDE), BDE-66 (2,3´,4,4´-Tetra-BDE), BDE-71 (2,3´,4´,6-Tetra-BDE), BDE-77 (3,3´,4,4´-Tetra-BDE), BDE-85 (2,2´,3,4,4´-Penta-BDE), BDE-99 (2,2´,4,4´,5-Penta-BDE), BDE-100 (2,2´,4´,4´,6-Penta-BDE), BDE-119 (2,3´,4,4´,6-Penta-BDE), BDE-126 (3,3´,4,4´,5-Penta-BDE), BDE-138 (2,2´,3,4,4´,5´-Hexa-BDE), BDE-153 (2,2´,4,4´,5,5´-Hexa-BDE), BDE-154 (2,2´,4,4´,5,6´-Hexa-BDE), BDE-183 (2,2´,3,4,4´,5´,6-Hepta-BDE) and BDE-209 (2,2´,3,3´,4,4´,5,5´,6,6´-Deca-BDE) (Table 1).

In brief, sample aliquots fortified with $^{13}C_{12}$-labelled internal standards were extracted using mixed organic solvents. PBDEs were chromatographically fractionated from the brominated dioxins and furans on activated carbon. Extracts were further purified using adsorption chromatography on basic alumina. Analytical measurement was carried out using high resolution gas chromatography coupled to high resolution mass spectrometry (HRGC-HRMS, Waters Autospec Ultima instrument fitted with a Hewlett Packard 6890N gas chromatograph). Quality control criteria for PBDE analysis was similar to regulated PCDD/Fs and PCBs measurements with the inclusion of a cod liver oil reference material (Fernandes et al., 2018) and procedural blanks which were evaluated prior to quantitation and reporting. Further quality assurance measures included the successful participation in international inter-comparison exercises on PBDEs (e.g. POPs in Food, 2018). Measurement uncertainty (expanded uncertainty with a coverage factor of 2) estimates range from around 20% at ≥ 10x the limit of detection, to around 200% at the limit of detection.

2.3. Intake estimates

Volumes of cod liver oil for intake estimation were based on recommended doses in tablespoons (teaspoon quantities for children) provided by the producers or other sources (Igya, 2019), as detailed elsewhere (Falandysz et al 2019a). Recommended doses were 1 to 4 tablespoons (adult), 1 to 2 tablespoons (teenager) and 1 to 2 teaspoons (child). These volumes were converted to a weight basis (12 g for a tablespoon, 4 g for a teaspoon) to allow better comparison. The corresponding weights are shown in Table 2. Body masses of 70 kg, 56 kg and 26 kg for adult, teenager and child respectively were used. It should be borne in mind that children and teenagers could be given cod liver oil daily for months beginning from early autumn until early spring for a couple of years. For the canned food, liver and liver pate, portions of 105 -150 g, 52-75 g and 26-37 g were used for adults, teenagers and children respectively. The daily intake of four PBDE congeners (BDE 47, 49, 99 and 100 were selected, based on occurrence) and the sum of the measured PBDEs (ΣPBDE), was estimated as the product of the contaminant concentration and the quantity of oil or food consumed, divided by the appropriate body mass.

3. Results and discussion

The concentrations of PBDE congeners detected in the cod liver oils and cod liver products are collated in conventional units, ng g^{-1} in Table 1. Concentrations for canned products are given in ng g^{-1} whole weight (ww), as well as on a fat basis in order to allow comparison to other data. All samples showed the presence of PBDEs, but concentrations varied widely and patterns of occurrence showed some differences between the canned cod liver products and cod liver oils. Some congeners such as Tetra-BDE-71, Penta-BDE-85 and Hexa-BDE-138 were not detected (LOD range < 0.002 to < 0.06 ng g^{-1}) in any of the samples, whilst others, Tetra-BDE-77, Penta-BDE-119 and -126, and Hepta-BDE 183 were observed at relatively low concentrations (0.003 to 0.09 ng g^{-1}) in some of the samples. BDE-209 was detected only in the liver products at 0.1 to 0.59 ng g^{-1}. The remaining nine measured congeners were detected (range 0.02 to 308 ng g^{-1}) in all the samples. The European Commission has recommended a set of ten congeners (BDE- 28, 47, 49, 99, 100, 138, 153, 154, 183 and 209) for investigation in member states, as part of an effort to identify the levels and patterns of PBDE occurrence in food and animal feeds (European Commission, 2014). Three of these congeners (BDE-138, 183 and 209) either did not occur or showed minor levels of occurrence. Of these, BDE-138 is rarely detected in foods or detected at very low concentrations, and BDE-183 is generally also observed at low concentrations (FSANZ, 2007; Mortimer et al., 2010). BDE-209, however does occur frequently in foods and can often be a major constitutent of summed PBDE occurrence (Fernandes et al., 2016b). This higher level of occurrence is more noticeable in more recent studies and may be due to Deca-BDE being the last of the PBDE commercial mixtures to be subjected to a ban on production and use. In this study its appearence only in the later (2017) samples may provide some support for this hypothesis. Tetra-BDE-47 and 49, and Penta-BDE-99 and 100 accounted for approximately 90% of the total PBDE in all samples. The dominance of BDE-47 (range 4.9 to 308 ng g^{-1}) is commonly observed in foods including fish and oils (Fernandes et al., 2009; 2016b; Mortimer et al., 2010).

