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Levels of PCDD/Fs, PCBs and PBDEs in breast milk of women living in the vicinity of a hazardous waste incinerator: Assessment of the temporal trend

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HIGHLIGHTS

- PCDD/Fs, PCBs and PBDEs were determined in milk from women in the vicinity of a HWI.
- Daily intake of PCDD/Fs, PCBs and PBDEs by infants via breastfeeding was estimated.
- The HWI does not pose a significant impact on the local population.

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ABSTRACT

The concentrations of polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs), polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) were determined in breast milk from women living in the vicinity of a hazardous waste incinerator (HWI) in Catalonia, Spain. The results were compared with the levels obtained in previous surveys carried out in the same area in 1998 (baseline study), 2002 and 2007. The current total concentrations of 2,3,7,8-chlorinated PCDD/Fs in breast milk ranged from 18 to 126 pg g^{-1} fat (1.1–12.3 pg WHO_{2005}-$TEQ_{PCDD/F}$), while the total levels of PCBs ranged from 27 to 405 pg g^{-1} fat (0.7–5.3 pg WHO_{2005}-TEQ_{PCB}). In turn, PBDE concentrations (sum of 15 congeners) ranged 0.3–5.1 g g^{-1} fat, with a mean value of 1.3 ng g^{-1} fat. A general decrease in the concentrations for PCDD/Fs, both planar and total PCBs, and PBDEs in breast milk was observed. The levels of PCDD/Fs, PCBs, and PBDEs in milk of women living in urban zones were higher than those corresponding to industrial zones (41%, 26%, and 8%, respectively). For PCDD/Fs and PCBs, the current decreases are in accordance with the reduction in the dietary intake of these pollutants that we have also observed in recent studies carried out in the same area of study.

1. Introduction

Polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans (PCDD/Fs) are persistent organic pollutants (POPs) formed during combustion processes and as by-products of industrial processes (Birch et al., 2007; Quina et al., 2011). Polychlorinated biphenyls (PCBs) are industrial chemicals that have been widely used in transformers, lubricants, plasticizers, inks, etc. However, their use has now been largely phased out (ATSDR, 2001). In addition, PCBs are also formed as by-products in combustion processes. PCDD/Fs and PCBs are toxic chemicals that can cause serious health effects such as cancer, hormone disruption, impaired reproduction, skin toxicity and immune system disorders, when exposure continues over an extended period (ATSDR, 1999; JECFA, 2002; Park et al., 2009). On the other hand, polybrominated diphenyl ethers (PBDEs) are widely used brominated flame-retardants. The general population is exposed to PBDEs through products such as upholstery, building materials, insulation, electronic equipment, combustion processes and also through dietary intake (Bocio et al., 2003; Schettgen et al., 2012). PBDEs have been detected in house dust, leaves, foods and human tissues due to high levels of production and the persistence and bioaccumulation of PBDEs in the environment (Bakker et al., 2008; Domingo et al., 2008; Domingo, 2012). Causal relationships between prenatal exposure to PBDEs and developmental and behavioral neurotoxicity have been observed in experimental animal models (Costa and Giordano, 2007; Heredia et al., 2012). PCDD/Fs, PCBs, and PBDEs can persist

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in the environment for long periods of time. These pollutants bioaccumulate into the biota, magnify up the food chain, and thereby pose threats to human health. Due to the lipophilic properties, they may be transferred from adipose tissue of the mother to the infant via breast milk (Pandelova et al., 2010). Exposure to these pollutants during stages of early life, including the breastfeeding period, has been associated with subtle developmental, immunological and endocrinological effects in children (Herbstman et al., 2010; Gascon et al., 2011; Hertz-Picciotto et al., 2011).

Breast milk is the most complete food in the human diet, providing almost all the necessary nutrients for the babies, as well as protection against a number of diseases, including diarrhea, acute respiratory infections, and otitis (Leon-Cava et al., 2002). Exclusive breastfeeding during the first six months of life can reduce child mortality rates (Jones et al., 2003), and the probability of developing diabetes, hypertension and cardiovascular disease in adulthood (Solomon and Weiss, 2002; Martin et al., 2005; Leaf and Winterson, 2009). However, milk is also an excretion pathway in mammals that may contain toxic compounds to which the mother has been exposed, mainly from dietary sources (Pandelova et al., 2010). Mature breast milk is used for non-invasive monitoring of environmental toxicants (Esteban and Castaño, 2009). Human milk is an ideal matrix for measurement of the body burden of lipophilic persistent organic pollutants (POPs) in nursing women, due to their relatively high lipid content (Tsang et al., 2011). Moreover, mother's milk levels of POPs give a good estimation of the exposure of the growing fetus and the breastfeeding infants to these contaminants. Therefore, in recent years, POPs have been extensively studied in human milk over the world; i.e., Italy (Ingelido et al., 2007), Belgium (Croes et al., 2012), Russia (Polder et al., 2003; Tsydenova et al., 2007; Polder et al., 2008a), Norway (Polder et al., 2008b), Philippines (Malarvannan et al., 2009), Japan (Fujii et al., 2012), USA (Schecter et al., 2010), China (Li et al., 2009; Shen et al., 2012), Hong Kong (Tsang et al., 2011), Asia (Haraguchi et al., 2009), South Africa (Darnerud et al., 2011), Sweden (Darnerud et al., 2010), and Spain (Lacorte and Ikonomou, 2009; Schuhmacher et al., 2009; Gómara et al., 2011).

