Project no: 022936
Project acronym: Beneris
Project title: Benefit-risk assessment for food: an iterative value-of-information approach

Instrument: STP-Specific Targeted Project

Deliverable 21:

Intake of contaminants - National registries

Due date of deliverable:	**1 Oct, 2007**
Actual submission date:	**15 Nov, 2009**
Dissemination level:	**PU**
Start date of project:	**April, 1st 2006**
Duration:	**3,5 years**

Organisation name of the lead contractor for this deliverable: **THL**

Intake of contaminants - National registries (D21)

This deliverable consists of a manuscript to be submitted to a peer reviewed scientific journal. At the time being, the manuscript is still at its draft stage. However, the draft is fairly extensive already. The introduction as well as the material and methods are already quite well established, and the results and the conclusions are being finalized.

The manuscript is about the intakes of POPs and Hg in Finnish children (1-6 years) and examines the safety margins and the proportion of the population exceeding tolerable daily intakes as set by international expert bodies.

Intakes of polychlorinated dibenzo-*p*-dioxins and furans, polychlorinated biphenyls, polybrominated diphenylethers, and mercury from food in Finnish children: risk assessment implications

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Research | Children's Health

Short running head: Contaminant intakes from food are high in children

Key words: children, contaminant intake, Finland, Hg, PBDEs, PCBs, PCDD/F, TDI.

Acknowledgment
We thank the DIPP research staff: nutritionists, nurses, doctors and the participating families. The study was supported by EU (Food-CT-2006-022936, BMH4-CT98-3314), Academy of Finland (63672, 79685, 79686, 80846, 201988, 210632, 126581), Finnish foundations (Diabetes Association; Diabetes Research; Finnish Pediatric Research; Juho Vainio; Yrjö Jahnsson; Medical Research Funds of Turku, Oulu and Tampere University Hospitals), JDRF (197032, 4-1998-274, 4-1999-731, 4-2001-435) and Novo Nordisk Foundation.

The authors declare they have no competing financial interests.

List of abbreviations: …..

Outline of section headers:

Abstract

Background: Food is contaminated by persistent organic pollutants (POP) and metals worldwide. Current major causes for concern include polychlorinated dibenzo-*p*-dioxins and furans (PCDD/F), polychlorinated biphenyls (PCB), polybrominated diphenylethers (PBDE), and mercury (Hg) that are detectable universally in any human individual. Previous data show intakes are elevated in children.

Objectives: We determined intakes of POPs and Hg in Finnish children. We examined safety margins and the proportion of the population to exceed the tolerable daily intakes set by international expert bodies.

Methods: We investigated the gender-specific food consumption of Finnish children aged 1 to 6 years, measured the contaminant concentrations in all the main food stuffs, and derived age-specific contaminant intakes as probability distributions to account for the variation in the intakes. Our data corresponds to years 2002-2005.

Results: The Hg intake ranged between 29-70 ng/kg bw/d. The reference dose for Hg was exceeded by 3-18 % of the study population. The mean ingestion rates for the sum of PCDD/Fs and sum of PCBs were 8.5 and 15.8 pg/kg bw/d. $WHO_{PCDD/F-PCB}$-TEQs indicated tolerable daily intakes were exceeded by remarkable proportion of the children. PBDEs were ingested on average 1.3 ng/kg bw/d. The highest POP intakes were observed in 3-year-old children.

Conclusions: The peak intakes at 3 years of age were within an intense growth burst in the age range under study. Regulating food intake in children so as to avoid using foodstuff contaminated the most is thus far the best means to decrease risk arising from food contamination to children's health.

INTRODUCTION

Polychlorinated dibenzo-*p*-dioxins and furans (PCDD/Fs), polychlorinated biphenyls (PCBs), mercury (Hg) recently also polybrominated diphenylethers (PBDEs) are omnipresent in the globe. They are persistent, lipophilic, resistant to metabolism in vertebrate species including humans. Biomagnification occurs in terrestrial and aquatic food chains resulting in high concentrations in top predator species. Over 90 percent of human background exposure to PCDD/Fs and PCBs is estimated to come from food of animal origin (WHO 1998). Hg in ecosystems converts into the organic form, methylmercury (MeHg) that is readily taken up by organisms (joku hyvä Hg-viite). MeHg can make up more than 90% of the total Hg in fish and fishery products (WHO 2003, EC 2008). Generally, fish is the main source of exposure to PCDD/Fs, PCBs and Hg in the Finns (Kiviranta et al. 2005, WHO 2003). There are recent indications that food and fish are the main sources for the exposure to PBDEs in Finland as well (Isosaari et al. 2006; Kiviranta et al. 2004, 2006).

Altogether there are 210, 209 and 209 individual congeners of PCDD/Fs, PCBs and PBDEs, respectively. Because of a mostly additive mode of action, a toxic equivalency concept has been established to facilitate risk assessment and management of 17 toxic 2,3,7,8-chlorine substituted PCDD/F congeners, four non-*ortho* and eight mono-*ortho* substituted dioxin-like PCB congeners (DL-PCBs). Effect potencies, relative to the reference toxicant, 2,3,7,8-TCDD (2,3,7,8-tetrachlorodibenzo-*p*-dioxin), has been defined by the World Health Organization (WHO) on several occasions, most recently 2006 (Van den Berg 2006), and by using TEF an operational sum of normalized concentrations of all congeners, the total toxic equivalent (TEQ) can be determined.

Treating children as a separate subgroup in intake assessment of persistent organic pollutants (POPs) and metals is crucial to the eventual usefulness and validity of the assessment made. There are three obvious reasons that favour separate children-specific intake assessments of POPs and heavy metals: 1) food consumption per weight is higher in children due to rapid growth and development, 2) children may be more vulnerable to development-disrupting effects of contaminants due to their yet maturing physiology, 3) the margins of safety are not very large, especially concerning some developmental dysfunctions. Also, their anatomy is still moulding and might therefore be more easily disturbed than adults. Although remarkable improvements in population estimates of contaminant intake have been made during the past decade in Finland, it has been generally agreed on that more should be invested in treating sensitive subgroups as their own both in intake and environmental health risk assessment of contaminants. Both are demanding tasks that require a highly multidisciplinary approach, but as they are performed to better manage the risks and thereby to lower population food-mediated exposure to contaminants, exclusively with a moderate extra effort of separate children-specific intake assessments these tasks can be adequately fulfilled.

The requirements for analytical procedures for PCDD/Fs, PCBs, PBDEs, and Hg are high. There are two critical quantification methods for individual congeners that are commonly used: upper bound and lower bound concentrations. They are calculated on the assumption that all the values of the individual congeners below the limit of quantification are equal to the limit of quantification or to zero, respectively. For risk management purposes, the European Commission (EC) currently engages with a precautionary principle and rather prefers to overestimate than underestimate the contaminant concentrations in various foodstuffs. It thus calls for upper bound-based concentrations of contaminants in foodstuffs from its member states (EC 2006). In practice this also means that intake estimations should be derived from upper bound concentrations as well. However, for authenticity of the data and to track for the whole range of the uncertainty at the bottom of the varying quantification methodology it is however crucial to obtain intake estimates based on lower bound concentrations as well. Because of these twofold requirements, we aimed at

estimating the daily intakes of contaminants in Finnish children using both the lower bound and the upper bound concentrations.

In the present study we introduce for the first time intake estimations of PCDD/F, PCBs, PBDEs, and Hg from food in Finnish children. These contaminants pose a greatest food-mediated risk for children's health in Finland at the moment so a priority to assess their intakes and risks has been made by the national authorities (Tuomisto, 2007). Two existing databases, food consumption data and food contamination data, were used in order to estimate daily intakes in 1, 3, and 6 years old Finnish children. In view of an effective intake and risk assessment (and management) of contaminants in children, one should not only pay attention to the mean daily intakes but particularly be able to tackle the high extremes. Representing the food consumption as probability distributions allows us to examine the whole probability range of daily intakes of contaminants from food – and determine the portion in the examined age groups to exceed tolerable daily intakes set by international expert bodies such as the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT), the Scientific Committee on Food of the European Commission (SCF), the U.S. Environmental Protection Agency (USEPA) and WHO. Additionally, intakes of individual PCDD/Fs, PCBs (non-*ortho*, mono-*ortho*, marker) and PBDE congeners are presented.

MATERIALS AND METHODS

Study subjects

Subjects in the present study were participants of the Finnish Type 1 Diabetes Prediction and Prevention Study (DIPP) that is a population-based cohort study (Kupila et al. 2001, http://www.dipp.fi/e_index.htm, Kyttälä et al. 2008, Virtanen et al. 2006). In the study parents of newborn infants from three university hospital areas were asked if the genetic susceptibility for type 1 diabetes can be screened from the cord blood of their child. Those children with increased genetic susceptibility were invited to take part in the DIPP-study (15% of the population). The subjects were followed for diet, growth, viral infections and type 1 diabetes-associated antibodies at 3 to 12 month intervals. The study was approved by the local Ethics Committees. All the families gave their written informed consent at the beginning of the study.

DIPP Nutrition Study was part of the DIPP-study. The subjects participating in the nutrition study were from two urban areas in Finland, Oulu and Tampere. A background questionnaire and structured dietary questionnaires with 3-day food records were collected at the ages of 3, 6, and 12 months, and annually thereafter. The series comprises at-risk children born in XXXX-XXXX. Food records were available from a sub sample of 1-year (n=963), 3-year (n=1045) and 6-year-olds (n=850). All food records were kept between the years 2003-2005.

Food consumption estimations

Each child's food consumption was recorded by parents and day care personnel using 3-day food records that included three consecutive days, two weekdays and one weekend day. The families and the day care personnel received written instructions to record with household measures, the type, brand and preparation method of all the foods eaten by the child. A trained study nurse reviewed the records item by item for completeness and accuracy and added information when needed.

Food consumption was calculated to ingredient level using in-house software and the Finnish Food Composition Databank FINELI® (www.fineli.fi). The children with food usage that had been recorded for less than 3 days (n=4,9%) were included in the study.

Food contaminant concentrations

PCDD/F, PCB, and PBDE concentrations

The occurrence data of PCDD/Fs, PCBs, and PBDEs originated from an annual national food monitoring program run by the Finnish Food Safety Authority (EVIRA) and from a specific research project on Finnish fish, "EU-fish" –project (Holocaine et al. 2004; Isosaari et al. 2006; Parmanne et al. 2006; Kiviranta et al. 2006). Samples included in this study, covering years 2002-2005, were meat, (n=29), liver (n=5), milk (n=18), egg (n=16), oil and fat (n=7), fish (n=175), and other food (n=8) samples (Wiborg et al. 2008).