The patterns of relative occurrence (Fig 1A) of the measured congeners are broadly similar in all of the samples, and there is barely any difference between the Baltic Sea and North Atlantic samples, but the canned products show some differences with BDE-154 and BDE-209 occurring to a relatively greater extent. The average profile (Fig 1B) for canned liver is very similar to the general profile (Fig 1C) for marine fish (Fernandes et al., 2018). As mentioned earlier the difference in the profile of the oils may be a result of the chronology of the sampling, but it is also possible that some PBDE congeners may be selectively lost/degraded during thermal processing (autoclaving) of canned liver products or purification of the oils.

As comparative literature to the more historic samples, De Boer (1989) reported on PBDEs in cod livers netted in the regions of the North Sea in 1977-1989. In cod samples from the southern part of the North Sea, Tetra-BDEs were recorded in the range of 110 – 360 ng g^{-1} fat, with sporadic detection of Penta-BDEs and Hexa-BDEs. However eels (*Anguilla anguilla*) from the North Sea and inland waters in the Netherlands were found to show far higher levels of contamination (de Boer, J., 1989; Falandysz, 1998). More recent data on retail cod liver oils from Spain showed a range of 8.7 - 18 ng g^{-1} (Marti et al., 2010), and separately, Boucher et al., 2018, reported a summed concentration of 11.6 ng g^{-1}. The concentrations of PBDEs in foods or indeed cod liver oils and other dietary supplements is not as yet regulated. As already mentioned, it is quite likely that for the more recent products, purification processes such as molecular distillation and activated carbon treatment that are used to remove regulated halogenated organic pollutants such as PCDD/Fs and PCBs (Oterhals et al., 2007) may effect decontamination from PBDEs as well, although the authors are not aware of activated carbon treatments for PBDEs as yet.

3.1. Estimated intake

Human exposure to PBDEs is likely to arise from multiple pathways (Bramwell et al., 2016) and the non-dietary route may be influenced by a number of variable such as proximity to sources, relative concentrations, temperature, personal habits (for hand to mouth transfer), etc. Dietary intake however is likely to be the dominant route to exposure as reported in other studies on European populations (Fromme et al., 2009; Roosens et al., 2009), accounting for over 90% of the body burden. For future scenarios, this level of attribution to dietary intake is not unreasonable as direct non-dietary exposure to PBDEs from household goods can be expected to decrease following the restrictions and phasing out of PBDE containing products.

As commercially produced cod liver oil involves the extraction of oil from the liver of several thousands of fish in batches, the resulting product represents an integration, and would therefore provide a much better estimate of contamination and intake rather than that from a single fish. Given the differences in relative abundance of congener occurrence, daily intakes were estimated for BDE-47, BDE-49, BDE-99, BDE-100 and the sum of PBDEs. Also, as different congeners may show different toxicological endpoints, individual congener intake estimates are perhaps most helpful at this stage, but for convenience and comparison with other literature, intake for the sum of PBDE congeners was also included. Estimates for intake based on recommended doses, for adults, teenagers and children are presented in Table 2. BDE-47 intakes from cod liver oil, depending on age were in the range of 1.3 to 211.5 ng kg^{-1} bm day^{-1} (Baltic Sea), 2.9 to 12.7 ng kg^{-1} bm day^{-1} (Atlantic, Norway) and 1.1 to 4.8 ng kg^{-1} bm day^{-1} (Atlantic, Iceland). During the periods covered by the production dates of the earlier samples (1972-2001), cod liver oil taken on a medicinal basis was prescribed for daily consumption over a period extending up to several months. Thus, on a weekly basis, estimated intakes for BDE-47 could range from 9 to 1480 ng kg^{-1} bm $week^{-1}$ (Baltic Sea), 20 to 89 ng kg^{-1} bm $week^{-1}$ (Atlantic, Norway) and 7.7 to 34 ng kg^{-1} bm $week^{-1}$ (Atlantic, Iceland).

Canned liver products sourced in the North Atlantic and Baltic Sea are currently retailed and consumed as a food in Europe. Apart from a break in production and supply (approximately from the late 1970s to the late 1980s), products sourced from the Baltic Sea (several varieties provided by a number of producers in recent years) have been continuously retailed in Poland, but there is no official estimate on the rate of consumption. During the optimal fishing season which runs from December to May, some consumers may be expected to eat the equivalent of a can (approximately 150-250 g total weight including oil) per week. The estimated intake of BDE-47 for all age groups after consuming the contents of one of the consignments per a week was in the range 5.3 to 12.2 ng kg^{-1} bm $week^{-1}$, with highest intake rates for adults (Table 2).