Incineration has demonstrated to be a commercially available technology for hazardous waste (HW) disposal. However, the stack emission of a number of inorganic and organic substances from HW incinerators (HWIs) has raised an important concern on their environmental and health risks. In 1996, the construction of the first and to date the only HWI in Spain was initiated in Constantí (Tarragona County, Catalonia, Spain). Regular operations began in 1999. Before the HWI started to operate, a wide surveillance program, consisting on biological and environmental monitoring studies, was initiated. This program was focused on determining the environmental impact and the human health risks derived from the emissions of PCDD/Fs and heavy metals from the HWI. In the baseline study (1998), samples of human blood, breast milk, and adipose tissue were collected from individuals living in the vicinity of the facility (Schuhmacher et al., 1999a,b,c). In 2002 and 2007, after approximately 3 and 8 years of regular operations, new surveys were again carried out using the same biological monitors (Schuhmacher et al., 2004a,b, 2009). Among these, breast milk is an ideal medium for assessing exposures to persistent organic pollutants (POPs) such as PCDD/Fs, PCBs, and PBDEs. Since 1998, breast milk surveys for PCDD/Fs and PCBs have been periodically performed. In addition, in 2002 PBDEs were also included in the monitoring program.

The main objective of the present study was to determine the levels of PCDD/Fs, PCBs, and PBDEs in breast milk of primiparae mothers living in the area under direct influence of the HWI. The current levels were compared with the concentrations obtained in previous surveys, and the daily intake of PCDD/Fs, PCBs, and PBDEs by infants via breastfeeding, was estimated.

2. Materials and methods

2.1. Breast milk sampling

Milk samples were collected in 2012 from women living in Tarragona County (Spain) in zones under potential influence of the emission of the HWI. The participants in the study were 26–44 years of age (mean value 32 years), who had lived in Tarragona County for at least the last 5 years. Only healthy primiparae mothers were included in this survey. All volunteers completed questionnaires about age, current and former area of residence, as well as dietary habits and lifestyles. Twenty milk samples were obtained. Fifteen samples corresponded to women living in urban zones (Tarragona downtown), while the remaining five samples belonged to women living near an important industrial area, which includes a big oil refinery, a chloralkali plant and other chemical facilities, a municipal solid waste incinerator, and the HWI here under study. The time elapsed between delivery and sampling was between one and two months. Milk samples of each participant were pooled (50–100 mL) and stored frozen (−20 °C) until analyses of PCDD/Fs, PCBs, and PBDEs. The study protocol was reviewed and approved by the Ethical Committee for Human Studies of the Hospital de la Vall d'Hebrón, Barcelona, Spain. An informed written consent was obtained from each of the participating women.

2.2. Analysis of human milk samples

Details about the analysis of the samples were previously reported (Schuhmacher et al., 2002). Briefly, fat from breast milk samples was extracted with a mixture of diethyl ether and hexane after addition of sodium oxalate and ethanol. Extraction solvent was exchanged to hexane only. Fat content of the breast milk sample was determined gravimetrically. An amount of 1.5 g of the fat was spiked with ^{13}C-labelled internal standards in order to analyze the 17 toxic 2,3,7,8-chlorine substituted PCDD/F-, PCB- and PBDE-congeners. The sample was defatted in a multilayer silica gel (MN-Kieselgel 60, 0.063-0.2/70-230 mesh ASTM, prewashed and activated) column containing acidic and neutral layers of silica and sodium sulfate (Merck, p.a., activated), and analytes were eluted with hexane PCDD/Fs and non-*ortho*-PCBs were purified and separated from other PCBs and PBDEs on aluminum oxide column (Merck, 90 1097) and on activated carbon column (Carbopack C, 60/80 mesh) connected to aluminum oxide column). The first fraction, including non-planar PCBs and PBDEs, was eluted with dichloromethane:hexane (20%/80% v/v), following a back elution of the second fraction (PCDD/Fs and non-*ortho*-PCBs) with toluene. Recovery standards (^{13}C-1,2,3,4-TCDD and ^{13}C-1,2,3,7,8,9-HxCDD for PCDD/Fs and ^{13}C-PCB60 for non-*ortho*-PCBs) were added before eluent was replaced by 10–15 μL of nonane. Recovery standards, ^{13}C-PCB-159 for other PCBs and ^{13}C-BDE118 and ^{13}C-BDE208 for PBDEs, were added in 0.5 mL hexane prior to analysis. Quantification was performed by selective ion recording using an an Autospec Ultima (Micromass Ltd., Manchester, UK) high-resolution mass spectrometer (resolution 10000) equipped with a HP 6890 gas chromatograph. A fused silica capillary column DB-5MS(60 m, 0.25 mm, 0.25 μm) was used. Two μL were injected into a split–splitless injector Limits of quantification (LOQ) for POPs varied between 0.01–4.9 pg g^{-1} in fat, depending on each individual congener. Recoveries for internal standards were higher than 60% for all congeners.

