Mol. Nutr. Food Res. 2008, *52*, 187 – 193 DOI 10.1002/mnfr.200700182



Research Article

# Temporal trends of polybrominated diphenyl ethers and hexabromocyclododecane in milk from Stockholm mothers, 1980–2004

**Britta Fängström[1], Ioannis Athanassiadis[1], Tjelvar Odsjö[2], Koidu Norén[3] and Åke Bergman[1]**

[1] Department of Environmental Chemistry, Stockholm University, Stockholm, Sweden
[2] Department of Contaminant Research, Swedish Museum of Natural History, Stockholm, Sweden
[3] Retired from Karolinska Institutet, Stockholm, Sweden

Environmental and human exposures to brominated flame retardants (BFR) have been of emerging concern since some BFR are persistent and bioaccumulative compounds. Among those, polybrominated diphenyl ethers (PBDE) have frequently been reported in low to high ng/g concentrations in human blood around the world while hexabromocyclododecane (HBCDD) only occasionally has been reported and then in the low ppb concentrations in human blood. The present study concerns PBDE congener and HBCDD concentrations in human milk from Stockholm from 1980 to 2004. HBCDD concentrations has increased four to five times since 1980 until 2002 but seems to have stabilized at this concentration in the last years (2003/04). Similarly, BDE-153 has continued to increase at least to 2001, after which it has stabilized in the mother's milk. Other PBDE congeners with four to five bromine substituents peaked 5 years earlier (1995) and are all decreasing. DecaBDE (BDE-209) is not a suitable biomarker for time trend studies according to the present results, showing no changes over time. This is likely due to its short apparent half-life in humans and poor transfer from blood to milk.

**Keywords:** Exposure / Human milk / Level / Hexabromocyclododecane / Polybrominated diphenyl ethers

Received: May 22, 2007; revised: August 16, 2007; accepted: August 20, 2007

## 1 Introduction

Polybrominated diphenyl ethers (PBDE) are one among several classes of brominated flame retardants (BFR) [1]; which are used in consumers products such as electronic equipment, textiles, plastics and in construction materials. PBDE have been produced since the 1970's [2] and were reported 1981 as an environmental contaminant in pike from a Swedish west coast river [3], and subsequently in the Japanese marine environment [4] and in human milk from Germany in 1988 [5]. These initial studies led to the need for authentic reference substances to allow identification and quantification of PBDE congeners in commercial products and in the environment. After these standards became available, a large number of PBDE assessments have been performed worldwide, as reviewed in *e.g.* [6–10]. Due to their widespread use, persistency and bioaccumulativity concern is also raised about their toxicity [11, 12].

Swedish researchers were in 1999, the first to show increasing concentrations of PBDE in human milk [13]. The temporal trend indicated a doubling time of PBDE concentrations every fifth year in milk for mothers living in Stockholm. An update with samples analyzed up to year 2000 indicated a decrease of particularly BDE-47 over the last 3 years [14]. A decrease of PBDE concentrations in Swedish milk was also indicated by Lind and co-workers in 2003 [15]. Ever since the initial report on increasing PBDE levels in human milk a very large number of studies have come out, first from Western Europe and North America [9, 13, 16–18] and more recently from many other countries worldwide [19–27]. Comparing the median or mean concentration of PBDE in human milk, the levels are approximately ten times higher in the United States than those hitherto reported for Europe [9, 13, 15, 24, 28, 29]. Concentra-

**Correspondence:** Dr. Åke Bergman; Department of Environmental Chemistry, Stockholm University, SE-106 91 Stockholm, Sweden
**E-mail**: ake.bergman@mk.su.se
**Fax**: +46-816-3979

**Abbreviations: ECNI,** electron capture negative ionization; **HBCDD**, hexabromocyclododecane; **PBDE**, polybrominated diphenyl ethers

tions as high as 1100 ng/g fat were observed in mother's milk from the U.S. [28].

The objective of the present study was to extend previous studies of PBDE in pooled human milk samples from Stockholm to cover the period 1980 to 2004 with emphasis on the last 10 years, to investigate any temporal concentration changes of PBDE congeners and of hexabromocyclododecane (HBCDD), to ascertain any temporal trend of decabromodiphenyl ether (BDE-209) and to add information on the PBDE time trend in human milk from Sweden. Further, these concentrations were compared to previous studies of PBDE performed in pooled human milk from Sweden. The inclusion of HBCDD in the present study is obvious since this is another BFR with properties similar to the 12 persistent organic pollutants (POP) [30, 31].