Intake from cod liver oil dietary supplements must also be considered in combination with intake from the rest of the diet. There is no total diet study (TDS) data available for Poland but as an example of exposure from another European country, the total diet study (TDS) for 2012 in the UK estimated a population intake range for BDE-47 of 0.20 to 0.61 ng kg^{-1} bm day^{-1} depending on age group from adults to toddlers (Mortimer et al., 2013). Similarly for the French population, the highest (95^{th} percentile) dietary exposure (for the sum of 8 PBDE congeners) was 1.18 ng kg-1 bm day-1for adults and 2.37 ng kg^{-1} bm day^{-1} for children (Riviere et al., 2014). These estimates integrate consumption from all common items of a normal diet and are substantially below any of the ΣPBDE intakes estimated in the present study (Table 2) which consider only a single item.

Intake estimates for the other congeners, BDE-49, BDE-99 and BDE-100, were relatively low in comparison to BDE-47, due to the correspondingly lower levels of occurrence. The estimated daily intakes of ΣPBDE from the Baltic cod liver oils were in the range 2.2 to 284.8 ng kg^{-1} bm day^{-1} for an adult, 2.8 to 178 ng kg^{-1} bm day^{-1} for a teenager and 2.0 to 127.8 ng kg^{-1} bm day^{-1} for a child. The corresponding intakes of ΣPBDE from the Norwegian cod liver oil were in the range 4.2 to 17, 5.3 to 10.6 and 3.8 to 7.6 ng kg^{-1} bm day^{-1}, and from Icelandic cod liver oil were 1.7 to 6.8, 2.1 to 4.2 and 1.5 to 3.0 ng kg^{-1} bm day^{-1} for adults, teenagers and children respectively. Estimated weekly intake of ΣPBDE from canned cod liver was highest for adults, ranging from 17.6 to 25.1 ng kg^{-1} bm $week^{-1}$ (Table 2).

Some studies suggest that PBDE-209 exposure during pregnancy and lactation impairs immune function in rats (Liu et al., 2012). However purified fish oils may contain lower concentrations of these contaminants (Covaci et al., 2007), and may be a more suitable alternative for certain population groups (e.g., pregnant women) for which fish consumption recommendations have been issued.

4. Conclusions

Given the current knowledge on marine contamination in the Baltic Sea and the North Atlantic, the relatively high levels of PBDEs measured in historic cod liver oils and contemporary cod liver is perhaps unsurprising. Although the highest concentrations encountered in this study date back to the 1990s, unpurified cod liver oils that were sold up to the mid-1980s were probably a very significant source of exposure to PBDE, particularly BDE-47, to those who were prescribed or generally consumed these oils as dietary supplements. Currently retailed canned cod liver products sourced from Baltic Sea would similarly pose significant levels of PBDE exposure to those who consume these products.

In the absence of relevant information on toxicology and risk, such as a tolerable intake level for PBDEs, the significance of the information presented here is unclear. EFSA's margin of exposure (MoE) approach (EFSA, 2011) concluded that, in Europe, BDE-47 did not raise health concerns, but estimated that the MoE for BDE-99 in one to three year old children was below the acceptable level of 2.5. The US EPA estimated reference doses (RfD) for daily intake of BDE-47 and BDE-99 at 100 ng kg^{-1} bm for both congeners (US EPA, 2010). It is clear that this is an information gap that requires expedient resolution.

Disclaimer

The authors assert no conflict of interest.

References:

Alaee, M., Arias, P., Sjödin A, Bergman, Å., 2003. An overview of commercially used brominated flame retardants, their applications, their use patterns in different countries/regions and possible modes of release. Environ. Int. 29, 683– 689.

ATSDOR, 2017. Public health statement polybrominated diphenyl ethers (PBDEs). https://www.atsdr.cdc.gov/ToxProfiles/tp207-c1-b.pdf (retrived on March 6, 2019).

Aznar-Alemany, Ò., Sala. B., Plön, S., Bouwman, H., Barceló, D., Eljarrat, E. 2019., Halogenated and organophosphorus flame retardants in cetaceans from the southwestern Indian Ocean. Chemosphere, 226, 791-799.

de Boer, J., 1989. Organochlorine compounds and bromodiphenylethers in livers of Atlantic cod (Gadus morhua) from the NorthSea 1977–1987. Chemosphere 18, 2131–2140.

Boucher, B.A., Ennis, J.K., Tsirlin, D., Harris, S.A., 2018. A global database of polybrominated diphenyl ether flame retardant congeners in foods and supplements. J. Food Compos. Anal. 69, 171–188.

Bramwell, L., Harrad, S., Abou-Elwafa Abdallah, M., Rauert, C., Rose, M., Fernandes, A., Pless-Mulloli, T., 2017. Predictors of human PBDE body burdens for a UK cohort. Chemosphere 189, 186–197.

Britannica, 2019. https://www.britannica.com/topic/cod-liver-oil (Retrieved on Feb. 28, 2019).