Chemical Exposure Unit at the National Institute for Health and Welfare of Finland, where the experimental work was performed, is a FINAS accredited testing laboratory (No. T077) (current standard: EN ISO/IEC 17025).

2.3. Data analysis

For calculations, non-quantified congener concentrations were assumed to be equal to one-half of the respective limit of quantification (ND = 1/2 LOQ). Statistical significance was performed by analysis of variance (ANOVA) or a Kruskal–Wallis test, depending on whether or not, data followed a normal distribution. A probability of 0.05 ($p < 0.05$) was considered as significant. The statistical software SPSS version 19.0 was used for data analyses. Toxic equivalents (TEQ) were calculated according to the 2005 WHO-TEFs (van den Berg et al., 2006). Furthermore, in order to compare TEQ values of the current study to those of our previous surveys, the latter were recalculated by applying the same 2005 WHO-TEFs.

3. Results and discussion

The individual concentrations of PCDD/Fs, PCBs, and PBDEs in breast milk of 20 women living in the vicinity of the HWI are shown in Table 1. In the present study, PCDD/Fs ranged from 18.0 to 126 pg g^{-1} fat (1.06 to 12.3 pg $WHO_{PCDD/F}$-TEQ g^{-1} fat), with a mean value of 48.9 pg g^{-1} fat (4.79 pg $WHO_{PCDD/F}$-TEQ g^{-1} - fat). The most toxic PCDD congener (2,3,7,8-TCDD) showed a mean concentration of 0.66 pg g^{-1} fat, being detected in all samples. The maximum concentration corresponded to OCDD, with a mean value of 24.1 pg g^{-1} fat. Regarding PCDFs, the highest mean value corresponded to 2,3,4,7,8-PeCDF (3.7 pg g^{-1} fat). In contrast, OCDF was under the quantitation limit in all samples. Total PCBs ranged from 26.9 to 405 ng g^{-1} fat (0.71–5.28 pg WHO_{PCB}-TEQ g^{-1} fat), with a mean value of 156 ng g^{-1} fat (2.48 pg WHO_{PCB}-TEQ g^{-1} fat). The most toxic PCB congeners, PCB 126 and PCB 169, showed mean concentrations of 16.3 and 17.3 pg g^{-1} fat, respectively. Non-planar congeners, PCB-153 and PCB-180 reached the highest levels (121 and 95 ng g^{-1} fat, respectively) (data of the individual PCB congeners not shown). In turn, ΣPBDE concentrations (sum of 15 congeners) ranged from 0.32 ng g^{-1} fat to 5.10 ng g^{-1} fat, with a mean value of 1.25 ng g^{-1} fat.

The results of the previous and current studies (baseline: 1998, 2002, 2008, and 2012) are summarized in Table 2. A general decrease of the concentrations in breast milk for PCDD/Fs, PCBs (both planar and total PCBs) and PBDEs, can be seen. Between 2007 and 2012, a general reduction was observed in breast milk for all the analyzed POPs. For the sum of 2,3,7,8-chlorinated PCDD/Fs, the reduction was 47%, being statistically significant ($p < 0.001$). When assessing PCDD/F concentrations in $WHO_{PCDD/F}$-TEQs, a similar decrease was noted between 1998 and 2002 (61% of reduction), while a 37% decrease between the 2007 and the current survey was observed. However, this decrease did not reach a level of statistical significance ($p > 0.05$). For planar PCBs, total concentrations and $WHO_{PL\text{-}PCB}$-TEQs decreased 39% and 49%, respectively, the latter reduction being significant ($p < 0.01$). For PCBs, both the concentration of the sum of PCBs and the WHO_{PCB}-TEQs decreased between 2002 and the current surveys (44% and 72%, respectively), being the TEQ decrease statistically significant ($p < 0.01$). Regarding the PBDE concentrations in breast milk, although no important changes were observed between 2002 and 2007, a significant decrease ($p < 0.001$; 52%) was noted between 2007 and 2012. Baseline data (1998) for PBDEs were not measured. With respect to the individual concentrations of the different PCDD/F congeners, the congener profile of PCDD/Fs in milk samples of women living in the vicinity of the HWI in 1998 (baseline) and 2012, is depicted in Fig. 1. Very similar PCDD/F congener profiles were found. However, when comparing individually each congener, samples collected in 2012 showed a slight increase of low-substituted congeners (2,3,7,8-TCDD,

Table 1
Concentrations of PCDD/Fs (in pg g^{-1} fat), PCBs (in pg g^{-1} fat) and PBDEs (in ng g^{-1} fat) in breast milk of 20 women living in the vicinity of a HWI in Catalonia, Spain.