## 2 Materials and methods

### 2.1 Samples

Milk was collected from healthy native Swedish mothers by the Mothers milk center in Stockholm. Milk samples are purchased from the center and banked annually. Fourteen milk pools were considered for analyses covering the years 1980 to 2004. The pools were prepared to be as similar in composition as possible, with 55 – 80% of the milk originating from mothers nursing their first infant. Equal amounts of milk from 116, 102, 20, 15 and 20 individual mothers were mixed constituting one pool for the years 1980, 1984/85, 1988 – 2002, 2003 and 2004, respectively. The average age of the mothers was 27 – 28 years in 1980 and 1984/85, and between 29 – 31 years in 1988 – 2004. Duplicate subsamples of 10 g milk were taken out for analysis from every pool and every sub-sample was subsequently divided in two and extracted in 5 g portions to better fit the extraction method used.

### 2.2 Chemicals

The individual PBDE congeners (numbered according to Ballschmiter *et al.* [32]) BDE-47, BDE-77, BDE-99, BDE-100, BDE-153 were synthesized as described elsewhere [33]. HBCDD was purchased from Cambridge Isotope Laboratory (Andover, MA, USA) and BDE-209 from Fluka Chemie, Switzerland. All solvents were of *pro analysis* quality. The 2-propanol from AnalaR (BDH laboratory supplies pool, UK) was glass-distilled prior to use. Silica gel (< 0.063 mm) was purchased from Merck (Darmstadt, Germany) and activated (300°C, 12 h) before use.

### 2.3 Instruments

The PBDE analysis was performed by GC/MS using a Finnigan TSQ 700 instrument (ThermoFinnigan, Bremen, Germany) connected to a Varian 3400 gas chromatograph equipped with an AS200S CTC autosampler. The transfer line temperature was set to 290°C and the ion source temperature maintained at 200°C. Automated 1-μL injections were made on a septum-equipped temperature programmable injector (SPI) fitted with a high performance insert directly connected to a DB-5 HT capillary column (15 m × 0.25 mm id, 0.1-μm film thickness; J&W Scientific) with helium as carrier gas at a head pressure of 3 psi. The injector temperature was programmed from 60 to 320°C at 150°C/min and the oven from 80°C (1 min), 15°C/min to 300°C (16 min). The PBDE congeners were analyzed with selected ion monitoring (SIM) for the negative bromide ion (isotopes *m/z* 79 and 81) formed by electron capture reactions at chemical ionization (electron capture negative ionization, ECNI) with methane (5.0, AGA, Stockholm, Sweden) as the electron thermalization buffer gas at 5.6 torr and a primary electron energy of 70 eV. All chromatographic data were collected, analyzed and quantified using the proprietary ICIS2 software from ThermoFinnigan. The linear relationship of the GC/MS system was determined and the quantifications were performed using a single point external standard within the concentration range of the linear relationship.

### 2.4 Extraction and cleanup procedure

The extraction and cleanup procedure for the milk samples is a modified method for analysis of organohalogen substances (OHS) in serum and has previously been applied for PBDE and polychlorinated biphenyl (PCB) analysis in human milk [27, 34, 35]. In the modified version of the method, formic acid and diethyl ether are used instead of hydrochloric acid and methyl *tert*-butyl ether [27]. Surrogate standard, BDE-77 was added to the samples prior to extraction. In short, formic acid (1 mL) and 2-propanol (6 mL) were added to a milk sample (5 g), subsequently extracted with a mixture of n-hexane/diethyl ether (1:1, 6 mL), and re-extracted once (3 mL). The lipid content was determined gravimetrically after gentle evaporation of the solvent. The bulk of lipids were removed with concentrated sulfuric acid and the samples were pooled (2 × 5 g). Additional cleanup was performed on two subsequently applied sulfuric acid/silica gel columns, according to Hovander *et al.* [34]. Finally, the sample was fractionated on a column of activated silica gel (0.7 g). Most of the PCB congener and major traditional organochlorine pesticide interferences were eluted with hexane (3 mL) and the PBDE were eluted with hexane : DCM (1:1, 8 mL). The solvent in the PBDE fraction was changed to hexane and reduced to 100 μL prior to GC/MS analysis. All samples were protected from daylight during handling and storage to prevent any photochemical degradation of the brominated compounds to be analyzed.