Cisneros, K.V., Agarwal, V., James, M.O., 2019. Sulfonation and glucuronidation of hydroxylated bromodiphenyl ethers in human liver. Chemosphere, 226, 132-139.

Covaci A, Voorspoels S, Vetter,V., Gelbin, A., Jorens, PG., Blust, R., Neels, H., (2007). Anthropogenic and naturally occurring organobrominated compounds in fish oil dietary supplements. Environ. Sci. Technol., 41, 5237–5244.

POPs in Food, 2018. 19th round of an inter-laboratory comparison study -Norwegian Institute of Public Health. Available at: https://fhi.no/en/publ/2018/interlaboratory-comparison-on-pops-in-food-2018/.

Dishaw, L.V., Macaulay, L.J., Roberts, S.C., Stapleton, H.M., 2014. Exposures, mechanisms, and impacts of endocrine-active flame retardants. Curr. Opin. Pharmacol. 19, 125-133.

Drobná, B, Fabišiková, A., Čonka, k., Gago, F., Oravcová, P., Wimmerová, S., Šovčíková, E., 2019. PBDE serum concentration and pre-school maturity of children from Slovakia. Chemosphere, submitted.

EFSA., 2011. European Food Safety Authority, Scientific Opinion on Polybrominated Diphenyl Ethers (PBDEs) in Food. EFSA Panel on Contaminants in the Food Chain (CONTAM). EFSA Journal 2011;9(5):2156.

European Commission (2014). Commission Recommendation 2014/118/EU of 3 March 2014 on the monitoring of traces of brominated flame retardants in food. Official Journal of the European Union, L65/39, 5.3.2014.

Eljarrat, E., Aznar-Alemany, Ò., Sala, B., Frías, Ó., Blanco, G., 2019. Decreasing but still high levels of halogenated flame retardants in wetland birds in central Spain. Chemosphere, 228, 83-92.

Falandysz, J., 1981. Organochlorine pesticides and PCBs in cod-liver oil of Baltic origin, 1971-80. Pest. Monit. J. 15, 51-53.

Falandysz J., 1997. Polybrominated diphenyl ethers in the environment (in Polish). Bromatol. Chem. Toksykol. 30, 175-182.

Falandysz J., 1998. Polybrominated diphenyl ethers in food (in Polish). Bromatol. Chem. Toksykol. 31, 5-8.

Falandysz, J., Kannan, K., Tanabe, S., Tatsukawa, R., 1994. Organochlorine pesticides and polychlorinated biphenyls in cod-liver oils: North Atlantic, Norwegian Sea, North Sea and Baltic Sea. Ambio. 23, 288-293.

Falandysz, J., Smith, F., Panton, S., Fernandes, A., 2019a. A retrospective investigation into the occurrence and human exposure to polychlorinated naphthalenes (PCNs), dibenzo-*p*-dioxins and furans (PCDD/Fs) and PCBs through cod liver products (1972 – 2017). Chemosphere, submitted.

Falandysz, J., Smith, F., Panton, S., Fernandes, A., 2019b. Contamination, compositional profile, persistency and exposure to poly-/chloronaphthalene (PCN) congeners through edible cod liver products in 1972-2017. Chemosphere. submitted

Fernandes A., White S., D'Silva K., Rose M. 2004. Simultaneous determination of PCDDs, PCDFs, PCBs and PBDEs in food. Talanta 63:1147–1155.

Fernandes, A., Rose, M., White, S., Mortimer, D., Gem, M., 2006. Dioxins and polychlorinated biphenyls (PCBs) in fish oil dietary supplements: occurrence and human exposure in the UK Food Add. Contam. 23, 939 – 947.

Fernandes, A., Tlustos, C., Smith, F., Carr, M., Petch, R., Rose, M., 2009. Polybrominated diphenylethers and Brominated dioxins in Irish Food of Animal Origin. Food Add. Contam. 2, 86-94.

Fernandes, A., Rose, M., Smith, F., 2016a. Report FS102036 to FSA, London.

Fernandes, A., Mortimer, D., Rose M., Smith, F., Panton, S., Garcia-Lopez, M., 2016b. Bromine content and brominated flame retardants in food and animal feed from the UK. Chemosphere, 150, 472-478.

Fernandes, A., Mortimer, D., Holmes, M., Rose, M., Zhihua, L., Smith, F., Panton, S., Marshall, L., 2018. Occurrence and spatial distribution of chemical contaminants in edible fish species collected from UK and proximate marine waters. Environ. Int. 114, 219-230.

Fernandes, A., Lake, I., Dowding, A., Rose, M., Jones, N., Petch, R., Smith, F., Panton, S. 2019. The potential of recycled materials used in agriculture to contaminate food through uptake by livestock. Sci. Tot. Environ. 667, 359–370.

Fromme, H., Korner, W., Shahin, N., Wanner, A., Albrecht, M., Boehmer, S., Parlar, H., Mayer, R., Liebl, B., Bolte, G., 2009. Human exposure to polybrominated diphenylethers (PBDE), as evidenced by data from a duplicate diet study, indoor air, house dust, and biomonitoring in Germany. Environ. Int. 35, 1125–1135.