Sample	PCDD/Fs		PCBs			PBDEs	
	ΣPCDD/Fs[a]	$WHO_{PCDD/F}$-TEQ	Sum of planar PCBs[b]	ΣPCBs[c]	WHO_{PCB}-TEQ	ΣPBDEs [d]	% fat
1	29.4	2.93	25.5	109	1.68	0.74	7.0
2	110	8.36	45.3	166	3.18	0.78	4.1
3	29.1	3.31	37.1	116	2.82	5.10	5.9
4	58.5	4.73	47.3	238	3.07	0.64	2.2
5	35.3	4.53	46.5	246	2.30	0.95	1.5
6	89.8	9.96	47.2	30.0	2.26	1.08	2.3
7	47.0	4.33	34.5	121	2.38	0.59	4.0
8	52.1	6.16	61.1	405	4.00	1.35	2.7
9	18.0	1.59	18.0	26.9	0.71	0.32	4.9
10	25.7	2.82	24.1	112	1.35	0.75	3.9
11	38.6	4.53	59.3	338	3.87	2.25	4.8
12	37.1	1.83	22.9	49.9	0.87	1.13	1.0
13	40.1	5.55	44.1	126	2.82	1.35	1.5
14	20.7	1.06	31.1	44.5	1.03	1.86	1.9
15	126	12.3	91.4	283	5.28	1.56	1.5
16	56.1	5.54	45.3	132	2.69	0.51	3.6
17	55.4	4.33	31.2	115	2.10	0.52	4.5
18	49.4	4.40	46.9	209	3.05	1.61	3.1
19	36.9	4.13	70.1	143	2.87	0.76	1.9
20	22.6	3.35	30.0	98.8	1.29	1.24	4.8
Mean	48.9	4.79	42.9	156	2.48	1.25	3.4
SD	28.9	2.76	17.8	102	1.15	1.03	1.7
Min	18.0	1.06	18.0	26.9	0.71	0.32	1.0
Max	126	12.3	91.4	405	5.28	5.10	7.0

[a] 17 toxic 2,3,7,8-chlorine substituted PCDD/F congeners (2,3,7,8-TCDD; 1,2,3,7,8-PeCDD; 1,2,3,4,7,8-HxCDD; 1,2,3,6,7,8-HxCDD; 1,2,3,7,8,9-HxCDD; 1,2,3,4,6,7,8-HpCDD; OCDD; 2,3,7,8-TCDF; 1,2,3,7,8-PeCDF; 2,3,4,7,8-PeCDF; 1,2,3,4,7,8-HxCDF; 1,2,3,6,7,8-HxCDF; 2,3,4,6,7,8-HxCDF; 1,2,3,7,8,9-HxCDF; 1,2,3,4,6,7,8-HpCDF; 1,2,3,4,7,8,9-HpCDF; OCDF).

[b] PCB congeners 77, 81, 126, and 169.

[c] 37 PCB congeners (PCB 18, 28/31, 33, 47, 49, 51, 52, 60, 66, 74, 77, 81, 99, 101, 105,110, 114, 118, 122, 123, 126, 128, 138, 141, 153, 156, 157, 167, 169, 170, 180, 183, 187, 189, 194, 206, and 209).

[d] 15 PBDE congeners (BDE 28, 47, 66, 71, 75, 77, 85, 99, 100, 119, 138, 153, 154, 183, 190).

Table 2
Mean levels and standard deviations of PCDD/Fs, planar PCBs, ΣPCBs (37) and PBDEs in samples of milk from women living in the vicinity of a HWI in Catalonia, Spain.