Because fish consumption, both domestic and imported, counts the majority of the total PCDD/F, PCB, PBDE (Wiborg et al. 2008) and Hg (WHO 2003) intake in Finns, also intakes from imported fish were included specifically in our study to add accuracy in intake estimations. Contaminant concentrations in imported fish species such as cod, salmon, farmed salmon, tuna, and saithe consumed substantially by the Finnish population were obtained from several sources (LeBlanc et al. 2006; Ásmundsdóttir et al. 2005; NIFES web page http://www.nifes.no/). The majority of the occurrence data of mercury in Finnish fish originated from a specific research project on Finnish fish, "EU-fish" –project in which 135 fish samples were analyzed for mercury by the laboratory at the Finnish Food Safety Authority (EVIRA) using a previously published method (Venäläinen et al. 2004). In brief, mercury was analyzed by treating samples of fish with a mixture of nitric, sulphuric, and hydrochloric acid. The quantification was performed with AAS (Atomic Absorption Spectrometer) utilizing cold vapor technique. Hg taken up in fish muscle consists mostly of its organic form, MeHg (WHO 2003, EC 2008). Hg analysed from both domestic and imported fish was regarded as MeHg without any correction. The assessed daily intakes are thus slight overestimates. Since mercury (Hg) was analysed from both domestic and imported fish the assessed daily intakes are slight overestimates for MeHg. Still, over 90% of the mercury in fish is methyl mercury. Concentrations of POPs in our study were analyzed in the Chemical Exposure Unit at the National Institute for Health and Welfare (THL) using a previously published method (Kiviranta et al. 2004). Analysis method of PCDD/Fs, PCBs, and PBDEs briefly, the occurrence of 17 2,3,7,8-chlorine substituted PCDD/F (toxic) congeners, of four non-*ortho* PCB congeners (77, 81, 126, and 169), of eight mono-*ortho* PCBs (105, 114, 118, 123, 156, 157, 167, and 189), of 24 other PCBs (PCB 18, 28, 33, 49, 51, 52, 60, 66, 74, 99, 101, 110, 122, 128, 138, 141, 153, 170, 180, 183, 187, 194, 206, and 209), and of fifteen PBDE congeners (BDE 28, 47, 66, 71, 75, 77, 85, 99, 100, 119, 138, 153, 154, 183, and 209) were measured. For PCDD/Fs and PCBs, toxic equivalents quantities (WHO-TEQ) were calculated with toxic equivalency factors (TEF) recommended by WHO in 1998 (Van den Berg et al., 1998).

Samples were spiked with ^{13}C-labeled PCDD/F, PCB, and PBDE standards and fat was extracted. Samples were defatted in a silica gel column after which PCDD/Fs were separated from PCBs and PBDEs on a carbon column. Both fractions were further cleaned by passing through an activated alumina column. The PCB-PBDE fraction was further fractionated in order to separate the non-*ortho* PCBs from other PCBs and PBDEs. The quantification was performed with a HRGC/HRMS (High-Resolution Gas Chromatography/High-Resolution Mass Spectrometry) instrument. Concentrations were calculated with both lower bound and upper bound methods. In the lower bound method, the results of congeners with concentrations below limit of quantification (LOQ) were designated as nil, while in the upper bound method they were denoted as the LOQ.

Quality control and assurance

Both laboratories and all methods used in this study were accredited according to standard EN ISO/IEC 17025.

Contaminant intake calculations

Contaminant daily intakes were calculated for 1-, 3- and 6-year old children separately for both sexes using the calculated mean daily consumption of the food items multiplied with the corresponding mean values of contaminant concentrations. Intakes were summed over each study day for all the subjects. To remove day-to-day variation and to adjust nuisance effects (e.g. day of the week, interview sequence) we used a method by Nusser et al. (1996) to obtain the long-run average of daily intakes, or usual intakes. Intake distributions were estimated using C-SIDE® (version 1.0; Department of Statistics, Center for Agricultural and Rural Development -CARD, Iowa State University, Ames), which implements the Nusser's method. Because there were no individual child weights available, we used age- and gender-specific proportional body weights (i.e. mean body weights from age-specific mean-heights) from Finnish child welfare clinics as specified in 1993 to adjust the intakes per body weights. The used body weights as kg were: 9.9, 14.6, 20.8 and 10.5, 15.0, 21.2 for 1-, 3- and 6-year-old girls and boys, respectively.

Comparison to limit values

In this study, the estimated daily intakes of PCDD/Fs and PCBs were paralleled by two separate TDI suggestions: the 2 pg/kg bw/d by SCF in the European Union and COT and the 1-4 pg/kg bw/d by the WHO (COT 2001, EC 2001, van Leeuwen and Younes 2002). The assessed daily intake of Hg was compared with the reference dose (RfD) of 0.1 μg/kg bw/day set by USEPA (1997) and independently reviewed by several experts by the Committee on the Toxicological Effects of Methylmercury of the National Research Council, the NRC (2000). For PBDEs, no threshold concentration has been suggested so far.

RESULTS

Contaminant intakes and comparison to limit values

The daily upper bound mean ingestion rates for the sum of PCDD/Fs were 9.58 (±5.11), 9.50 (±4.66), 7.51 (±2.86) and 9.50 (±4.61), 8.25 (±3.44), 6.85 (±2.88) pg/kg bw for 1, 3 and 6-year-old boys and girls (Table 2, suppl). For the sum of PCBs the same were 12.61 (±15.85), 22.81 (±21.15), 20.45 (±14.35) and 12.69 (±12.9), 19.52 (±14.61), 17.51 (±11.25) pg/kg bw. The mean intakes for marker PCBs, non-*ortho* PCBs and mono-*ortho* PCBs were 9.89, 27.22 and 2.32 pg/kg bw/d, respectively (Table 1, suppl). The boys intakes were slightly higher than those in girls although not differing significantly. The intakes were at their highest in the three year-old boys and girls but relieving, appeared to decrease from three to six years by both boys and girls. For children aged one year in this study the total daily dietary intake of PCDD/Fs and PCBs was 1.2 (±1.8) and 1.0 (±1.2) pg/WHO-TEQ/kg bw for boys and girls. For three-year-old boys and girls they were 2.0 (±2.2) and 1.8 (±1.4) pg/WHO-TEQ/kg bw, and for six-year-old boys and girls the intakes were 1.8 (±1.5) and 1.7 (±1.4) pg/WHO-

TEQ/kg bw. The lower bound intakes for the sum of PCDD/Fs, sum of PCBs, marker PCBs, non-*ortho*-PCBs and mono-*ortho*-PCBs were 67 (±6), 88 (±5), 90 (±6), 76 (±8) and 94 (±6) % of those measured upper bound, respectively.

Lower bound $WHO_{PCDD/F-PCB}$-TEQs were 77 (±15) % of those measured upper bound. They both indicated TDIs were exceeded by remarkable proportion of the children (Fig 1). The immediate target of 4.0 pg/kg bw/d by WHO was exceeded by 2.5, 10-12.5, 5-7.5 % and 2.5, 5-7.5, 5 % of the 1, 3 and 6-year-old boys and girls, respectively (Table 2, suppl). The WHO's long-term goal 1.0 pg/kg bw/d was exceeded 28-45, 58-68, 65-78 % and 35-48, 63-73, 63-73 % of the 1, 3 and 6-year-old boys and girls, respectively. Ten to fourty percent of the children exceeded the bodyweight-adjusted TDI of 2.0 pg set by COT and SCF. Minimum intakes slightly exceeded the COT's 2 pg/kg bw/d in 3 to 6 years-old boys and girls. Only roughly 5% of lower bound-measured intakes in 1-year-old (both sexes) were below the WHO's TDI of 1.0 pg/kg bw. The maximum intakes were 6-6.7, 7-7.4, 7.2-7.9 and 9.5-8.9, 11.3-12.8, 7.9-8.3 times higher than WHO's TDI of 1.0 and 4.0 pg/kg bw, respectively.

PBDEs were taken up from food on average 0.98 (±0.87), 1.51 (±1.16), 1.49 (±0.93) and 1.03 (±0.92), 1.41 (±0.83), 1.11 (±0.60) ng/kg bw/d by the boys and girls of 1, 3 and 6-years of age, respectively (Fig 2; Table 3, suppl). The intake was at its highest in the three-year-old children, both boys and girls, but it had decreased by the age of six. For PBDEs the lower bound intakes were on average 78 (±6) % of those measured upper bound based (Figure 2; Table 3, suppl).

The lower and upper bound concentrations revealed practically the same Hg intakes in each age group (lower bound-based intakes being 99.99 ± 0.01 % of the upper bound results). Thus only lower bound intakes are presented for Hg (Fig 3). Hg intake from food in Finnish 1, 3 and 6-year-old boys and girls was on average 29 (±29), 46 (±40), 66 (±42) and 32 (±40), 33 (±30), 70 (±71) ng/kg bw/d, respectively (Table 4, suppl). At the smallest, the Hg intakes in 1-year-old boys and girls were nil (fractiles 0.01 for boys and 0.25 for girls). The lowest five percentiles of the three to six-year-old boys and girls took in Hg at a daily ingestion level of 6-9 ng/kg bw. A systematic increasing trend in the intake of Hg in age appeared for both boys and girls.

Probability to exceed the USEPA reference dose of 0.1 µg/kg bw/d for Hg was 2.5, 7.5, 17.5 and 5.0, 2.5, 17.5 % in 1, 3 and 6-year-old boys and girls, respectively (Fig 1; Table 1, suppl). At its highest the USEPA RfD was exceeded times 1.5 (1-year-old boys and 3 year-old girls), ca. two times (1-year-old girls and 3-year-old boys) and times 2.8-3.6 in 6-year-old boys and girls, respectively.

Congener profiles

Nine of the 17 analyzed PCDD/F congeners were ingested by the children in our study. These congeners were in descending order of their average daily ingestion levels: OCDD>2,3,7,8-TCDF>2,3,4,7,8-PeCDF≈1,2,3,4,6,7,8-HpCDF>1,2,3,4,6,7,8-HpCDD>1,2,3,6,7,8-HxCDD≈1,2,3,7,8-PeCDD>1,2,3,4,7,8-HxCDF≈1,2,3,6,7,8-HxCDF (Fig. 4).

The marker PCBs in descending order of their intake levels were: 153, 138, 118, 101, 180, 28_31, 52. Their mean intakes ranged between 0.19-3.60 ng/kg bw/d (Fig 5). The non-*ortho*- and mono-*ortho*-PCBs in descending order of their intakes were: 77, 126, 169, 81; and 118, 105, 156, 123, 167, 157, 189; respectively (Figs 6, 7). The total dietary daily ingestion levels for non-*ortho*-PCBs were 0.42-15.80 ng/kg bw. The same for mono-*ortho*-PCBs were 0.01-1.32 ng/kg bw. Seventeen other PCBs that appeared in the intakes by Finnish children in the mean range of 0.02-0.71 ng/kg bw/d were 18, 33, 47, 49, 51, 60, 66, 74, 99, 110, 128, 141, 170, 183, 187, 194, 209 (Fig 8).

As with the PBDE congeners, BDE-47 was ingested the most. Other congeners detected of the measured were in descending order of their mean daily ingestion levels: 99>100>154≈153>183>66>119>85 (Fig. 9). BDEs 28, 71, 75, 77, 138 and 209 were not detected in the foodstuffs analysed.

DISCUSSION

Contaminant intakes

Due to their higher food consumption in relation to their body weight, children ingest higher doses of environmental contaminants than adults. Because of rapid growth and development, exposure may vary significantly between children and adults but also between children of different age groups. It became mostly evident that the intakes of PCDD/Fs, PCBs and PBDEs were at their highest in the boys and girls aged three years, thus during the most intensive growth burst period in the age distribution included in our study. Just recently for instance, higher PBDE concentrations in the blood sera of young children (6-month age up to 4-years-old) have been detected in Australia as compared with infants and adults (Toms et al. 2009).

The POP intakes by children herein were on average higher than those of adults in Finland. In the late 90s, the total daily dietary intake of PCDD/Fs and PCBs based on a 24-h recall study with an average Finnish adult population (weighing 76 kg) was 1.3 pg TEQ/kg bw (Kiviranta et al. 2001) and so within the range of TDI of 1-4 pg TEQ/kg bw proposed by the WHO. The corresponding intakes by one-year-old Finnish children in this study were similar, 1.1 pg TEQ/kg bw. PCDD/F and PCB intakes almost doubled in the three- and six-year-old children (1.9 and 1.8 pg TEQ/kg bw). Notably, the daily TEQ intakes can be a factor of 2-3 times higher when DL-PCBs are also considered (WHO 1998) like in this study. In our opinion, as humans may be exposed to dozens of dioxin and DL-PCB congeners simultaneously that mostly act additively, such an inclusion should be always made. When comparing the $WHO_{PCDD/F\text{-}PCB}$-TEQ dietary intakes of the children herein to those estimated for German ca. 1-4 years-old children as $WHO_{PCDD/F}$-TEQs only by Wittsiepe et al. (2001), and by correcting their estimates to the $WHO_{PCDD/F\text{-}PCB}$-TEQs, it becomes evident that the children's intakes in both these countries form a pretty much uniform distribution in the very same range mostly in the WHO's TDI range of 1.0-4.0 pg/kg bw/d.