FSANZ, 2007. Food Standards Australia New Zealand. Polybrominated diphenyl ethers (PBDEs) in food in Australia. Available at: https://www.foodstandards.gov.au/science/surveillance/documents/PBDE_Report_Dec_07.pdf.

Garcia Lopez, M., Driffield, M., Fernandes A., Smith, F., Tarbin, J., Lloyd, A.S., Christy, J., Holland, M., Steel, Z., Tlustos, C., 2018. Occurrence of polybrominated diphenylethers, hexabromocyclododecanes, bromophenols and tetrabromobisphenols A and S in Irish foods. Chemosphere, 197, 709-715.

Geyer , H.J., Rimkus, G.G., Scheunert, I., Kaune, A., Kettrup, A., Zeeman, M., Muir, D.C.G., Hansen, L.G., Mackay, D., 2000. Bioaccumulation and occurrence of endocrine-disrupting chemicals (EDGs), persistent organic pollutants (POPs), and other organic compounds in fish and other organisms including humans. Pp. 1-165. *In* Bio-accumulation. New aspects and developments. B. Beek (Ed.) the Handbook of Environmental Chemistry. vol. 2. Reactions and processes. Part J. Springer-Verlag Berlin Heidelberg.

Hanari, N., Kannan, K., Miyake, Y., Okazawa, T., Kodavanti, P. R., Aldous, K. M., Yamashita, N., 2006. Occurrence of polybrominated biphenyls, polybrominated dibenzo-*p*-dioxins, and polybrominated dibenzofurans as impurities in commercial polybrominated diphenyl ether mixtures. Environ. Sci. Technol. 40, 4400–4405.

Hanari, N., Falandysz, J., Nakano, T., Petrick, G., Yamashita, N., 2013. Separation of closely eluting chloronaphthalene congeners by two-dimensional gas chromatography/quadrupole mass spectrometry: An advanced tool in the study and risk analysis of dioxin-like chloronaphthalenes. J. Chrom. A. 1301, 209-214.

Hites, R. A., 2004. Polybrominated diphenyl ethers in the environment and in people: a meta-analysis of concentrations. Environ. Sci. Technol. 38, 945–956.

Ishikawa, Y., Noma, Y., Mori, S., Sakai, S., 2007. Congener profiles of PCB and a proposed new set of indicator congeners. Chemosphere, 67, 1838-1851.

Knutsen, H.K., Kvalem, H.E., Thomsen, C., Frøshaug, M., Haugen, M., Becher, G., Alexander, J., Meltzer, H.M., 2008. Dietary exposure to brominated flame retardants correlates with male blood levels in a selected group of Norwegians with a wide range of seafood consumption. Mol. Nutr. Food Res. 52, 217–227.

La Guardia, M.J., Hale, R.C., Harvey, E., 2006. Detailed polybrominated diphenyl ether (PBDE) congener composition of the widely used penta-, octa-, and deca-pbde technical flame-retardant mixtures. Environm. Sci. Technol. 40, 6247-6254.

Liu, X., Zhan, H., Zeng, X., Zhang, Ch., Chen, D., 2012. The PBDE-209 exposure during pregnancy and lactation impairs immune function in rats. Mediators Inflamm. 2012: 692467. doi: 10.1155/2012/692467.

Lundstedt, S., Sindiku,O., Ortuño N, Lundin L., Brominated dioxins in plastics–Emissions during fires, in PIC2015 – the 14th International Congress on Combustion By-Products and Their Health Effects, 14-17 June 2015: Umeå, Sweden.

Lyche, J.L., Rosseland, C., Berge, G., Polder, A., 2015. Human health risk associated with brominated flame-retardants (BFRs). Environ. Int. 74, 170–180.

Martí, M., Ortiz, X., Gasser, M., Martí, R., Montaña, M., Díaz-Ferrero, J., 2010. Persistent organic pollutants (PCDD/Fs, dioxin-like PCBs, marker PCBs, and PBDEs) in health supplements on the Spanish market. Chemosphere, 78, 1256-62.

Mortimer, D., Gem, M., Fernandes, A., Rose, M., 2010. Investigation of Polybrominated Diphenyl Ethers in UK Retail Food Samples. Proceedings, BFR 2010. Available at: https://www.researchgate.net/publication/229088182_Investigation_of_Polybrominated_Diphenyl_Ethers_in_UK_Retail_Food_Samples.

Mortimer, D., Acheampong, R., Fernandes, A., Rose, M., 2013. Consumer exposure to chlorinated and brominated dioxins and biphenyls and polybrominated diphenyl ethers: new uk total diet study. Organohalogen Compounds, 75, 1138-1141.

Oli, J., Breivik, H., Thorstadt, O., 2013. Removal of persistent organic pollutants in fish oils using short-path distillation with a working fluid. Chemosphere, 92, 273-278.