	Baseline				% Variation	
	1998 (n = 15)	2002 (n = 15)	2007 (n = 15)	2012 (n = 20)	98–12	07–12
PCDD/Fs						
Sum PCDD/Fs (pg g^{-1} fat)	242 ± 69	118 ± 72.3	92.2 ± 31.8	48.9 ± 28.9	−80**	−47**
(pg $WHO_{PCDD/F}$-TEQ g^{-1} fat)	12.2 ± 2.8	10.6 ± 9.6	7.6 ± 2.4	4.8 ± 2.8	−61**	−37
Planar PCBs						
Sum of planar PCBs (pg g^{-1} fat)	128 ± 37	74 ± 24	69.9 ± 32	42.9 ± 17.7	−66**	−39
(pg WHO_{PL-PCB}-TEQ g^{-1} fat)	8.2 ± 2.7	4.4 ± 1.5	4.3 ± 2.1	2.2 ± 0.9	−73**	−49*
Total PCBs						
Σ PCBs (37) (ng g^{-1} fat)	471 ± 147	255 ± 97	280 ± 137	156 ± 102	−66**	−44
(pg WHO_{PCB}-TEQ g^{-1} fat)	17.6 ± 5.8	9.4 ± 3.1	9.0 ± 4.4	2.5 ± 1.1	−86**	−72**
PCDD/Fs + PCBs						
(pg $WHO_{PCDD/F+PCB}$-TEQ g^{-1} fat)	29.7 ± 8.3	20.0 ± 11.5	16.6 ± 6.4	7.3 ± 3.7	−75**	−56*
PBDEs						
Σ PBDEs (15) (ng g^{-1} fat)	[a]	2.4 ± 1.7	2.5 ± 1.6	1.2 ± 1.0	−50^{**,b}	−52**

Differences are statistically significant at $^{*}p < 0.01$, $^{**}p < 0.001$.
[a] PBDE concentrations were not measured in the baseline (1998) survey.
[b] Percentage variation between 2002 and 2012.

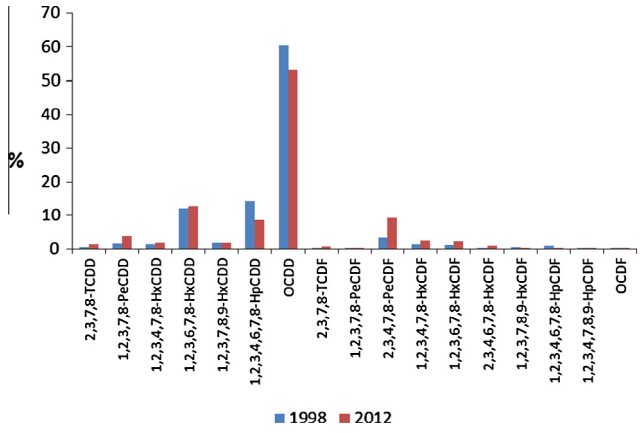

Fig. 1. PCDD/F congener profile in human milk in 1998 (baseline survey) and 2012 (current study).

1,2,3,7,8-PeCDD, 2,3,4,7,8-PeCDF, 1,2,3,4,7,8-HxCDF, and 1,2,3,6,7,8-HxCDF), and a slight decrease in high-chlorinated congeners (OCDD and 1,2,3,4,6,7,8-HpCDD).

Comparative data on the concentrations of POPs in breast milk from different regions of the world have been generated in collaborative studies coordinated by the WHO. Five of these studies were carried out in the periods 1987–1988, 1992–1993, 2000–2003, 2005–2007 and 2008–2009 (van Leeuwen and Malisch, 2002; Colles et al., 2008; WHO, 2009). The results of these studies have shown a consistent decline in the concentrations of PCDD/Fs and PCBs in breast milk over the last 20 years (van Leeuwen and Malisch, 2002; Lignell et al., 2009). Also other studies found a time-related decrease in the concentrations of POPs in breast milk (Bordajandi et al., 2008; Nakamura et al., 2008; Polder et al., 2008b; Schuhmacher et al., 2009; Ulaszewska et al., 2011).

For the general population, dietary intake is the main route of exposure to PCDD/Fs, PCBs, and probably also for PBDEs (Wang and Needham, 2007; Perelló et al., 2009; Domingo, 2012). In the present study, the decrease observed in PCDD/F and PCB concentrations in relation to those of the baseline survey, is probably due to the general reduction of PCDD/F and PCB emissions, as well as the continued decrease in the dietary exposure to PCDD/Fs and PCBs of the population living in the neighborhood of the HWI (Domingo et al., 2012). It has been shown that the body burdens of PCDD/Fs and PCBs significantly decreased in most developed countries during the last two decades after governmental regulations were enacted to reduce their emissions (Polder et al., 2008a). As a result of the 2001 Stockholm Convention, stringent treatment and disposal requirements have been imposed on industrial wastes potentially involved in contamination with POPs, such as PCDD/Fs and PCBs. In contrast, levels of PBDEs in human specimens, including breast milk and blood, have increased in the past two decades (1980–1990s), although there is some signs that the concentrations are decreasing after 2000 (Norén and Meironyté, 2000; Sjödin et al., 2003).