For Hg, a slightly increasing trend in its intake in age up to six years was observed. No such a trend is seen in the MeHg intakes in Swedish children aged 4 to 12 years (Concha et al. 2006). Drawing on their report it appears that the mean daily body weight adjusted Hg intakes of 0.036 μg in the German children aged 1 to 6 years and of 0.03 μg in the Swedish 4-12 years-old boys and girls were a bit lower than the mean of 0.046 μg measured in the present study. If we however make a Hg correction to MeHg (that was not made for the analyzed food samples here but was made in the Concha's report), we get an average intake of 0.041 μg/kg bw/d for the study population here and so converge with the German and Swedish intakes.

Congener profiles

Octachloro dibenzo-*p*-dioxin (OCDD) has been detected as the most abundant congener in the Finnish total diet baskets (Kiviranta et al. 2004), and it was clearly the most abundant in the children's intakes as well (Fig. 4). In addition to OCDD, the congener profile of the sum of PCDD/F intakes was dominated by 2,3,7,8-tetrachloro dibenzofuran (2,3,7,8-TCDF), 2,3,4,7,8-pentachloro dibenzofuran (2,3,4,7,8-PeCDF), 1,2,3,4,6,7,8-heptachloro dibenzofuran (1,2,3,4,6,7,8-HpCDF), 1,2,3,4,6,7,8-heptachloro dibenzo-*p*-dioxin

(1,2,3,4,6,7,8-HpCDD) and 1,2,3,6,7,8-hexachloro dibenzo-*p*-dioxin (1,2,3,6,7,8-HxCDD). This is an average Finnish exposure pattern to dioxins. The congener profiles in Figure 4 indicate a slightly descending trend of intakes by three to six years-old children.

As with the PBDE congeners, BDE-47 was ingested the most. Other congeners detected of the measured were in the order of their daily ingestion levels: 99>100>154≈153>183>66>119>85. This is a typical exposure pattern to PBDEs by humans and other top predator species worldwide (Boon et al. 2002, Concha 2006, Hites 2004, Isosaari et al. 2004, Law et al. 2006, Swedish Naturhistoriska Riksmuseet 2009). BDEs 28, 71, 75, 77, 138 and 209 were not detected in the foodstuffs analyzed. As the BDE-209 analysis includes a number of analytical difficulties (de Boer and Cofino 2002), its analysis was not under the control of our laboratory.

Comparison to limit values

The reassessed TDI of 0.01 pg/kg bw/d for PCDD/Fs and DL-PCBs by the USEPA (2000) is based on an assumption that exposure to even one molecule of the toxicant may induce cancer (viite, joku muu kuin NRC 2006). It thus retains an unrealistic precautionary principle incorporated in the TDI. It is criticized by the National Research Council of the National Academies (2006) for its scientific robustness, lack of clarity and transparency of the key data sets in the dose-response analysis, lack of justification for selecting an appropriate benchmark dose as a point of departure and failure to characterize variability and uncertainty incorporated throughout the analysis. Thus the USEPA TDI was not considered herein. The TDI of the Nordic Expert Group of 5 pg/kg bw/d (viite) on the other hand, is grounded on an ad hoc derogation until 31 December 2011 Finland and Sweden has received from the EC to place on the market certain fish species originating from the Baltic region that may contain high levels of dioxins and dioxin-like PCBs (EC 2006). This limit value was neither considered.

The TWI (tolerable weekly intake) of 14 pg TEQ/kg bw by SCF (2001) and COT (2001) is within the range of 1-4 pg WHO-TEQ/kg bw. In its latest re-evaluation (1998), WHO has specified the upper range of the TDI (i.e. 4 pg TEQ/kg bw) should be considered as a maximal tolerable intake on a provisional basis, and that the ultimate long-term target is to reduce human intake levels below 1 pg TEQ/kg bw/d. However, no means how nor during which time window these aims should be received has been put forward. According to our results, in Finland, remarkable portion of children younger than 6 years exceed tolerable daily intakes. Because the foundation of TDI lays on a lifetime exposure, children aged 1 to 6 years to exceed the upper range of 4 pg/kg bw/d by WHO even with occasional short-term overrun would have no health consequences later in their life according to WHO (1998) provided that the averaged intake over long periods is not exceeded. Several causal dependencies behind the derivation of TDIs are however highly uncertain. This uncertainty is simply dealt with a safety factor of 10 to increase the margin from the uncertainties in dose-response estimations and another safety factor of 10 to account for children's overall higher vulnerability. Because fish contributes 72-94% of a relevant average market basket of PCDD/Fs and PCBs in Finland (Kiviranta et al. 2001, 2003, 2004), the most obvious mean to increase the margin of safety for potential hazardous health effects of PCDD/Fs and DL-PCBs in children in Finland would be reducing fish usage in children and women of fertile age (because of the congener's long biological half-life), especially those species heavily contaminated with POPs in the Baltic Sea.

With the PBDEs, the situation is of the same kind for 55 % of their Finnish market baskets result from fish (Kiviranta et al. 2004). Based on a preliminary LOAEL of 1 mg/kg

bw/d (Darnerud et al. 2001) and on the maximum intake observed in our data (5.8 ng/kg bw/d for 3-year-old boys), a safety margin in the intakes of Finnish children – if we base our estimation to a benchmark dose approach and roughly assume a NOAEL to be one order of magnitude lower – is in the order of 10^4. For PBDEs, no provisional tolerable intake or corresponding resting on any solid critical threshold has been established so far (FAO/WHO JECFA, 2005).

Because fish is clearly the only significant source of MeHg from food for most populations exclusive some rare cases (WHO 2003), its intake can be diminished by reducing consumption of fish loaded with the compound such as e.g. pike and pike-perch in children and pregnant or nursing women (for its biological $t_{1/2}$ is on average shorter than that of PCDD/Fs and PCBs). The RfD by the USEPA (1997) at a daily ingestion level of 0.1 μg/kg bw is anticipated to be protective of methylmercury-induced neurotoxicity (fetal and postnatal periods) over a lifetime. A safety factor of up to ten at its highest, one by one, has been incorporated in the RfD to account for uncertainties such as extrapolation from animal to human data, extrapolation of data to sensitive subpopulations, lack of chronic data, use of a LOAEL (lowest-observable-adverse-effect-level) in the absence of NOAEL (no-observable-adverse-effect-level), and lack of some other critical (e.g. toxicokinetic) data (NRC, 2000; Rice 2004). Thus the children exceeding the RfD in this study times 1.5 to 3.6 do not have by definition an elevated risk for neurotoxic effects of MeHg to the developing nervous system.

When we assessed quantitatively with Monte Carlo analysis the net health effects of maternal consumption of MeHg- and the long-chain omega-3 polyunsaturated fatty acids (MeHg being adverse and omega-3 PUFAs being essential for optimum neural development) containing fish in Finland using the child's intelligence quotient (IQ) as a composite endpoint, net health effects between slightly beneficial to slightly adverse were concluded with solely fatty fish and solely lean fish consumption patterns, respectively (Leino et al. 2009). Therefore, in our opinion the current MeHg intake in children does not pose a risk to children's cognitive development. Indeed, Clewell et al. (1999) and Stern (1997) have proposed a RfD of 0.1-0.3 μg/kg bw/d to MeHg when only the uncertainties in the dose conversion factor from hair mercury concentration to chronic MeHg ingestion rate (this conversion used in our analysis) was analysed using Monte Carlo analyses. An observational cohort study in the USA by Hibbeln et al. (2007) also indicates that limiting maternal seafood consumption during pregnancy to diminish MeHg risk to the child could actually be detrimental to optimal fetal neurodevelopment. However, just as USEPA (1997) itself denotes "the risk following exposures above the RfD is uncertain, but risk increases as exposures to methylmercury increase", the Hg intake in Finnish children surely needs to be carefully monitored and should be diminished. Particularly, as it appears according to our results that Hg intake increases in age at least from one to six years.

We lack means other than total banning of fishing and/or usage for food-source of the most contaminated Baltic Sea fish species such as herring (*Clupea harengus*) and wild salmon (*Salmo salar*) to achieve the long-term goals in the intakes. For instance, increasing herring fishing pressure is a far less effective way to decrease the risk PCDD/Fs and PCBs pose for human health than regulating the consumption of the most contaminated fish species (Kiljunen et al. 2007). Because of many beneficial health benefits of fish usage (Dalbokova et al. 2007, Mozaffarian and Rimm 2006, Tuomisto et al. 2004, Tuomisto and Pekkanen 2005) the Finnish authorities (Evira; National Institute for Health and Welfare, THL) have tipped the balance in favour of recommending fish consumption. However, specific recommendations were given so that 1) pregnant and nursing women should not consume pike at all (due to Hg), and 2) children, adolescents and people of fertile age could eat large herring (>17 cm in length) OR alternatively wild salmon caught from the Baltic Sea AND sea or lake caught pike only 1-2 times a month (due to PCDD/Fs, PCBs). These recommendations together with the general instruction to eat fish at least twice a week with varying species as such are justifiable. They rest on the current knowledge about relevant dose-responses and toxicokinetics of these compounds and aim as long-term goals to TDI of

1-2 pg TEQ/kg bw/d recommended by EFSA (2006), SCI (2001) and WHO (1998). Whether they are feasible as a whole in practice, has been questioned (e.g. Kiljunen et al. 2007). In overall, the limitations of the current guidelines is that they reach those citizens that are conscious of the food-mediated risks and benefits from the very start, but require too much awareness e.g. from those that cope with more fundamental issues in their every-day life. Indeed, according to the latest surveys by Evira (2007), Finnish youth know poorly the restrictions given by it for fish consumption. We highlight, that intake of fish oil supplements or corresponding instead of fish itself is not a resolution to the problem for two reasons: 1) contaminant concentrations in supplements are not controlled neither regulated and unrefined supplements can enter today's markets (Wiborg et al. 2008), 2) one can never mimic the wide variety of beneficial effects fish retains in only one product.

Uncertainties and suggestions for further work

Obvious goals for further specifications in population contaminant intake estimations from food (in Finland) using a probabilistic approach presented herein should be gender-specific intakes of infants, juvenile, pubescent, adults and elderly people. A corrective to the intake estimations presented in this study could be received by using longer than 3-d food records as well as individual body weights rather than those based in the early nineties (1993) herein. As it seems that Finnish children today weigh more than in the nineties (Virtanen, unpublished data), the intakes presented herein can be slightly overestimated. These means would provide firmer grounds for lifetime exposure estimations and comparisons to the TDIs set by international expert bodies. Because safety margins to threshold levels of PCDD/Fs, DL-PCBs are still narrow, calculations should be performed on how different children-specific food consumption scenarios influence the likelihood of exceeding the WHO-TEQ-derived TDIs of dioxins and DL-PCBs. Similarly as with MeHg (Leino et al. 2009), these calculations should be implemented as quantitative benefit-risk comparisons if feasible, to include in the analysis any possible food-related beneficial aspects such as the omega-3 PUFAs in fish that may outweigh the potential contaminant risks. These would be useful corrective means to enable successful risk management founded on the net health benefit of the public. Currently, food-mediated contaminant risks can anyway be managed successfully only as trade-offs, especially in the case of fish. Remarkably useful information for dietary intake estimates would be a verified relationship between the parent's and their child's food consumption habits since it would allow a relevant tool to estimate intake in children solely by knowing the food consumption habits of their parents.