 

**Table 1.** Concentrations (pmol/g fat) of PBDE congeners in pooled human milk double samples (A/B) from Sweden 1980 – 2004

| Year | BDE-47 (A/B)[a)] | BDE-99 (A/B)[a)] | BDE-100 (A/B)[a)] | BDE-153 (A/B)[a)] | HBCDD (A/B)[a)] |
|---|---|---|---|---|---|
| 1980 | 0.28/0.23 | 0.15/0.064 | 0.11/0.048 | 0.082/0.034 | 0.17/0.087 |
| 1984 | 0.48/0.59 | 0.079/0.073 | 0.13/0.13 | 0.13/0.13 | 0.14/0.16 |
| 1988 | 1.3/1.1 | 0.46/0.47 | 0.29/0.29 | 0.36/0.40 | 0.34/0.41 |
| 1990 | 2.1/2.1 | 1.1/1.1 | 0.51/0.47 | 0.46/0.42 | 0.32/0.30 |
| 1992 | 2.8/3.1 | 0.88/0.81 | 0.57/0.52 | 0.79/0.71 | 0.48/0.41 |
| 1994 | 3.6/3.5 | 1.5/1.4 | 0.57/0.51 | 0.74/0.66 | 0.64/0.54 |
| 1995 | 4.6/4.1 | 1.3/1.3 | 0.90/0.91 | 1.0/1.1 | 0.79/0.81 |
| 1996 | 3.9/4.1 | 1.3/1.3 | 0.77/0.76 | 0.81/0.82 | 0.50/0.54 |
| 1997 | 3.2/3.4 | 1.2/1.2 | 0.65/0.64 | 1.0/1.0 | 0.45/0.46 |
| 1999 | 4.4/4.4 | 0.94/0.94 | 0.57/0.47 | 1.4/1.2 | 0.60/0.54 |
| 2001 | 3.6/3.7 | 1.0/0.98 | 1.1/1.1 | 2.1/1.9 | 0.82/0.85 |
| 2002 | 3.0/2.8 | 0.60/0.57 | 0.44/0.52 | 1.2/1.0 | 1.0/0.83 |
| 2003 | 2.5/2.5 | 0.51/0.52 | 0.62/0.47 | 1.7/1.9 | 0.77/0.76 |
| 2004 | 1.9/1.9 | 0.46/0.47 | 0.50/0.51 | 1.4/1.5 | 0.58/0.62 |

a) Two pool samples from the same pool were analyzed in parallel.

### 2.5 Analysis

Five PBDE congeners, BDE-47, BDE-99, BDE-100, BDE-153 and BDE-209 and HBCDD were analyzed by GC/MS (ECNI). Solvent blank samples representing every fifth sample were cleaned up and analyzed in the same way as the other samples. Control and solvent blank samples were run in parallel throughout the whole procedure. For quantification, the PBDE amount in the sample had to be three times higher than the average PBDE amount in the solvent blank samples to be considered quantifiable. The LOQ for BDE-47 (0.041 pmol), BDE-99 (0.01 pmol), BDE-100 (0.002 pmol), BDE-153 (0.005 pmol), BDE-209 (0.019 pmol) and HBCDD (0.007 pmol) in this study were set in direct relation to the amount of the PBDE measured in the blank samples. The average in the blank samples was then subtracted from the amount in the milk samples. A recovery study was performed on cow's milk (5 g) with a fat content at 3% to validate the recovery of the method at two different spike levels (0.1 ng/sample and 1 ng/sample) [27]. The overall recovery for BDE-47, BDE-99, BDE-100 and BDE-153 were about 90% within a range of 79 – 107% [27]. The overall recoveries and SD of the surrogate standard BDE-77 were 84%, SD 5.5.