PCDD/F, PCB, and PBDE concentrations in human milk samples were also evaluated according to the specific place of residence of the participants (urban or industrial zones). The results for the baseline 1998, 2002, 2007 and current surveys are shown in Table 3. In the present survey, the mean concentration of PCDD/Fs in milk of women living in urban areas was 41% higher than that corresponding to the industrial zones (5.3 and 3.1 pg $WHO_{PCDD/F}$-TEQ g^{-1} fat, respectively). This difference was similar to that observed in our previous surveys (2002 and 2007). However, in the baseline survey women living in industrial areas presented higher levels than in urban areas. Planar PCBs and total PCBs were also higher in the urban than in the industrial area (26% and 23%, respectively) with values of (2.3 vs. 1.7 pg WHO_{PL-PCB}-TEQ g^{-1} fat and 2.6 vs. 2.0 pg WHO_{PCB}-TEQ g^{-1} fat, respectively). Yang et al. (2002) also observed higher PCB levels in breast milk of primiparae mothers living in urban areas of Korea than in those living in industrial areas (7.34 pg TEQ g^{-1} fat and 5.42 pg TEQ g^{-1} fat, respectively). Regarding the current PBDE levels, they were slightly higher (8%) in the urban than in the industrial zone (1.3 and 1.2 ng g^{-1} fat, respectively). In our previous survey, PBDE levels were slightly lower in the urban than in the industrial zone (2.4 vs. 2.7 ng g^{-1} fat) (Schuhmacher et al., 2009). Škrbić et al. (2010) did not find any differences between donors from urban and ruralareas. Several studies have shown that dietary habits have a strong effect on PCDD/F and PCB intakes: diets rich in fish and seafood have frequently been associated with higher levels in human breast milk (Polder et al., 2008b; Li et al., 2009). Although human milk congener composition may vary widely due to differential partitioning or metabolism of compounds, residue profiles in human milk may also differ locally because of the wide variation of dietary habits (Nadal et al., 2004a). Population from industrial areas may have some different food habits compared to

Table 3
Concentrations (mean ± standard deviations) of PCDD/Fs, PCBs and PBDEs in samples of milk from women living in the vicinity of a HWI in Catalonia, Spain, according to the specific place of residence (urban or industrial zones).

	Baseline 1998		2002		2007		2012	
	Urban (n = 9)	Industrial (n = 6)	Urban (n = 7)	Industrial (n = 8)	Urban (n = 9)	Industrial (n = 6)	Urban (n = 5)	Industrial (n = 15)
PCDD/Fs	11.5 ± 2.8	13.1 ± 2.7	13.9 ± 13.4	7.8 ± 3.5	9.0 ± 1.7	5.5 ± 1.8	5.3 ± 2.9	3.1 ± 1.4
Planar PCBs	7.4 ± 2.6	9.3 ± 2.7	5.1 ± 1.2	3.7 ± 1.4	5.1 ± 2.0	3.0 ± 1.6	2.3 ± 0.8	1.7 ± 1.2
Total PCBs	16.0 ± 5.5	20.0 ± 5.7	11.1 ± 2.5	7.9 ± 3.0	10.9 ± 4.2	6.3 ± 3.3	2.6 ± 1.0	2.0 ± 1.4
Σ PBDEs	Not determined		2.2 ± 1.9 8	2.5 ± 1.5	2.4 ± 1.6	2.7 ± 1.8	1.3 ± 1.1	1.2 ± 0.8

PCDD/F and PCB concentrations are expressed in pg WHO-TEQ g^{-1} fat. PBDE levels are expressed in ng g^{-1} fat.

those in urban areas, as socioeconomic levels are frequently different. Higher quantities of fish and seafood are consumed in the urban areas (Nadal et al., 2004b), explaining the observed differences.

To identify any common profile, principal component analysis (PCA) was applied to the sum of PCDD/Fs (17), sum of planar PCBs (4), sum of PCBs (37), and sum of PBDEs (15) for the current 20 human milk samples. PCA is a data compression technique that aims to explain most of the variance in the data, while transforming the set of correlated measured variables into a smaller set of new uncorrelated variables or principal components (PCs), attempting at the same time to preserve and emphasize the relevant relationships present in the original data (Boruvka et al., 2005). The main goal of this multivariate statistical technique is to extract useful information and provide an easier visualization of the relations among objects and variables determined in large or complex data sets (Rovira et al., 2011). The scatter plot of component scores on both principal components (PCs) showed that most breast milk samples were included in a main cluster with only a few outliers (Fig. 2). The first PC, which explains 52% of the variance, was correlated with the sum of planar PCBs (r = 0.938), the sum of PCBs (r = 0.789), and the sum of PCDD/Fs (r = 0.765). The second PC (27% of the variance) was mainly correlated with the sum of PBDEs (r = 0.942). These results indicate that samples collected in urban and industrial zones have similar profiles, which corroborates that breast milk from women living in industrial zones are not influenced by the presence of the HWI. Furthermore, chlorinated (PCDD/Fs and PCBs) and brominated (PBDEs) compounds were represented in different PCs, reflecting probably different exposure sources.