As with the food-mediated exposure to brominated flame retardants, the development trend of their concentrations in the environment and food as well as the intakes in the public needs to be carefully monitored despite the fact that the biomagnification of PBDEs in the Baltic Sea seem to have leveled off or even decreased (Swedish Naturhistoriska Riksmuseet, 2009). In the near future, we will also focus on assessing the biomagnification potential and public intake of a newcomer cause for concern, hexabromocyclododecane (HBCD).

Risk communication of dioxins, dioxin-like PCBs and PBDEs is also hindered because of varying analytical quantification procedures. It is generally well known that using upper bound concentrations is likely to exceed the real intake while using lower bound concentrations may underestimate them. We do not state opinion here on which of the quantification method to use for risk assessment purposes. Merely, that as long as no single commonly accepted and adopted quantification procedure is introduced, it would be upmost important to report the whole range of intake estimations obtained with both methods. For risk assessment purposes, the difference does not really count (because other uncertainties weigh heavily over) but for time scale and inter-country comparisons the introduced quantification methodology matters.

CONCLUSIONS

Based on the exposure profile reported herein, children should be clearly considered as a specific sub-population in food-mediated contaminant risk assessment. The child-specific characteristics should be taken into account more transparently in risk assessments aimed to protect children.

The long term goals should be the decrease of new anthropogenic releases of POPs and heavy metals into the environment….

REFERENCES

Boon JP, Lewis WE, Tjoen-A-Choy MR, Allchin CR, Law RJ, de Boer J, Ten Hallers-Tjabbes CC and Zegers BN. 2002. Levels of Polybrominated Diphenyl Ether (PBDE) Flame Retardants in Animals Representing Different Trophic Levels of the North Sea Food Web. *Environ Sci Technol* 36: 4025-4032.

Clewell H.J, Gearhart JM, Gentry P.R, Covington TR, VanLandingham CB, Crump KS, Shipp AM. 1999. Evaluation of the Uncertainty in an Oral Reference Dose for Methylmercury Due to Interindividual Variability in Pharmacokinetics. *Risk Analysis* 19: 547-558.

Concha G, Grawé KP, Aune M, Darnerud PO. 2006. Svensk intagsberäkning av dioxiner (PCDD/PCDF), dioxinlika PCBer ach metylkvicksilver för barn baserad på aktuella analysdata samt kostundersökningen 2003. Resultatrapport till Naturvårdsverkets Miljöövervakning. Livsmedelsverket, 2006-11-24, 2150312, pp. 28. (in Swedish).

COT. 2001. Statement on the Tolerable Daily Intake for Dioxins and Dioxin-like polychlorinated biphenyls. Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment. 2001/07, available at http://cot.food.gov.uk/pdfs/cot-diox-full.pdf. pp. 26.

Darnerud PO, Eriksen GS, Johannesson T, Larsen PB, Viluksela M. 2001. Polybrominated diphenyl ethers: occurrence, dietary exposure and toxicology. Environ Health Perspect 109 (suppl 1): 49-68.

De Boer J and Cofino WP. 2002. First world-wide interlaboratory study on polybrominated diphenylethers (PBDEs). *Chemosphere* 46: 625-633.

DIPP web page http://www.dipp.fi/e_index.htm

EC 2001. Scientific Committee on Food. Opinion of the Scientific Committee on Food on the risk assessment of dioxins and dioxin-like PCBs in food. Update based on new scientific information available since the adoption of the SCF opinion of 22nd November 2000. CS/CNTM/DIOXIN/20 final, adopted 30 May 2001.

EC 2006. Setting maximum levels for certain contaminants in foodstuffs. *Off J Eur*, Commission regulation (EC) No 1881/2006 of 19 December 2006, adopted 1 March 2007, L364/5-24.

EC 2008. Methyl mercury in fish and fishery products. Information note by the Health and Consumers directorate-General. Safety of the Food chain; E3 Chemicals, Contaminants, Pesticides. 21 April, 2008, D530/286, pp. 3.

EFSA 2006. Risk-benefit analysis of foods. Scientific colloquium summary report of European Food Safety Authority (EFSA), 13-14 July 2006, Parma, Italy.

Evira 2007. Finnish youth know poorly the restrictions of fish usage. A press release of Finnish Food Safety Authority, www.evira.fi (in Finnish).

FAO/WHO JECHA. 2005. Joint FAO/WHO expert Committee on Food Additives. 64th meeting, Rome, 8-17 February, 2005, 64/SC, available at ftp://ftp.fao.org/es/esn/jecfa/jecfa64_summary.pdf. pp. 47.

Hallikainen, A., Kiviranta, H., Isosaari, P., Vartiainen, T., Parmanne, R., Vuorinen, P.J. (2004). Kotimaisen järvi- ja merikalan dioksiinien, furaanien, dioksiinin kaltaisten PCB-yhdisteiden ja polybromattujen difenyylieettereiden pitoisuudet: EU-KALAT. Concentration of dioxins, furans, dioxin-like PCB compounds and polybrominated diphenyl ethers in domestic fresh water and salt water fish. Publications of the National Food Agency 1/2004, Helsinki, Finland. (in Finnish, abstract in English)

Hibbeln JR, Davis JM, Steer P, Emmett P, Rogers I, Williams C, Golding J. 2007. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study. Lancet 369: 578-585.

Hites RA. 2004. Polybrominated Diphenyl Ethers in the Environment and in People: A Meta-Analysis of Concentrations. *Environ Sci Technol* 38: 945-956.

Isosaari P., Hallikainen, A., Kiviranta, H., Vuorinen, P.J., Parmanne, R., Koistinen, J., Vartiainen, T. (2006). Polychlorinated dibenzo-*p*-dioxins, dibenzofurans, biphenyls, naphthalenes and polybrominated diphenyl ethers in the edible fish caught from the Baltic Sea and lakes in Finland. *Environmental Pollution* **141**, 213-225.

Kiljunen M, Vanhatalo M, Mäntyniemi S, Peltonen H, Kuikka S, Kiviranta H, Parmanne R, Tuomisto JT, Vuorinen P, Hallikainen A, Verta M, Pönni J, Jones RI, Karjalainen J. 2007. Human dietary intake of organochlorines from Baltic herring: implications of individual fish variability and fisheries management. Ambio 36:257-264.

Kiviranta H, Hallikainen A, Ovaskainen M-L, Kumpulainen J, Vartiainen T. 2001. Dietary intakes of polychlorinated dibenzo-p-dioxins, dibenzofurans and polychlorinated biphenyls in Finalnd. *Food Additives and Contaminants* 18:945-953.

Kiviranta, H., Hallikainen, A., Ruokojärvi, P., Rantakokko, P., Vartiainen, T. (2006) PCDD/F, PCB, and PBDE levels in Finnish foodstuffs in 2003-2005. *Organohalogen Compounds* **68**, 1898-1901.

Kiviranta, H., Ovaskainen, M-L., Vartiainen, T. (2004). Market basket study on dietary intake of PCDD/Fs, PCBs, and PBDEs in Finland. *Environment International* **30**, 923-932.

Kiviranta H, Vartiainen T, Parmanne R, Hallikainen A, Koistinen J. 2003. PCDD/Fs and PCBs in Baltic herring during the 1990s. Chemosphere 50:1201-1216.

Kupila, A., Muona, P., Simell, T., *et al*; Juvenile Diabetes Research Foundation Centre for the Prevention of Type I Diabetes in Finland (2001) Feasibility of genetic and immunological prediction of type I diabetes in a population-based birth cohort. *Diabetologia* **44**, 290-297.

Kyttälä, P., Ovaskainen, M, Kronberg-Kippilä, C., Erkkola, M., Tapanainen, H., Tuokkola, J., Veijola, R., Simell, O., Knip, M., Virtanen, S.M. (2008). Lapsen ruokavalio ennen kouluikää. The diet of Finnish preschooler. Publications of the National Public Health Institute B32/2008, Helsinki.Finland. (in Finnish, abstract in English)

Law K, Halldorson T, Danell R, Stern G, Gewurtz S, Alaee M, Marvin C, Whittle M, Tomy G. 2006. Bioaccumulation and Trophic Transfer of Some Brominated Flame Retardants in a Lake Winnibeg (Canada) Food Web. *Environ Toxicol Chem* 25:2177-2186.

LeBlanc, J-C., Sirot, V., Volatier, J-L., Bemrah-Aouachria, N. (2006). Fish and seafood consumption study and biomarker of exposure to trace elements, pollutants and omega 3. CALIPSO report. 162 p.

Leino, O., Karjalainen, A.K. and Tuomisto, J.T. 2009. Effects of maternal fish consumption on children's cognitive health. (manuscript)

Mozzaffarian D and Rimm EB. 2006. Fish intake, contaminants, and human health. Evaluating the risks and the benefits. JAMA 18:1885-1899.

NIFES web page http://www.nifes.no/.

NRC. 2000. Toxicological effects of methylmercury. Committee on the Toxicological Effects of Methylmercury, Board on Environmental Studies and Toxicology, Commission on Life Sciences, National Research Council. The National Academies Press, Washington DC, available at http://www.nap.edu/openbook.php?record_id=9899&page=R1. pp. 344.

NRC. 2006. Health risks form dioxin and related compounds. Evaluation of the EPA reassessment. National Research Council (NRC) of the National Academies, July 2006, Public Summary, available at http://dels.nas.edu/dels/rpt_briefs/dioxin_brief_final.pdf. pp. 6.

Nusser, S., Carriquiry, A., Dodd, K. and Fuller, W. (1996) A semiparametric transformation approach to estimating usual daily intake distributions. *Journal of American Statistical Association* **91**, 1440-1449.

Parmanne, R., Hallikainen, A., Isosaari, P., Kiviranta, H., Koistinen, J., Laine, O., Rantakokko, P., Vuorinen, P.J., Vartiainen, T. (2006). The dependence of organohalogen compound concentrations on herring age and size in the Bothnian Sea, northern Baltic. *Marine Pollution Bulletin* **52**, 149-161.

Rice DC. 2004. The US EPA reference dose for methylmercury: sources of uncertainty. *Environ Res* 95: 406-413.

Stern AH. 1997. Estimation of the Interindividual Variability in the One-Compartment Pharmacokinetic Model for Methylmercury: Implications for the Derivation of a Reference Dose. *Reg Tox Pharmacol* 25: 277-288.

Swedish Naturhistoriska Riksmuseet. 2009. Övervakning av metaller och organiska miljögifter i marin biota. Sakrapport, överenskommelse 2120818, dnr 235-3405-08-Mn. English summary report of the monitoring activities within the national Swedish contaminant programme in marine biota. pp. 154.

Toms L-M.L., Sjödin A, Harden F, Hobson P, Jones R, Edenfield E, Mueller J.F. 2009. Serum Polybrominated diphenyl ether (PBDE) Levels are higher in children (2-5 years of age) than in infants and adults. *Environ Health Perspect* 117:1461-1465.

Tuomisto, J. 2007. Safe food: crucial for child development. In: Dalbokova D, Krzyzanowski M, Lloyd S. (eds.), Children's health and the environment in Europe: a baseline assessment. World Health Organization, WHO, Copenhagen, Denmark, pp. 88-97.

Tuomisto JT, Tuomisto J, Tainio M, Niittynen M, Verkasalo P, Vartiainen T, Kiviranta H and Pekkanen J. 2004. Risk-benefit analysis of eating farmed salmon. *Science*, Letters 305:476.

Tuomisto and Pekkanen 2005. Assessing environmental health risks or net health benefits? *Scandinavian Journal of Public Health*, Editorial 33:162-163.