## 3 Results

The concentrations from duplicate samples of the four major PBDE congeners (BDE-47, -99, -100 and -153) and of HBCDD in the milk pool samples from 1980 to 2004 are presented in Table 1. The agreement between the duplicate samples where very good as presented by comparing the two sets of samples being analyzed, with $R^2$ values ranging from 0.92 – 0.99, the comparison is presented in Table 2. The concentrations are given on a molar basis to promote direct comparisons between analytes with substantial differences in molecular weight. All analytes were well above LOQ except for the decabromodiphenyl ether (BDE-209), where the concentrations were very low. BDE-209 was detected in all samples analyzed but with 20% of the samples falling below the LOQ. The concentrations ranged from LOQ to 0.10 pmol/g fat after blank levels were subtracted but still it is not possible to make any conclusion regarding temporal changes for the BDE-209 concentrations.

**Table 2.** Correlation between the duplicate samples, the linear correlation equation and $R^2$ values are given in the Table.

| | Correlation | $R^2$ |
|---|---|---|
| BDE-47 | $y = 0.98x + 0.0158$ | 0.97 |
| BDE-99 | $y = 0.98x - 0.0048$ | 0.99 |
| BDE-100 | $y = 0.97x - 0.0069$ | 0.96 |
| BDE-153 | $y = 0.99x - 0.0146$ | 0.97 |
| HBCDD | $y = 0.91x + 0.0194$ | 0.93 |

## 4 Discussion

The present study is, to our knowledge, the first to report on any temporal concentrations trends of HBCDD in mother's milk. The Stockholm human milk shows a fluctuating increase over time (Fig. 1). From 1980, the concentration has increased from around 0.1 to 0.6 pmol/g fat in 2004. During the last 10 years, the concentrations have varied between 0.45 and 1.0 pmol/g fat. These concentrations are in a similar range as BDE-99, BDE-100 and BDE-153 and even higher during the last few years than for BDE-99 and BDE-100 (c.f. Table 1). In a recently reported study on regional differences of PBDE in human milk from Sweden,

 

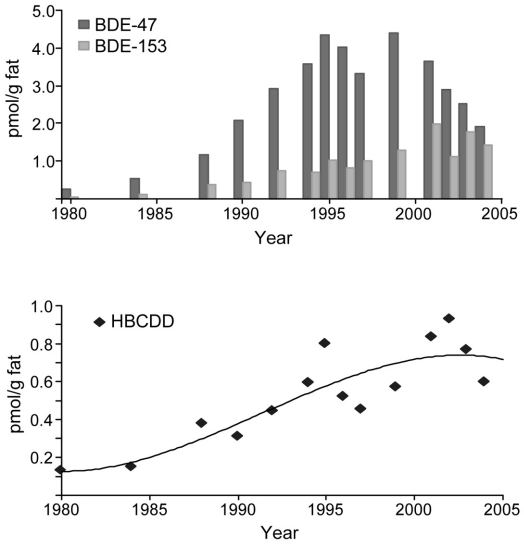


**Figure 1.** Temporal trend of BDE-47, BDE-153 (above) and HBCDD (below) concentrations in pmol/g fat in pooled milk samples from Sweden 1980 to 2004.

similar HBCDD concentrations were reported, ranging from 0.14 to 16 pmol/g fat [36]. The result shows that HBCDD are transferred to the milk and hence both persistent and bioaccumulative. However, it was beyond the scope of the present study to identify the isomer and enantiomer composition of the HBCDD in the mother's milk. Further, it was not yet possible to determine if the HBCDD levels have stabilized or are decreasing, a fact needing further attention.

It is worth commenting that the present study involves HBCDD quantification by GC/MS (ECNI), which has been claimed to be less reliable than LC/MS analysis [37, 38]. However, according to the procedure applied in this study we have chosen to report HBCDD concentration without isomer specific analysis, which is a prerequisite if GC/MS is applied. The analysis is performed by injection via an SPI to the GC column, which has shown no observable degradation of HBCDD (unpublished). In addition, standard dilution curves are always established prior to analysis of the analytes, including HBCDD. Further, the results presented for HBCDD in mother's milk are similar to other reports [38], strengthening the quantifications presented herein. Our results are supported by Petersen and coworkers [39] who have compared GC/MS methodology for analysis of HBCDD with LC/MS analysis for quantification. Their results show the usefulness also of GC/MS for quantification of HBCDD. Still, to enable isomer-specific analysis it is necessary to apply LC/MS. In addition, the LC/MS technique has to be performed by applying great care to avoid pitfalls related to this technique.