Oterhals, A., Solvang, M., Nortvedt, R., Berntssen, M., 2007. Optimization of activated carbon-based decontamination of fish oil by response surface methodology. E.J. Lipid Sci. Tech. 109, 691-705.

Pajurek, M., Pietroń, W., Maszewski, S., Mikolajczyk, Sz., Piskorska-Pliszczyńska, J., 2019. Poultry eggs as a source of PCDD/Fs, PCBs, PBDEs and PBDD/Fs. Chemosphere, 223, 651-658.

Pan, Y., Tsang, D.C.W., Wang, Y., Li, Y., Yang, X., 2018. The photodegradation of polybrominated diphenyl ethers (PBDEs) in various environmental matrices: Kinetics and mechanisms. Chemical Eng. J., 297, 74-96.

Petrlik, J., Behnisch, P., DiGangi, J., 2018. Toxic soup Dioxins in plastic toys. https://papersmart.unon.org/resolution/uploads/3_dioxin_in_recycled_plastics_toxic_soup_brochure_en_web04.pdf.

Pietroń, W., Pajurek, M., Mikolajczyk, Sz., Maszewski, S., Warenik-Bany, M., Piskorska-Pliszczyńska, J., 2019. Exposure to PBDEs associated with farm animal meat consumption. Chemosphere, 224, 58-64.

Quasimeme, 2007. Quasimeme Round 37 exercise 618, Data Assessment report. (Nov 2004) Quasimeme Project Office, Aberdeen, UK.

Rivière, G., Sirot, V., Tard, A., Jean, J., Marchand, P., Veyrand, B., Le Bizec, B., Leblanc, J. 2014. Food risk assessment for perfluoroalkyl acids and brominated flame retardants in the French population: Results from the second French total diet study. Sci. Tot. Environ. 491–492, 176–183.

Rauert C, Harrad S., 2015. Mass transfer of PBDEs from plastic TV casing to indoor dust via three migration pathways-A test chamber investigation. Sci. Total Environ. 536, 568-574.

Roosens, L., Abdallah, M.A., Harrad, S., Neels, H., Covaci, A., 2009. Factors influencing concentrations of polybrominated diphenyl ethers (PBDEs) in students from Antwerp, Belgium. Environ. Sci. Technol. 43, 3535–3541.

Stockholm Convention, 2019. Stockholm Convention on Persistent Organic Pollutants. http://chm.pops.int/ (retrieved on Feb. 26, 2019).

US-EPA, 2010. An Exposure Assessment of Polybrominated Diphenyl Ethers. https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=210404.

Van den Berg, M., Denison, M.S., Brinbaum, L.S., DeVito, M., Fiedler, H., Falandysz, J., Rose, M., Schrenk, D., Safe, S., Tohyama. C., Tritscher, A., Tysklind, M., Peterson, R.E., 2013. Polybrominated dibenzo-*p*-dioxins (PBDDs), dibenzofurans (PBDFs) and biphenyls (PBBs) - inclusion in the toxicity equivalency factor concept for dioxin-like compounds. Toxicol. Sci. 133, 197-208.

Vuong, A.M., Yolton, K., Dietrich, K.N., Braun, J.M., Lanphear, B.P., Chen, A., 2018. Exposure to polybrominated diphenyl ethers (PBDEs) and child behavior: Current findings and future directions. Horm. Behav. 101, 94–104.

Wang, D., Tian Chen, T., Yang, L., Kong, F., Wang, Y., Wang, Y., Shi, Z., 2019. Exposure of occupational workers to polybrominated diphenyl ethers or decabromodiphenyl ethane in brominated flame retardants manufacturing plants: Occurrence and health risk assessment. Chemosphere, submitted.

Wojtalewicz, D., Grochowalski, A., Wegiel, M., 2008. Determination of polybrominated diphenyl ethers (PBDEs) as persistent organic pollutants (POPs) in Polish food using semipermeable membranes (SPMs) *In*: The Fate of Persistent Organic Pollutants in the Environment. (eds.) E. Mehmetli and B. Koumanova, pp. 459 - 469. Springer

Wu X, Wu G, Xie J, Wang Q, Liu G, Liu W, Yang L, Zheng M., 2019. Thermochemical formation of multiple unintentional persistent organic pollutants on metallurgical fly ash and their correlations. Chemosphere, 226, 492-501.

Figure legends

Figure 1. Typical congener-specific PBDE profiles for A. Cod liver oil, B. Canned cod liver, and C. Commonly consumed fish species.