USEPA. 1997. Mercury Study Report to Congress. Vol I: Executive Summary. EPA, December 1997, EPA-452/R-97-003, available at __ pp. 95.

USEPA. 2000. Exposure and human health reassessment of 2,3,7,8-tetrachloro-dibenzo-*p*-dioxin (TCDD) and related compounds. Draft Final. National Center for Environmental Assessment, US Environmental Protection Agency, Washington DC.

Van den Berg, M., Birnbaum, L., Bosveld, A.T.C., Brunström, B., Cook, P., Feeley, M., et al. (1998). Toxic equivalency factors (TEFs) for PCBs, PCDDs, PCDFs for humans and wildlife. *Environment Health Perspectives* **106**, 775-792.

Van den Berg M, Birnbaum Ms, Denison M, De Vito M, Farland W, Feeley M, Fiedler H, Hakansson H, Hanberg A, Haws L, Rose M, Safe S, Schrenk D, Tohyama C, Tritcher A, Tuomisto J, Tysklind M, Walker N, Peterson RE. 2006. The 2005 World Health Organization Re-evalution of Human and mammalian Toxic Equivalency Factors for Dioxins and Dioxin-like Compounds. *Tox Sci Advace Access* ____.

Van Leeuwen FXR, Younes MM. 2000. Assessment of the health risk of dioxins: re-evaluation of the tolerable daily intake (TDI). *Food Addit Contam* 17: 223-240.

Venäläinen, E-R., Hallikainen, A., Parmanne, R., Vuorinen, P.J. (2004). Kotimaisen järvi- ja merikalan raskasmetallipitoisuudet. Heavy metal contents in Finnish sea and fresh water fish. Publications of the National Food Agency 3/2004, Helsinki, Finland. (in Finnish, abstract in English)

Virtanen SM 2009. unpublished data.

Virtanen, S.M., Kenward, M.G., Erkkola, M., Kautiainen, S., Kronberg-Kippila, C., Hakulinen, T., Ahonen, S., Uusitalo, L., Niinisto, S., Veijola, R., Simell, O., Ilonen, J. and Knip, M. (2006) Age at introduction of new foods and advanced beta cell autoimmunity in young children with HLA-conferred susceptibility to type 1 diabetes. Diabetologia 49, 1512-1521.

WHO 1998. Assessment of the health risk of dioxins: re-evaluation of the Tolerable Daily Intake (TDI). Executive summary. WHO Consultation, May 25-29 1998, Geneva, Switzerland, pp.28.

WHO 2003. Joint FAO/WHO Expert Committee on Food Additives and Contaminants. 61st meeting, Rome, 10-19 June 2003, 61/SC. Summary and Conclusions. Available at: http://www.who.int/ipcs/food/jecfa/summaries/en/summary_61.pdf.

Wiborg, M.L., Knutsen, H.K., Andersson, Ö., Büchert, A., Cederberg, T., Darnerud, P.O., Hallikainen, A., Kiviranta, H., Ólafsdóttir, K., Peters, K. 2008. EU maximum levels for dioxins and dioxin-like PCBs – Impact on exposure and food supply in the Nordic countries. TemaNord2008:531. 70 p. + appendixies 35 p.

Wittsiepe J, Schrey P, Wilhelm M. 2001. Dietary Intake of PCDD/F by Small Children with Different Food Consumption Measured by the Duplicated Method. *Chemosphere* 43:881-887.

Ásmundsdóttir, ÁM., Auðunsson, GA. Gunnlaugsdóttir, H. (2005). Undesirable substances in seafood products-results from the monitoring activities in 2004. IFL-report 33-05. 37 p.

Figures

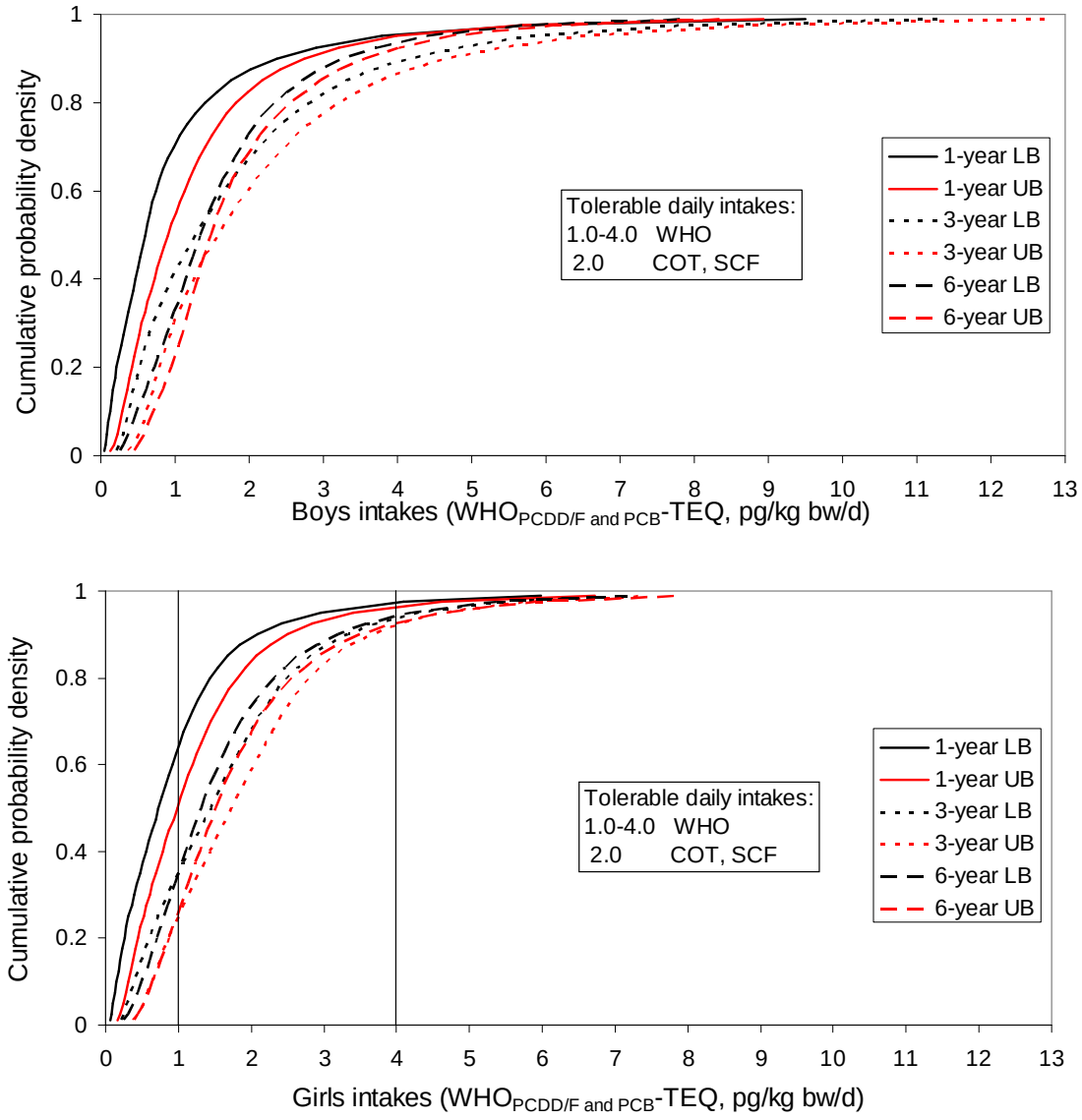

Figure 1. The cumulative probability density of lower bound and upper bound $WHO_{PCDD/F\ and\ PCB}$-TEQ intakes (pg/kg bw/d) in Finnish 1, 3 and 6 year-old boys and girls based on a 3-d food record study. The limits for tolerable daily intakes by the WHO (1.0-4.0) and COT (2.0) (see text for further information).

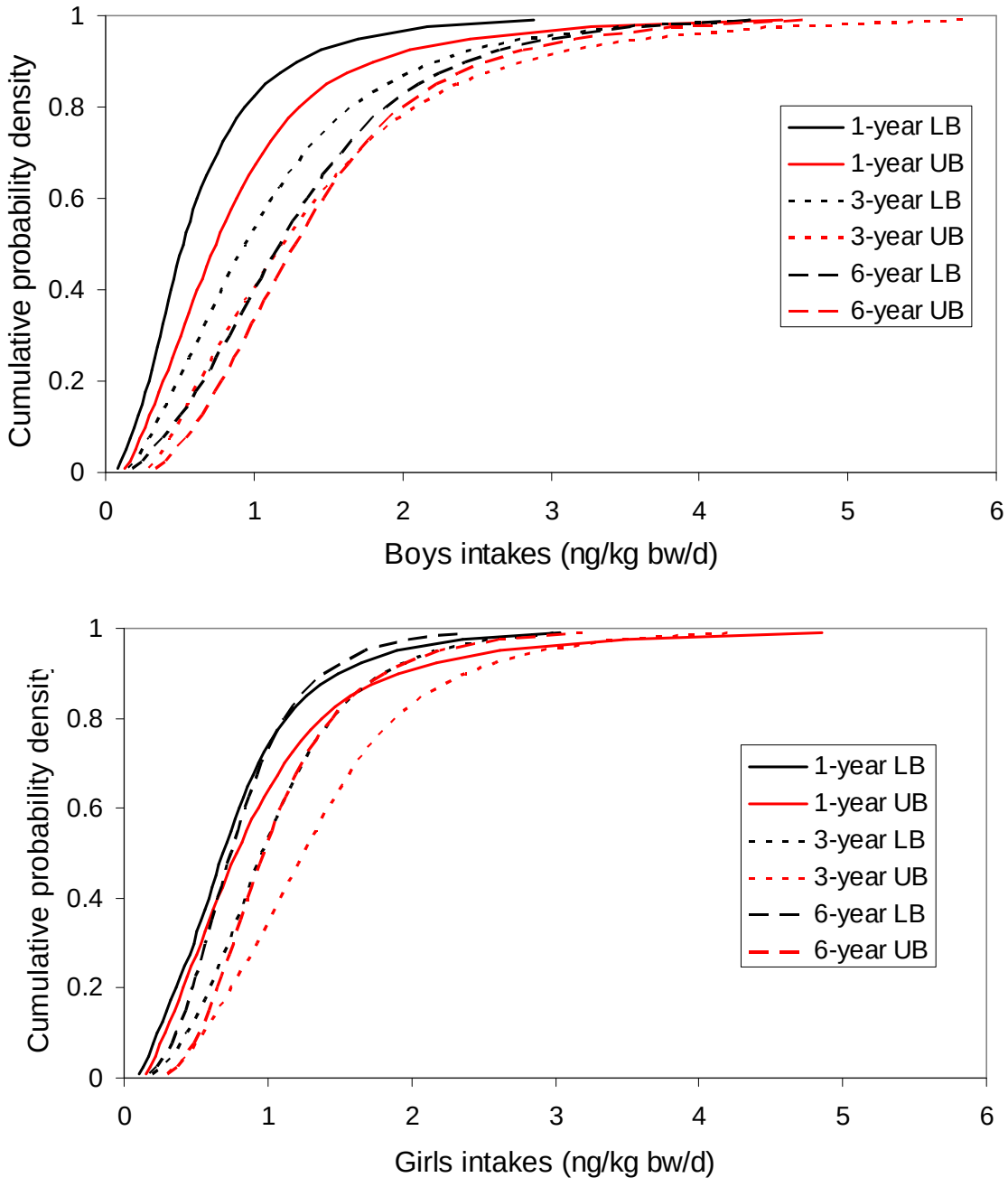

Figure 2. The cumulative probability density of lower bound and upper bound sum of PBDE intakes (ng/kg bw/d) in Finnish 1, 3 and 6 year-old boys and girls based on a 3-d food record study. A preliminary LOAEL of 1 mg/kg bw/d suggested by Darnerud et al. (2001) (see text for further information).