This study stresses the results from previous studies on PBDE in human milk from Stockholm, where the concentrations of the lower brominated PBDE, *i. e*. BDE-47, BDE-99 and BDE-100, were shown to decrease from the mid 1990's, after an increase from 1970 to 1995 (Table 1, Fig. 1) [13, 14]. Meanwhile, the concentrations of higher brominated PBDE, *i. e*. BDE-153 show increasing concentrations. The ratio BDE-153/BDE-47 (ng/g fat) in 1980 to 2004 has changed from 0.30 to 0.99. This is also in accordance with the previous study of human milk from Sweden where PBDE concentrations were studied until year 2000 [13, 14]. A higher influence of BDE-153 compared to BDE-47 on PBDE blood concentrations has also been seen in humans from USA, Norway, The Netherlands and the Faroe Islands [27, 40 – 43]. No such relation has been observed in the recent studies of PBDE in human milk from neither Australia [23] nor the USA [24]. The reason for the relative higher concentrations of BDE-153 may be due to a higher persistence of BDE-153 than of BDE-47. BDE-47 has been reported to metabolize to a large number of hydroxylated metabolites in mice and rats [44], and several of the corresponding metabolites have been identified in human blood plasma [45]. Far less metabolism is expected to occur for BDE-153 if relating it to compounds such as CB-153 and BB-153 that both are present at the highest concentration between PCB and polybrominated biphenyls (PBB), respectively. Possibly the change is influenced by the fact that PBDE products containing the lower brominated diphenyl ethers (PentaBDE and OctaBDE) are phased out, in Sweden on a voluntary basis over the last 10 – 15 years.

It is not possible to see any time trend for BDE-209 in the milk samples due to low and similar concentrations over the period studied. A similar result is shown by She *at al*. 2007 [24] with only low concentrations in human milk from Northwest Pacific in almost all subjects analyzed for BDE-209. The levels of tetraBDE-hexaBDE are in the expected concentration range in the milk from these mothers [24]. Previous studies on paired human milk and blood plasma samples showed that the BDE-153/BDE-47 ratio was lower in milk compare to blood, 28 and 67%, respectively [46]. This difference between milk and blood for BDE-153 has also been observed in Norwegian milk, where the relative amount of BDE-153 was lower in breast milk compared to serum [47]. Similar results have also been reported from the US where the partitioning between blood and milk was studied, and these data suggest that it may be easier for the less brominated congeners to move from blood to milk [48]. The transfer from blood to milk seems therefore less efficient for higher brominated diphenyl ethers than for the lower brominated diphenyl ethers. Therefore, serum seems to be a more suitable matrix for assessing human exposure to higher brominated diphenyl ethers, *i. e*. those with six bromine atoms or more. Still concentration of up to 3.4 pmol/g fat have been reported for BDE-209 in Faroese mother's milk [27], confirming that this compound can be transferred to the milk, but the overall conclusion is that BDE-209 in mother's milk is not a good indicator of BDE-209 exposure. This is an observation that is supported by

 

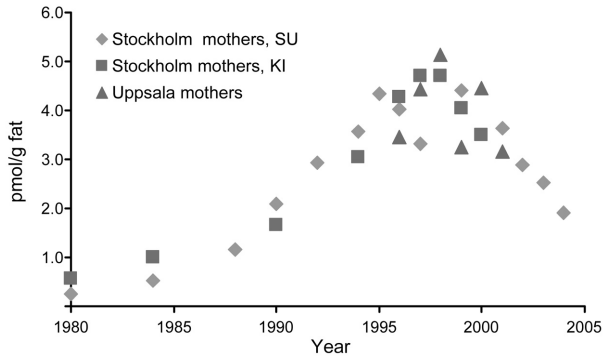


**Figure 2**. BDE-47 concentrations in human milk as determined in the present study and two previous studies performed in Sweden; among Stockholm mothers [13, 14] and Uppsala mothers [15].

the short apparent half-life of BDE-209 in humans [49]. A recent study on BDE-209 in cows and its poor transfer to the milk supports our results [50].