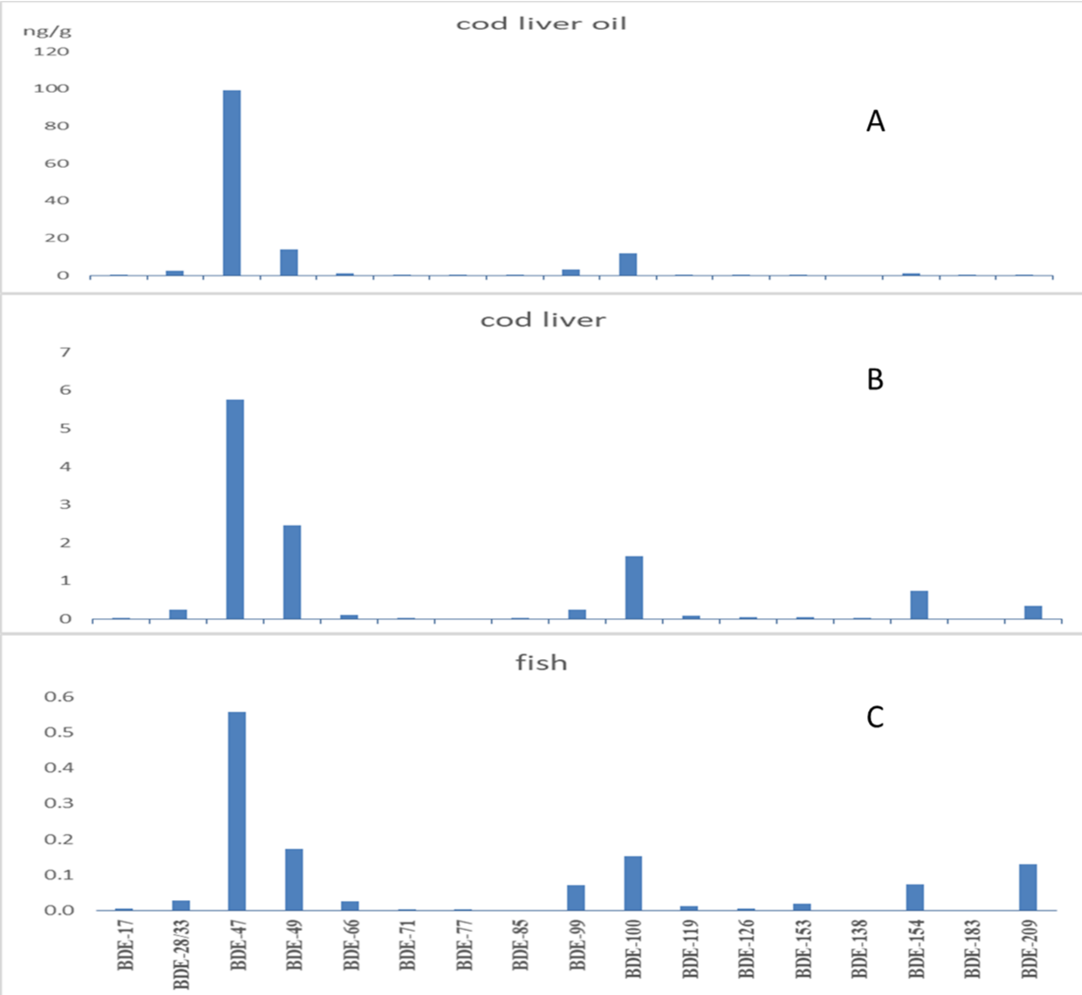

cod liver oil
ng/g
120
100
80
60
40
20
0
A
cod liver
7
6
5
4
3
2
1
0
B
fish
0.6
0.5
0.4
0.3
0.2
0.1
0.0
C
BDE-17
BDE-28/33
BDE-47
BDE-49
BDE-66
BDE-71
BDE-77
BDE-85
BDE-99
BDE-100
BDE-119
BDE-126
BDE-153
BDE-138
BDE-154
BDE-183
BDE-209

Table 1. PBDEs (ng g-1 fat) in cod liver oil and canned liver products (ng g-1 fat // ng g-1 ww) sourced from regions of the North Atlantic (1972 – 2017)