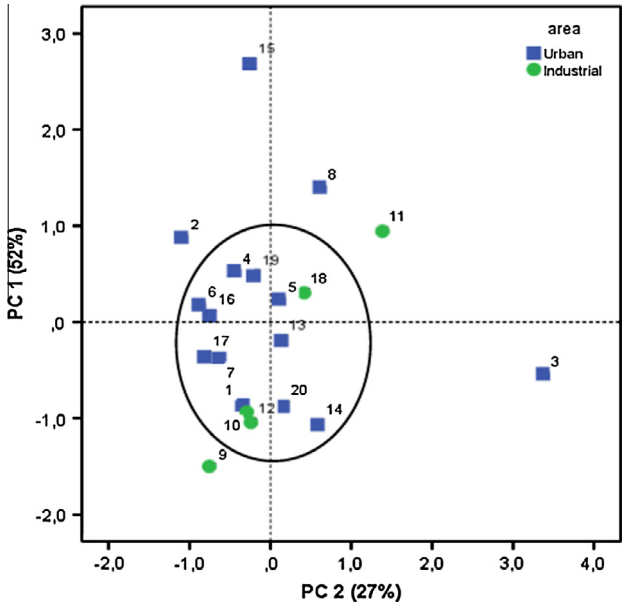

Fig. 2. PCA for milk samples collected in 2012 in urban and industrial zones.

Breast-milk feeding is essential for the growth, development, and wellbeing of infants, as indicated by a decreased incidence of infectious diseases and enhanced performance on tests of cognitive development (American Academy of Pediatrics, 2005). However, exposure assessments have indicated that breast milk is a major source of POPs for infants (Hsu et al., 2007). In recent years, various international organizations have established a tolerable daily intake (TDI) for PCDD/Fs, including that of dioxin-like PCBs. Thus, the WHO established a TDI for PCDD/Fs (plus dioxin-like PCBs) in the range of 1–4 pg WHO-TEQ kg^{-1} body weight per d for the non-carcinogenic effects of these organic pollutants (van Leeuwen et al., 2000). In turn, the Joint FAO/WHO Expert Committee on Food Additives (JEFCA) also evaluated the health implications of PCDD/Fs, suggesting a provisional maximum tolerable monthly intake of 70 pg TEQ kg^{-1} body weight (JECFA, 2002). Based on practical reasons, currently the weekly and monthly maximum intakes are being handled as if it was a TDI of 2 pg WHO-TEQ kg^{-1} (Domingo et al., 2012). In relation to PBDEs, limit values based on toxicological evaluations (such as a TDI) have not been established yet. Bakker et al. (2008) have calculated the expected human NOAEL (no adverse effect level) of daily intake for neurodevelopmental toxicity concerning lactational exposure to BDE-99, which ranged from 18.8 to 41.4 ng kg^{-1} d^{-1}.

In order to evaluate the potential risks, the daily intake of PCDD/Fs (plus dioxin-like PCBs) and BDE-99 by infants via breastfeeding for 8, 16 and 24 weeks, were calculated. To evaluate the accumulated intake of PCDD/Fs, PCBs, and BDE-99 from breastfeeding in newborns, we used a probabilistic model. Probabilistic exposure calculations were performed by means of Crystal Ball (Decisioneering Inc., Denver, USA). Monte Carlo simulations with 10 000 iterations per simulation were applied. The following equation, proposed by Patandin et al. (1999), was applied.

$$I = \left(F \times V \times [\mathrm{BMF}] \times [C]_{\mathrm{breastmilk}} \times \int_0^t e^{-0.017}dt\right) \Big/ BW \qquad (1)$$

where F is the fraction of intestinal absorption in breast-milk (unitless), this is, 0.95 for PCDD/Fs and dioxin-like PCBs, and 0.85 for BDE-99 (EPA, 2008; Ulaszewska et al., 2011), V is the weekly consumption of milk (in mL), BMF is the milk fat concentration (in g fat mL^{-1}), t is the duration of breast feeding (in weeks), C is the concentration in breast milk (pg WHO-TEQ g^{-1} fat for PCDD/Fs and dioxin-like PCBs, and ng g^{-1} fat for BDE-99). We assumed that infants consume only breast milk in their first 24 weeks. The input variables included in the present probabilistic exposure calculations, as well as the probability distributions and parameters for each variable, are given in Table 4. In turn, Table 5 shows the intake estimation of PCDD/F + DL-PCB and PBDE-99 by newborns (8, 16 and 24 weeks) of breastfeeding. The accumulated mean values of PCDD/Fs and dioxin-like PCBs were 600, 1008 and 1282 pg WHO-TEQ after 8, 16 and 24 weeks of breastfeeding. The highest

Table 4
Probability distributions and distribution parameters for each variable used in the probabilistic exposure calculation.