The PBDE concentrations in the pooled human milk samples in the present study are in close agreement with concentrations reported in previous studies on human milk from Sweden [13 – 15] (Fig. 2). Comparison of the results from the Stockholm mother's milk, where pooled samples have been used, with the results of milk from Uppsala mothers, for which individual samples were analyzed and median values are given, reveals very good agreement between the two studies (Fig. 2). To make long-time trend studies possible it is almost a prerequisite to use pooled samples to minimize the number of samples to be analyzed. The present data show rather good agreement between pooled and individual analysis [13 – 15, 27]. To some extent, the same pools were used in the present study and in previous studies by Meironyté and co-workers [13, 14]. The agreement between these studies is good although the extraction method, standards, analytical instrumentation and time of the analyses differ. When pooled samples are analyzed no individual variation is taken into account, therefore the composition of the pools is very important. All pools were prepared to be as comparable as possible, *e. g.* with 55 – 80% of the milk coming from mothers nursing their first infant. In the beginning of the 1980s, the number of mothers in each pool was about 100; thereafter from 1988 to 2004, only 15 – 20 mothers were included in each pool. The average age of the mothers was 27 – 31 years. Despite these rather similar requirements in the pools, there are differences between the pools, which may have some influence on the temporal trend.

Human milk is a good matrix for monitoring OHS in general, since it can provide exposure information about the mother and the breastfed infant through a non-invasive method of collection. On a weight basis, breast milk exposure for nursing infants is about six times higher than adult exposure via food. The benefits due to the optimal composition of the human milk to meet the nutritional needs early in life make the milk the best way to feed infants with regard to the healthy growth and development of the infant. WHO recommendation is indeed that infants should be breastfed [51].

In conclusion, the temporal trend of PBDE must be expressed on a congener basis since the fate of the individual PBDE congener concentrations differ. BDE-47, -99 and -100 concentrations reached a peak in the mid 1990's and are now clearly showing decreasing levels. BDE-153 concentrations increased until the year 2000 and thereafter the concentrations may level off but it is yet not clear how the concentrations of this PBDE congener will develop over the next few years. BDE-209 is not showing any temporal trend in mother's milk and likely is not a good indicator of BDE-209 exposure. HBCDD concentrations have increased approximately four times from 1980 to 2004. It is too early to judge if the levels are decreasing or leveling off for the HBCDD. The HBCDD concentrations are in a range between BDE-47, BDE-99 and BDE-100. HBCDD and the lower and medium brominated diphenyl ethers are transferred to a significant degree to the nursing baby via the milk.

*We like to express our gratitude to Anna Strid and Lotta Hovander for their valuable contributions to the present project. This study was financially supported by the Swedish EPA and Stockholm University.*

*The authors have declared no conflict of interest.*

## 5 References

[1] Örn, U., Bergman, Å., An attempt to assess the present commercial production of brominated flame retardants, *The Third International Workshop on Brominated Flame Retardants*, Toronto, Canada 2004, 467 – 472.

[2] Alaee, M., Arias, P., Sjödin, A., Bergman, Å., An overview of commercially used brominated flame retardants (BFRs) and their applications, changes in their use pattern in different countries/regions over time and possible modes of release, *Environ. Int.* 2003, *29*, 683 – 689.

[3] Andersson, Ö., Blomkvist, G., Polybrominated aromatic pollutants found in fish in Sweden, *Chemosphere* 1981, *10*, 1051 – 1060.

[4] Watanabe, I., Kashimoto, T., Tatsukawa, R., Polybrominated biphenyl ethers in marine fish, shellfish and river and marine sediments in Japan, *Chemosphere* 1987, *16*, 2389 – 2396.

[5] Kruger, C., (1988), Polybromierte Biphenyle und polybromierte Biphenylether-Nachweis und Bestimmung in ausgewählten Lebensmittel, Westfälischen Wilhelms Universität zu Münster, Münster, Germany.

[6] de Wit, C. A., Alaee, M., Muir, D. C. G., Levels and trends of brominated flame retardants in the Arctic, *Chemosphere* 2006, *64*, 209 – 233.