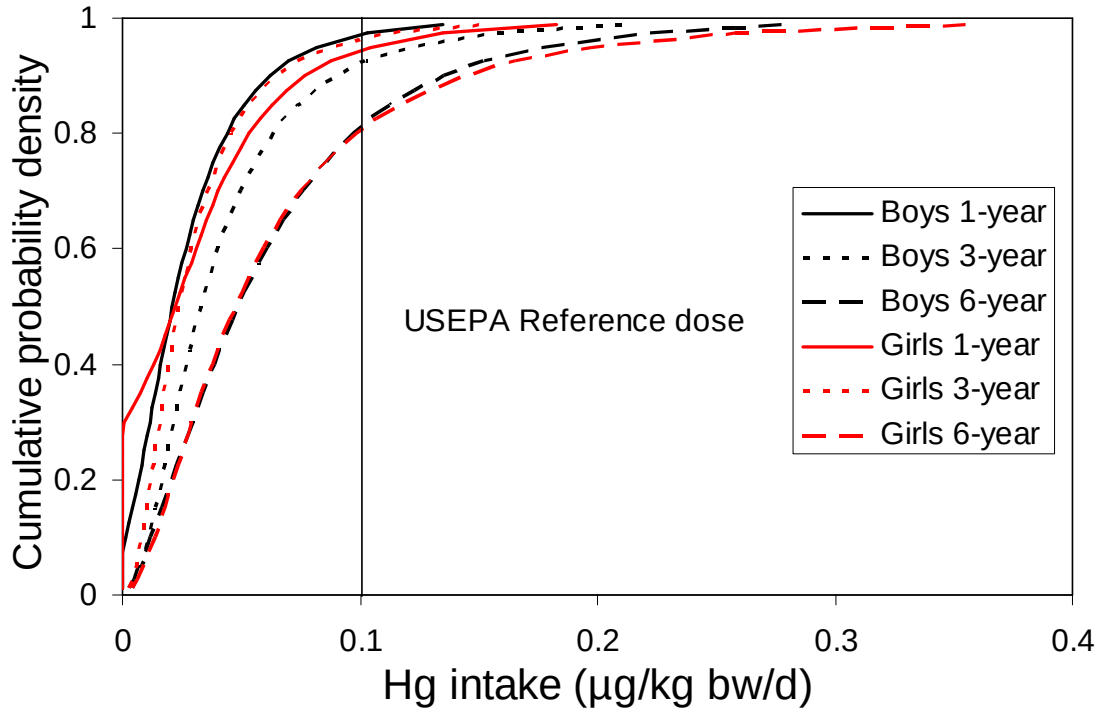

Figure 3. The cumulative probability density of gender-specific methylmercury intake (µg/kg bw/d) in Finnish 1, 3 and 6 year-old children based on a 3-d food record study. USEPA RfD for MeHg is 0.1 µg/kg bw/d (see text for further information).

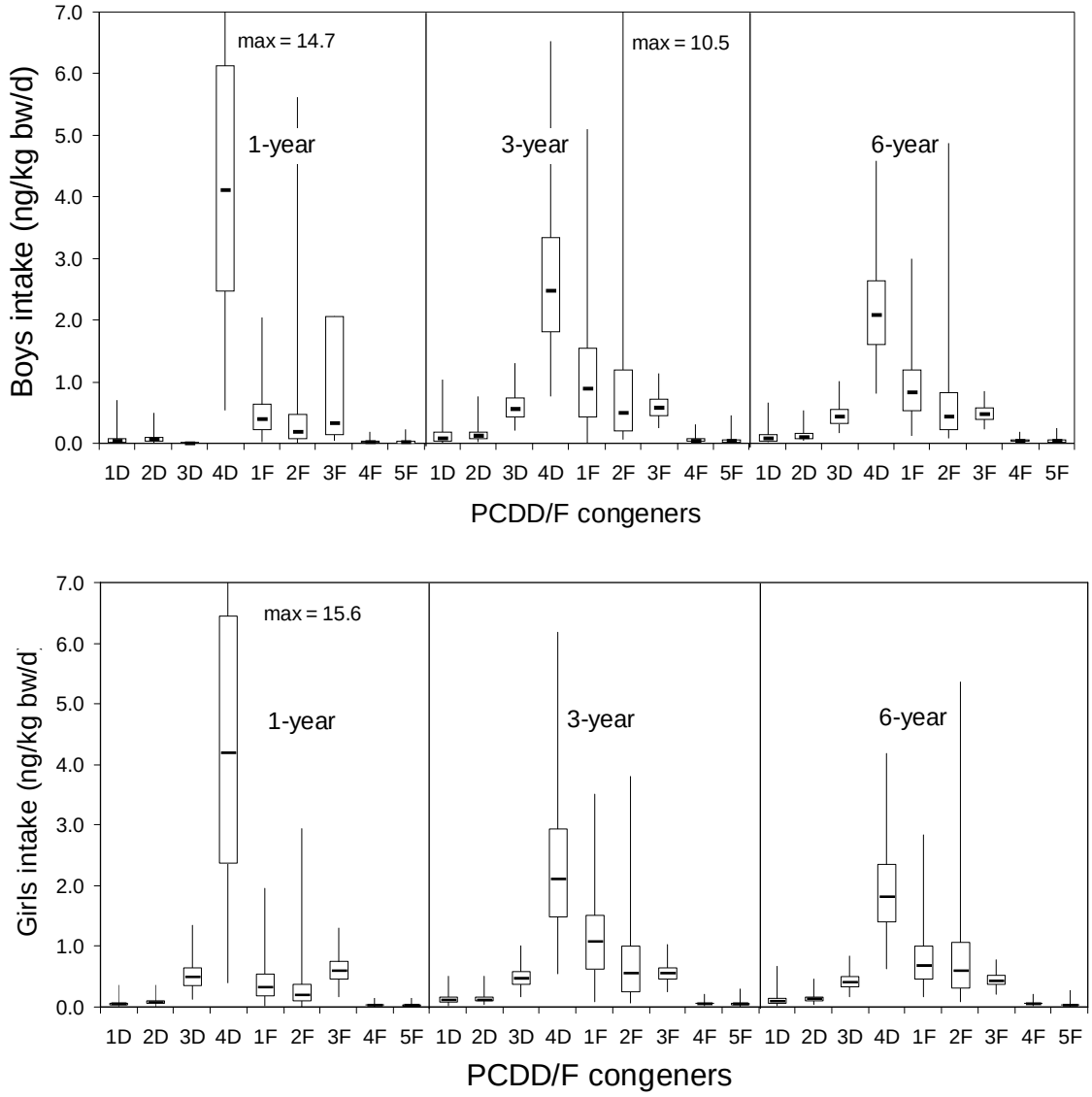

Figure 4. PCDD/F congener-specific lower bound intakes (min, 1st quartile, median, 3rd quartile, max) in Finnish 1, 3 and 6 year-old boys and girls. Congeners: 1D: 1,2,3,7,8-PeCDD; 2D: 1,2,3,6,7,8-HxCDD; 3D: 1,2,3,4,6,7,8-HpCDD; 4D: OCDD; 1F: 2,3,7,8-TCDF; 2F: 2,3,4,7,8-PeCDF; 3F: 1,2,3,4,6,7,8-HpCDF, 4F: 1,2,3,4,7,8-HxCDF; 5F: 1,2,3,6,7,8-HxCDF.

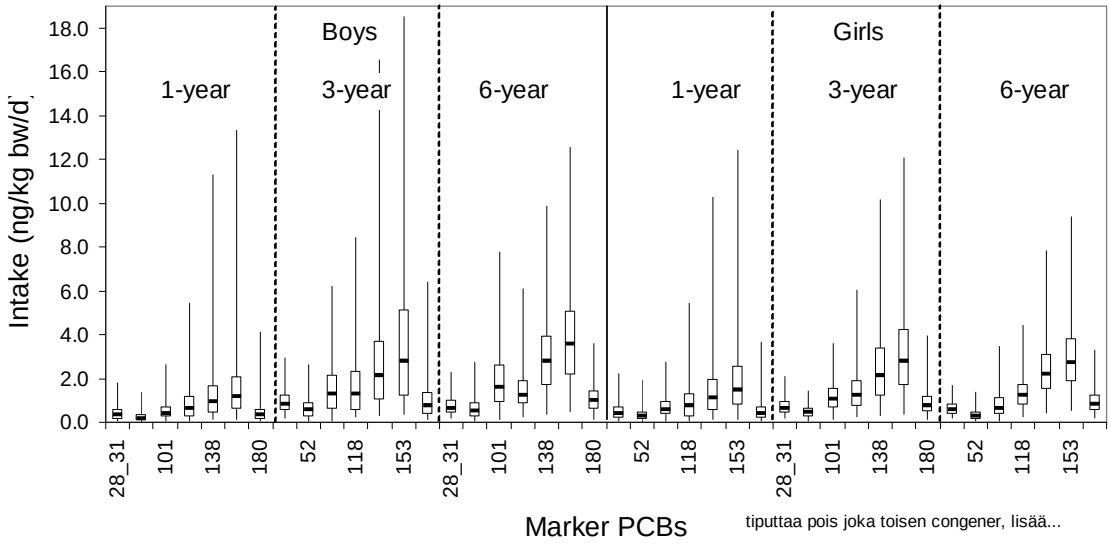

Figure 5. Congener-specific lower bound intakes for the seven marker PCBs (min, 1st quartile, median, 3rd quartile, max) in Finnish 1 to 6 year-old boys and girls.

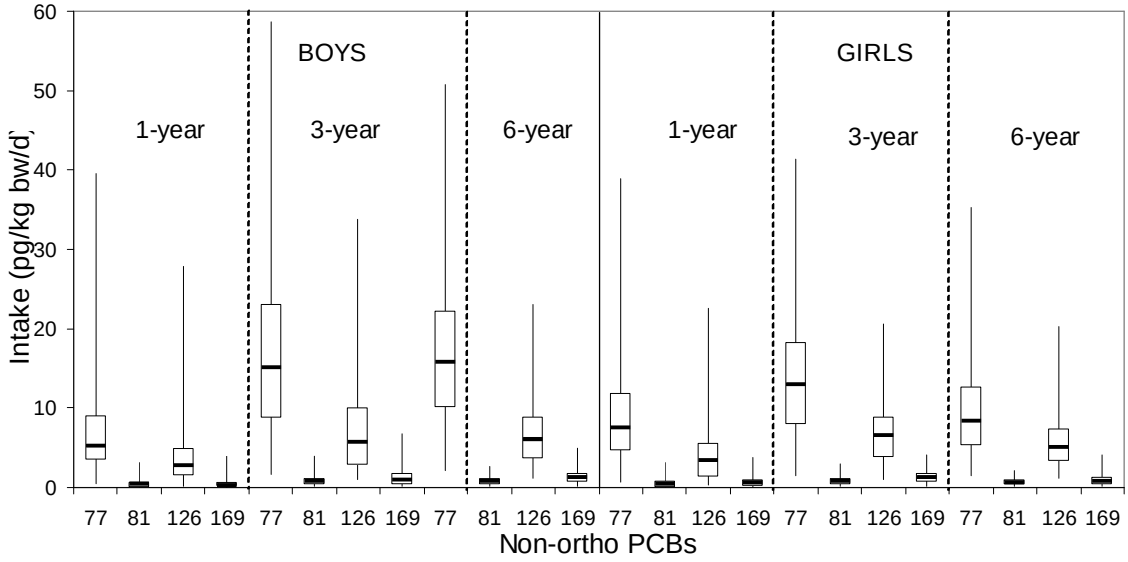

Figure 6. Congener-specific lower bound intakes for non-*ortho* substituted PCBs (min, 1st quartile, median, 3rd quartile, max) in Finnish 1 to 6 year-old boys and girls.