Variable	Distribution	Weeks		
		8	16	24
V (mL week^{-1})	Normal	5292 ± 1190	5670 ± 994	6272 ± 854
BW (kg)	Log normal	4.0 ± 3.7	5.1 ± 4.7	6.0 ± 5.5
BMF (% fat)	Log normal		3.4 ± 1.7	
PCDD/Fs + PCBs (pg WHO-TEQ g^{-1} fat)	Log normal		7.3 ± 3.7	
PBDE-99 (ng g^{-1} fat)	Log normal		0.090 ± 0.094	

Probability distributions given as mean ± standard deviation.

Table 5
Estimated intakes of PCDD/Fs + PCBs (pg WHO-TEQ) and BDE-99 (ng kg^{-1}) via breast milk in 8, 16 and 24 weeks-old Spanish infants using a probabilistic approach.

Weeks	Variable	Mean	SD	Percentiles		
				10th	50th	90th
8	PCDD/Fs + PCBs	600.2	767.6	77.4	358.2	1272.9
	BDE-99	3.64	21.60	0.01	0.28	5.43
16	PCDD/Fs + PCBs	1008.4	1362.4	154.3	538.5	2336.1
	BDE-99	8.12	114.94	0.02	0.45	9.43
24	PCDD/Fs + PCBs	1281.8	1636.3	193.1	732.5	2795.5
	BDE-99	9.31	89.67	0.03	0.58	13.04

SD: Standard deviation.

daily intake was noted in the first 8 weeks, with a mean value of 10 pg WHO-TEQ kg^{-1} bw per d. Afterwards, daily intake by breastfeeding was reduced to mean values of 6.8 pg WHO-TEQ kg^{-1} and 4.6 pg WHO-TEQ kg^{-1} at 16 and 24 weeks, respectively. On the other hand, 10% of the infants (percentile 90th) had daily intakes above 21.2, 17.7, and 7.7 pg WHO-TEQ kg^{-1} bw at 8, 16, and 24 weeks, respectively. These values are higher than the TDI proposed by the WHO, 1–4 pg TEQ kg^{-1} bw per d, and the JEFCA (2002) recommendation of 70 pg TEQ kg^{-1} body weight per month. Even though the exposure to dioxin-like compounds in individual infants decreases during the breastfeeding period, it is clear that newborn exposure continues to be elevated compared to adults. However, the risk of this exposure should not be overestimated because the TDI refers to life-span exposure, while lactation is restricted to a clearly limited period of a few months. In Catalonia, the prevalence of exclusive breastfeeding is around 50% at 3 months of age, decreasing to 20% 6 months after birth. Notwithstanding, a reduction in human exposure to these POPs is required in order to protect breastfeeding newborns, since a baby in a fastdeveloping stage may be even more vulnerable to toxic compounds than adult. Regarding BDE-99, a huge variability in the results can be observed. The accumulated mean values were 3.64, 8.12, and 9.31 ng d^{-1} at 8, 16 and 24 weeks, respectively. The daily intake in relation to bw increases during the first 8 weeks, and then it decreases. Mean daily intake was 0.06, 0.08, and 0.02 ng kg^{-1} bw 8, 16, and 24 weeks after birth, respectively. These results are well below the range 18.8–41.4 ng kg^{-1} bw per d, which is considered as potentially adverse to human health (Bakker et al., 2008). Due to the high variability observed in the current results, we propose to consider a deterministic approach only as a first tier in human exposure assessments, by using the worst-case scenario approach to protect public health. However, if more information on the human exposure is required (e.g., sensitivity analysis, uncertainty and variability analysis), or the purpose is to estimate the probability of occurrence at a certain risk level, the probabilistic approach should be applied. Therefore, the demand of more specific food safety recommendations can be satisfied through more effective risk assessment and risk management studies.

In summary, the results of the present study show that in terms of exposure to PCDD/Fs, PCBs, and PBDEs, the HWI of Constantí (Catalonia, Spain) does not pose a significant impact on the population living in the neighborhood. The results of the current biological surveillance program are in agreement with the significant reduction of PCDD/F and PCB concentrations in breast milk of non-occupationally exposed people observed in recent years in most developed countries. In turn, this decrease is also in accordance with the reduction in the dietary intake of PCDD/Fs and PCBs, reduction that has been observed in concurrent studies carried out in the same area of study (Domingo et al., 2012). Using a probabilistic approach and biomonitoring data, we were able to calculate reliable estimates of infant exposure to environmental pollutants in breast milk at different time points during breastfeeding, as well as the cumulative intake. Although these values are higher than the TDI proposed by the WHO, the risk derived from this exposure should not be overestimated, taking into account that TDI refers to life-span exposure, while lactation is restricted to a limited period.

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