	Region of the North Atlantic							
	Baltic Sea						North Atlantic - Iceland	North Atlantic - Norway
	Medicinal Tran (cod liver oil)	Cod liver oil (tran)	Cod liver oil (tran)	Cod liver oil (tran)	Canned liver products		L-Tran (cod liver oil)	M-Tran (cod liver oil)
Compound	1972	1993	2001	2001	2017[A]	2017[B]	1980	1982
BDE-17	0.031	0.426	0.238	0.249	0.046 // 0.029	0.059 // 0.019	0.026	0.081
BDE-28/33	0.412	7.023	2.661	2.718	0.371 // 0.233	0.861 // 0.278	0.31	1.004
BDE-47	8.8	308.4	124.9	128.1	7.8 // 4.9	20.4 // 6.6	7.0	18.6
BDE-49	1.59	48.6	15.1	14.8	4.8 // 2.5	7.4 // 2.4	1.0	2.2
BDE-66	0.104	3.844	0.912	0.938	0.20 // 0.126	0.334 // 0.108	0.068	0.2
BDE-71	< 0.003	< 0.057	< 0.012	< 0.016	< 0.036 // < 0.022	< 0.11 // < 0.035	< 0.002	< 0.013
BDE-77	< 0.002	0.09	< 0.011	0.008	0.028 // 0.018	0.034 // 0.011	< 0.002	< 0.002
BDE-85	< 0.002	< 0.002	< 0.002	< 0.002	< 0.002 // < 0.002	< 0.006 // < 0.002	< 0.002	< 0.002
BDE-99	0.352	4.7	6.3	6.3	0.557 // 0.35	0.406 // 0.131	0.217	0.308
BDE-100	1.4	37.8	14.2	13.9	2.06 // 1.3	6.2 // 2.0	1.0	2.1
BDE-119	< 0.011	0.35i	< 0.078	< 0.048	< 0.025 // < 0.015	0.28 // 0.09	< 0.003	< 0.027
BDE-126	< 0.005	0.059	0.006	0.007	0.077 // 0.048	0.192 // 0.062	< 0.005	0.003
BDE-138	< 0.005	< 0.005	< 0.005	< 0.005	< 0.003 // < 0.002	< 0.006 // < 0.002	< 0.005	< 0.005
BDE-153	0.017	0.425	0.145	0.144	0.104 // 0.065	0.050 // 0.016	0.016	0.015
BDE-154	0.258	3.5	1.1	1.1	1.25 // 0.786	2.19 // 0.707	0.246	0.218
BDE-183	< 0.002	0.032	0.008	0.007	0.005 // 0.003	< 0.006 // < 0.002	< 0.002	< 0.002
BDE-209	< 0.181	< 0.16	< 0.159	< 0.155	0.165 // 0.104	1.82 // 0.589	< 0.184	< 0.157
Sum PBDEs[#]	12.96	415	166	168	16.7 // 10.46	40.2 // 13.0	9.9	24.7

Notes: 2017[A] is "Cod livers in cod liver oil" (the fat content was 62.8%) and 2017[B] is "pate, cod liver & vegetables" (the fat content was 32.3%) produced in Łeba (Poland) February 2017;

#Lower bound (excludes values < LOQ)

Table 2. Estimated intakes of PBDEs arising from the consumption of typical daily doses of cod liver oils and from portions of canned livers products (one package per week)

Parameters	Product intake (g)	Contaminant intake				
		BDE-47	BDE-49	BDE-99	BDE-100	ΣPBDE
Cod liver oil		(ng kg^{-1} bm day^{-1})				
Baltic Sea - Poland						
Adult (70 kg bm)	12	1.5 - 52.9	0.27 - 8.3	0.06 - 1.08	0.24 – 6.5	2.2 - 71.2
	24	3.0 - 105.7	0.54 - 16.7	0.12 - 2.16	0.48 - 13	4.4 - 142.4
	48	6.0 - 211.5	1.09 - 33.3	0.24 - 4.32	0.96 - 26	8.9 - 284.8
Teen age 14 (56 kg bm)	12	1.9 – 66.1	0.34 – 10.4	0.75 – 1.35	0.3 – 8.1	2.8 – 89.0
	24	3.8 – 132.2	0.68 – 20.8	0.15 – 2.7	0.6 – 16.2	5.6 – 178.0
Child age 7 (26 kg bm)	4	1.3 – 47.4	0.24 – 7.5	0.05 – 0.97	0.21 – 5.8	2.0 – 63.9
	8	2.7 – 94.9	0.49 – 14.9	0.11 – 1.94	0.43 – 11.6	4.0 – 127.8
Atlantic - Norway						
Adult (70 kg bm)	12	3.2	0.38	0.053	0.36	4.2
	24	6.4	0.75	0.11	0.72	8.5
	48	12.7	1.5	0.21	1.4	17
Teen age 14 (56 kg bm)	12	4.0	0.47	0.066	0.45	5.3
	24	8.0	0.94	0.13	0.9	10.6
Child age 7 (26 kg bm)	4	2.9	0.34	0.047	0.32	3.8
	8	5.7	0.68	0.095	0.65	7.6
Atlantic - Iceland						
Adult (70 kg bm)	12	1.2	0.17	0.037	0.17	1.7
	24	2.4	0.34	0.074	0.34	3.4
	48	4.8	0.69	0.15	0.69	6.8
Teen age 14 (56 kg bm)	12	1.5	0.21	0.046	0.21	2.1
	24	3.0	0.43	0.093	0.43	4.2
Child age 7 (26 kg bm)	4	1.1	0.15	0.033	0.15	1.5
	8	2.1	0.31	0.067	0.31	3.0
Canned cod livers (ww)		(ng kg^{-1} bm week^{-1})				
Adult (70 kg bm)	105	8.5	3.6	0.36	2.4	17.6
	150	12.2	5.1	0.51	3.4	25.1
Teenager 14 (56 kg bm)	52^{A}	5.3	2.2	0.22	1.5	10.9
	75^{A}	7.6	3.2	0.32	2.1	15.7
Child age 7 (26 kg bm)	26^{B}	5.7	2.4	0.24	1.6	11.7
	37^{B}	8.1	3.4	0.34	2.3	16.7

Notes: A (a half of a package); B (a quarter of a package)