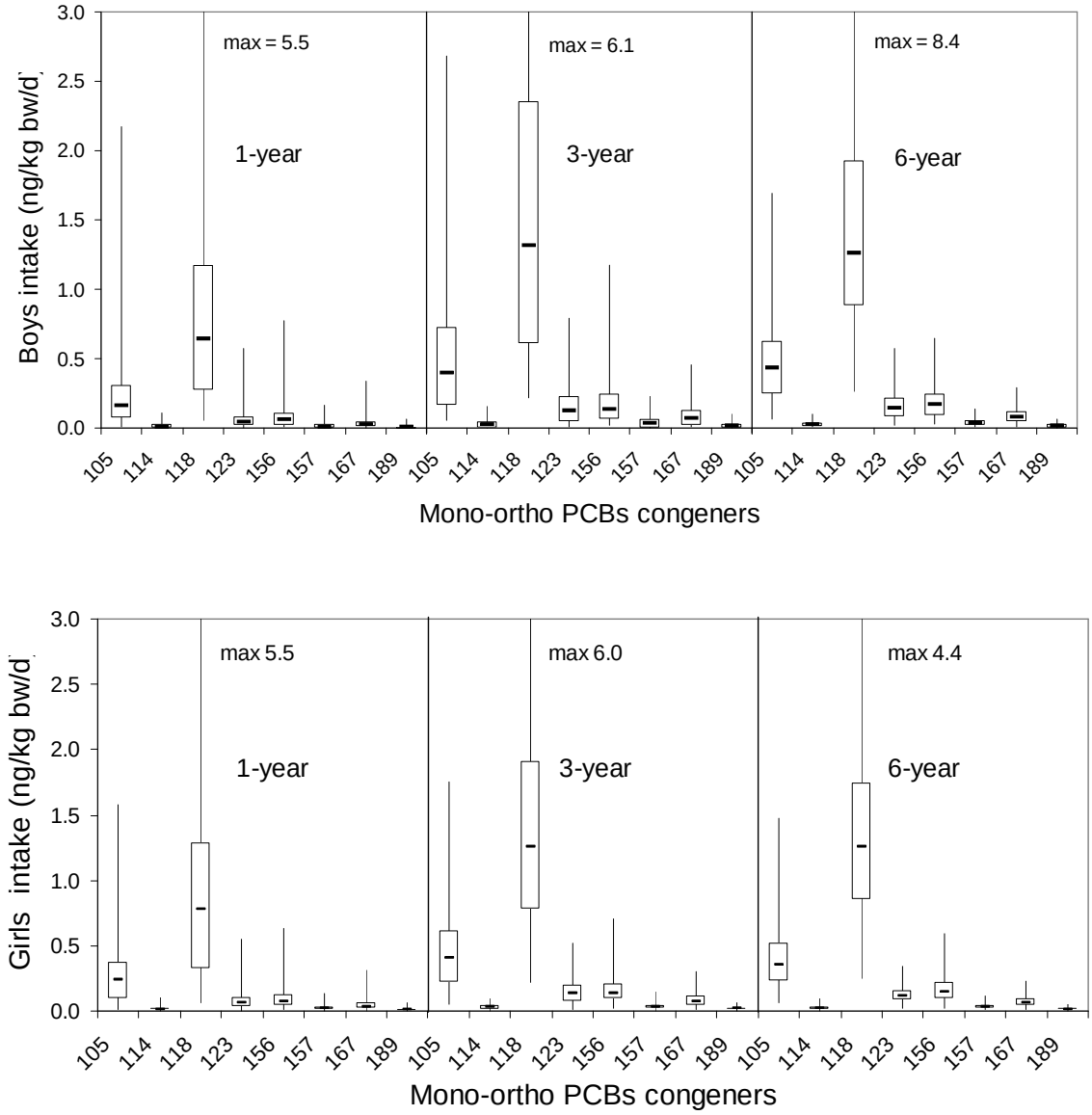

Figure 7. Congener-specific lower bound intakes for mono-*ortho* substituted PCBs (min, 1st quartile, median, 3rd quartile, max) in Finnish 1 to 6 year-old boys and girls.

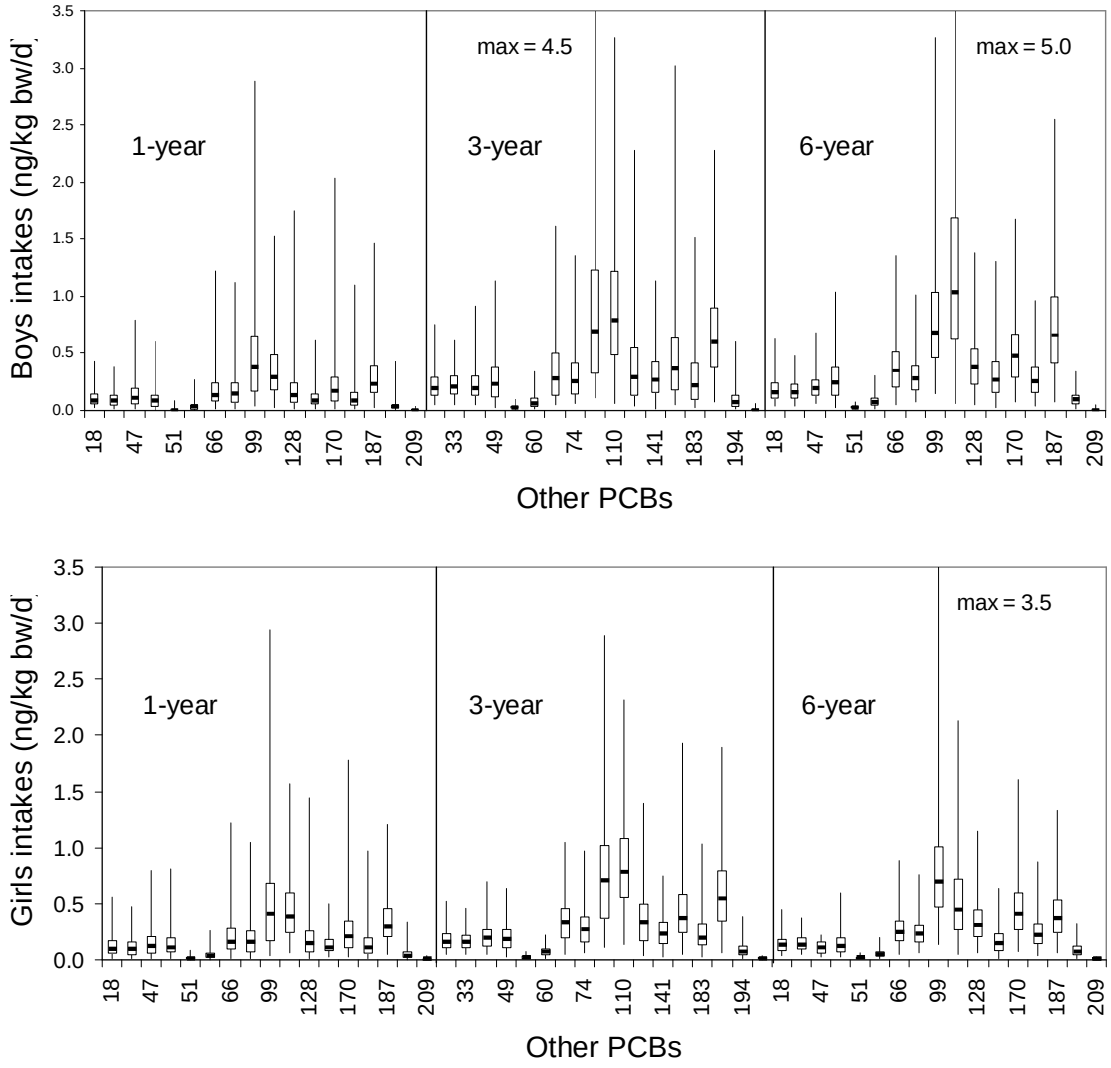

Figure 8. Congener-specific lower bound intakes for 17 other PCBs (min, 1st quartile, median, 3rd quartile, max) in Finnish 1 to 6 year-old boys and girls. Congeners: 1: 18; 2: 33; 3: 47; 4: 49; 5: 51; 6: 60; 7: 66; 8: 74; 9: 99; 10: 110; 11: 128; 12: 141; 13: 170; 14: 183; 15: 187; 16: 194; 17: 209.

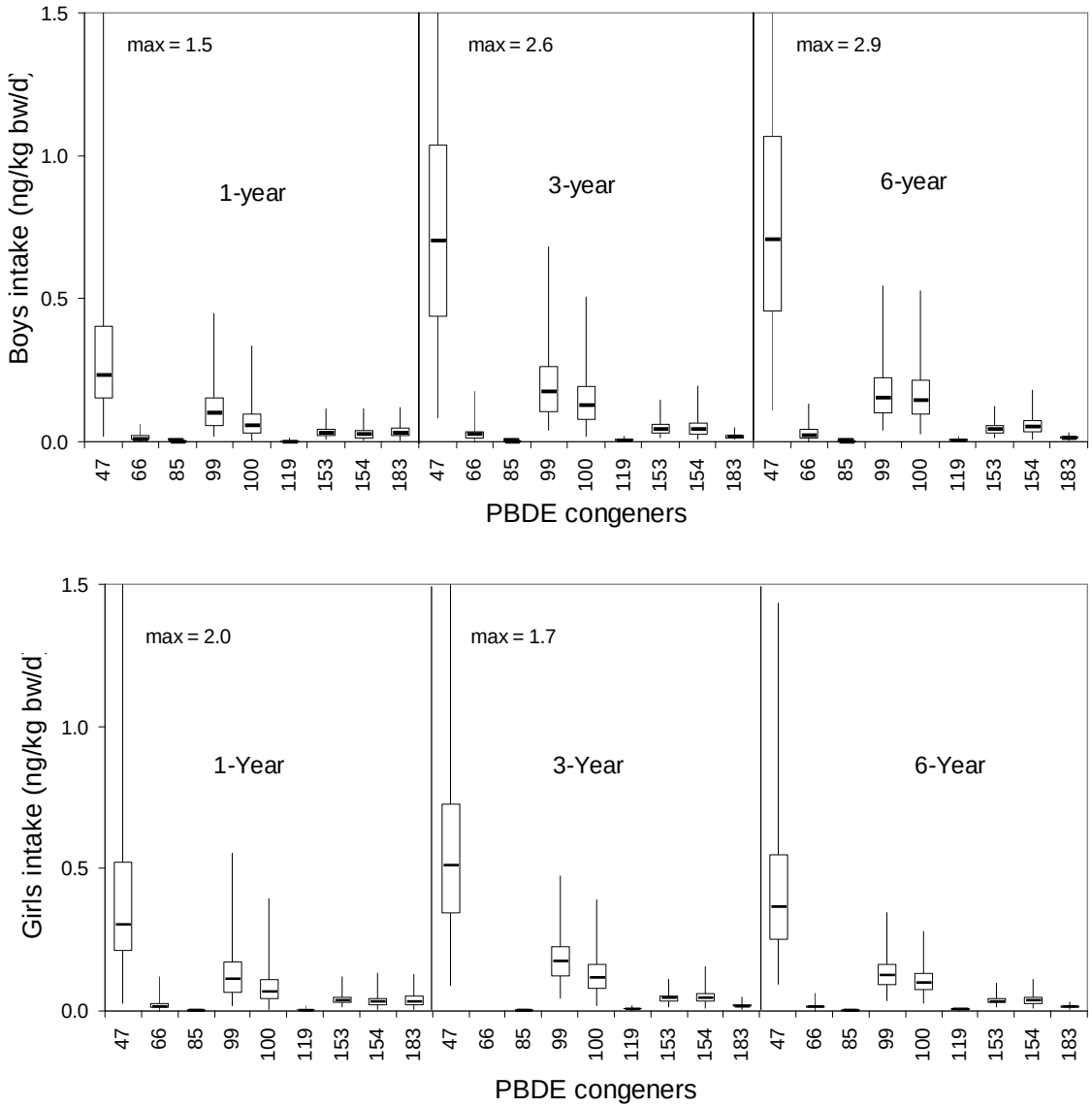

Figure 9. PBDE congener-specific lower bound intakes (min, 1st quartile, median, 3rd quartile, max) in Finnish 1, 3 and 6 year-old boys and girls.

Supplemental material:

Correlation matrix for sum of PCDD/F, sum of $WHO_{PCDD/F}$-TEQs, sum of PCBs, sum of WHO_{PCB}-TEQs, and sum of PBDE intakes.

group	_TYPE_	_NAME_	icpcddsumma	iWHOPCDD_F_TEQ	iPCBSumma	iWHOPCB_TEQ	BDESumma_209
11	CORR	icpcddsumma	1.00	0.34	0.34	0.32	0.52
11	CORR	iWHOPCDD_F_TEQ	0.34	1.00	0.96	0.98	0.77
11	CORR	iPCBSumma	0.34	0.96	1.00	0.99	0.87
11	CORR	iWHOPCB_TEQ	0.32	0.98	0.99	1.00	0.81
11	CORR	BDESumma_209	0.52	0.77	0.87	0.81	1.00
12	CORR	icpcddsumma	1.00	0.20	0.20	0.17	0.39
12	CORR	iWHOPCDD_F_TEQ	0.20	1.00	0.95	0.98	0.73
12	CORR	iPCBSumma	0.20	0.95	1.00	0.99	0.85
12	CORR	iWHOPCB_TEQ	0.17	0.98	0.99	1.00	0.80
12	CORR	BDESumma_209	0.39	0.73	0.85	0.80	1.00
31	CORR	icpcddsumma	1.00	0.63	0.61	0.60	0.66
31	CORR	iWHOPCDD_F_TEQ	0.63	1.00	0.93	0.96	0.80
31	CORR	iPCBSumma	0.61	0.93	1.00	0.98	0.93
31	CORR	iWHOPCB_TEQ	0.60	0.96	0.98	1.00	0.88
31	CORR	BDESumma_209	0.66	0.80	0.93	0.88	1.00
32	CORR	icpcddsumma	1.00	0.57	0.55	0.55	0.63
32	CORR	iWHOPCDD_F_TEQ	0.57	1.00	0.93	0.96	0.79
32	CORR	iPCBSumma	0.55	0.93	1.00	0.99	0.92
32	CORR	iWHOPCB_TEQ	0.55	0.96	0.99	1.00	0.88
32	CORR	BDESumma_209	0.63	0.79	0.92	0.88	1.00
61	CORR	icpcddsumma	1.00	0.58	0.58	0.56	0.63
61	CORR	iWHOPCDD_F_TEQ	0.58	1.00	0.91	0.95	0.80
61	CORR	iPCBSumma	0.58	0.91	1.00	0.99	0.94
61	CORR	iWHOPCB_TEQ	0.56	0.95	0.99	1.00	0.90
61	CORR	BDESumma_209	0.63	0.80	0.94	0.90	1.00
62	CORR	icpcddsumma	1.00	0.57	0.53	0.53	0.55
62	CORR	iWHOPCDD_F_TEQ	0.57	1.00	0.92	0.96	0.78
62	CORR	iPCBSumma	0.53	0.92	1.00	0.99	0.92
62	CORR	iWHOPCB_TEQ	0.53	0.96	0.99	1.00	0.88
62	CORR	BDESumma_209	0.55	0.78	0.92	0.88	1.00

Tables

Table 1. Mean, **median**, *SD* and (min-max) gender-specific upper bound intakes of sum of PCDD/Fs (pg/kg bw/d) and sum of PCBs, marker PCBs, non-*ortho* PCBs and mono-*ortho* PCBs (ng/kg bw/d) in Finnish 1 to 6-year-old children based on a 3-d food record study.

	Age, years					
	1		3		6	
Congener sums	Boys (n=___)	Girls (n=___)	Boys (n=___)	Girls (n=___)	Boys (n=___)	Girls (n=___)
Sum of PCDD/Fs	9.58, **8.60**, *5.11* (2.26-27.14)	9.50, **8.72**, *4.61* (2.35-23.98)	9.50, **8.37**, *4.66* (3.49-26.11)	8.25, **7.51**, *3.44* (3.40-19.86)	7.51, **6.86**, *2.86* (3.55-17.26)	6.85, **6.22**, *2.88* (2.90-16.59)
Sum of PCBs	12.61, **7.83**, *15.85* (0.82-85.21)	12.69, **9.65**, *12.98* (0.96-68.38)	22.81, **16.68**, *21.15* (2.99-104.30)	19.52, **16.02**, *14.61* (2.90- 73.72)	20.45, **17.44**, *14.35* (3.50-71.56)	17.51, **15.24**, *11.25* (3.16-56.87)
Marker PCBs	7.04, **4.33**, *8.96* (0.44-48.17)	7.08, **5.36**, *7.29* (0.52-38.34)	12.84, **9.38**, *11.93* (1.65-58.77)	10.91, **8.92**, *8.25* (1.59,-41.61)	11.56, **9.23**, *8.16* (1.93-40.64)	9.93, **8.25**, *6.88* (1.79-34.99)
Non-*ortho* PCBs	20.39, **13.91**, *22.91* (1.41-118.03)	20.71, **14.95**, *21.43* (1.67-112.20)	36.42, **25.49**, *35.76* (4.43-181.43)	30.61, **27.17**, *21.21* (5.04-106.07)	30.16, **26.45**, *19.69* (6.34-100.15)	25.02, **21.22**, *17.10* (5.08-87.41)
Mono-*ortho* PCBs	1.73, **1.01**, *2.31* (0.09-12.39)	1.71, **1.20**, *1.89* (0.12-10.07)	3.06, **2.14**, *3.36* (0.34-17.54)	2.61, **2.35**, *1.84* (0.36-8.97)	2.62, **2.03**, *2.01* (0.44-10.34)	2.19, **1.86**, *1.53* (0.36-7.67)

Table 2.Lower bound and **upper bound** $WHO_{PCDD/F\ and\ PCB}$-TEQs (pg/kg bw/d) in Finnish 1 to 6 year-old boys and girls based on a 3-d food record study. Prob to exceed 1.0, 2.0 and 4.0 stands for probability of exceeding the TDI (tolerable daily intake) as pg/kg bw/d WHO-TEQs of 1.0 by the WHO as a long-term goal, 2.0 by the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT), and 4.0 by the WHO as an immediate goal. Regular values indicate lower bound and bold values upper bound intakes.

	Age, years					
	1		3		6	
Intake statistics	Boys (n=)	Girls (n=___)	Boys (n=___)	Girls (n=___)	Boys (n=___)	Girls (n=___)
Mean	1.146, **1.405**	1.043, **1.324**	1.998, **2.371**	1.756, **2.043**	1.757, **1.963**	1.698, **1.929**
Median	0.590, **0.906**	0.731, **0.979**	1.277, **1.582**	1.440, **1.734**	1.345, **1.477**	1.310, **1.514**
SD[1]	1.741, **1.642**	1.151, **1.270**	2.212, **2.432**	1.444, **1.472**	1.509, **1.566**	1.405, **1.514**
Percentiles						
0.05	0.085, **0.222**	0.107, **0.246**	0.302, **0.520**	0.301, **0.522**	0.373, **0.580**	0.378, **0.521**
0.25	0.276, **0.484**	0.320, **0.522**	0.604, **0.884**	0.724, **0.999**	0.834, **1.054**	0.802, **0.978**
0.75	1.158, **1.590**	1.263, **1.606**	2.444, **2.813**	2.262, **2.565**	2.092, **2.273**	2.065, **2.300**
0.95	3.785, **3.982**	2.966, **3.408**	5.824, **6.517**	4.313, **4.643**	4.381, **4.708**	4.209, **4.618**
Min	0.047, **0.133**	0.059, **0.163**	0.213, **0.374**	0.207, **0.385**	0.258, **0.445**	0.245, **0.386**
Max	9.497, **8.933**	5.977, **6.723**	11.290, **12.770**	7.082, **7.432**	7.891, **8.389**	7.173, **7.925**
Prob to exceed 1.0	0.275, **0.450**	0.350, **0.475**	0.575, **0.675**	0.625, **0.725**	0.650, **0.775**	0.625, **0.725**
Prob to exceed 2.0	0.125, **0.150**	0.100, **0.150**	0.325, **0.375**	0.300, **0.400**	0.250, **0.300**	0.250, **0.300**
Prob to exceed 4.0	0.025, **0.025**	0.025, **0.025**	0.100, **0.125**	0.050, **0.075**	0.050, **0.075**	0.050, **0.050**

[1] Standard deviation

Table 3. Gender-specific upper bound-based sum of PBDE intake statistics (ng/kg bw/d) in Finnish 1 to 6 year-old children based on a 3-d food record study.

	Age, years					
	1		3		6	
Intake statistics	(n=___)		(n=___)		(n=___)	
	Boys	Girls	Boys	Girls	Boys	Girls
Mean	0.976	1.034	1.506	1.407	1.491	1.105
Median	0.742	0.781	1.195	1.250	1.277	0.968
SD[1]	0.865	0.922	1.160	0.833	0.926	0.602
Percentiles						
0.05	0.200	0.218	0.391	0.436	0.482	0.433
0.25	0.447	0.472	0.715	0.840	0.865	0.707
0.75	1.165	1.230	1.875	1.740	1.835	1.331
0.95	2.451	2.613	3.599	2.892	3.163	2.191
Min	0.132	0.152	0.290	0.305	0.337	0.309
Max	4.559	4.853	5.835	4.240	4.742	3.191

[1] Standard deviation

Table 4. Gender-specific (B, boys; G, girls) Hg intake statistics (µg/kg bw/d) in Finnish 1 to 6 year-old children estimated from the 3-d food record study. Prob to exceed RfD stands for probability of exceeding the current USEPA reference dose [1] of 0.1 µg/kg bw/d for MeHg.

	Age, years					
	1		3		6	
Intake statistics	Boys (n=508)	Girls (n=420)	Boys (n=516)	Girls (n=471)	Boys (n=426)	Girls (n=377)
Mean	0.029	0.032	0.046	0.033	0.066	0.070
Median	0.021	0.023	0.033	0.024	0.049	0.048
SD[2]	0.029	0.040	0.042	0.030	0.060	0.071
Percentiles						
0.05	0	0	0.008	0.006	0.007	0.009
0.25	0.009	0	0.019	0.014	0.025	0.025
0.75	0.039	0.046	0.056	0.040	0.086	0.086
0.95	0.082	0.104	0.121	0.087	0.176	0.197
Min	0	0	0.004	0.003	0.003	0.004
Max	0.135	0.183	0.212	0.153	0.282	0.356
Prob to exceed RfD	0.025	0.050	0.075	0.025	0.175	0.175

[1] The reference dose (RfD) is an amount of methylmercury, which when ingested daily over a lifetime is anticipated to be without adverse health effects to humans, including sensitive subpopulations. At the RfD or below, exposures are expected to be safe. The risk following exposures above the RfD is uncertain, but risk increases as exposures to methylmercury increase (USEPA, 1997).

[2] Standard deviation

– Not detected