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

 

[8] Law, R. J., Allchin, C. R., de Boer, J., Covaci, A., *et al*., Levels and trends of brominated flame retardants in the European environment, *Chemosphere* 2006, *64*, 187 – 208.

[9] Schecter, A., Pavuk, M., Päpke, O., Ryan, J. J., *et al*., Polybrominated diphenyl ethers (PBDEs) in U.S. mothers' milk, *Environ. Health Perspect.* 2003, *111*, 1723 – 1729.

[10] Schecter, A., Paepke, O., Tung, K. C., Joseph, J., *et al*., Polybrominated Diphenyl ether flame retardants in the U.S. population: Current levels, temporal trends, and comparison with dioxins, dibenzofurans, and polychlorinated biphenyls, *JOEM*, 2005, *47*, 199 – 211.

[11] Birnbaum, L. S., Staskal, D. F., Brominated flame retardants: Cause for concern? *Environ. Health Perspect.* 2004, *112*, 9 – 17.

[12] Gill, U., Chu, I., Ryan, J. J., Feeley, M., Polybrominated diphenyl ethers: Human tissue levels and toxicology, *Rev. Environ. Contam. Toxicol.* 2004, *182*, 55 – 96.

[13] Meironyté, D., Norén, K., Bergman, Å., Analysis of polybrominated diphenyl ethers in Swedish human milk. A time-related trend study, 1972 – 1997, *J. Toxicol. Environ. Health Part A* 1999, *58*, 329 – 341.

[14] Meironyté Guvenius, D., Norén, K., Polybrominared diphenyl ethers in Swedish human milk. The follow-up study, *The Second International Workshop on Brominated Flame Retardants*, Stockholm, Sweden 2001, 303 – 305.

[15] Lind, Y., Darnerud, P. O., Atuma, S., Aune, M., *et al*., Polybrominated diphenyl ethers in breast milk from Uppsala county, Sweden, *Environ. Res.* 2003, *93*, 186 – 194.

[16] Fürst, P., Organochlorine pesticides, dioxins, PCB and polybrominated biphenylethers in human milk from Germany in the course of time, *Organohalogen Compounds* 2001, *52*, 185 – 188.

[17] Darnerud, P. O., Atuma, S., Aune, M., Cnattingius, S., *et al*., Polybrominated diphenyl ethers (PBDEs) in breast milk from primiparous women in Uppsala county, Sweden, *Organohalogen Compounds* 1998, *35*, 411 – 414.

[18] Kalantzi, O. I., Martin, F. L., Thomas, G. O., Alcock, R. E., *et al*., Different levels of polybrominated diphenyl ethers (PBDEs) and chlorinated compounds in breast milk from two U.K. Regions, *Environ. Health Perspect.* 2004, *112*, 1085 – 1091.

[19] Bi, X., Qu, W., Sheng, G., Zhang, W., *et al*., Polybrominated diphenyl ethers in South China maternal and fetal blood and breast milk, *Environ. Pollut.* 2006, *144*, 1024 – 1030.

[20] Eslami, B., Koizumi, A., Ohta, S., Inoue, K., *et al*., Large-scale evaluation of the current level of polybrominated diphenyl ethers (PBDEs) in breast milk from 13 regions of Japan, *Chemosphere* 2006, *63*, 554 – 561.

[21] Inoue, K., Harada, K., Takenaka, K., Uehara, S., *et al*., Levels and concentration ratios of polychlorinated biphenyls and polybrominated diphenyl ethers in serum and breast milk in Japanese mothers, *Environ. Health Perspect.* 2006, *114*, 1179 – 1185.

[22] Lopez, D., Athanasiadou, M., Athanassiadis, I., Estrade, L. Y., *et al*., A preliminary study on PBDEs and HBCDD in blood and milk from Mexican women., *The Third International Workshop on Brominated Flame Retardants*, Toronto, Canada 2004, 483 – 487.

[23] Toms, L. M., Harden, F. A., Symons, R. K., Burniston, D., *et al*., Polybrominated diphenyl ethers (PBDEs) in human milk from Australia, *Chemosphere* 2007, *68*, 797 – 803.

[24] She, J., Holden, A., Sharp, M., Tanner, M., *et al*., Polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) in breast milk from the Pacific Northwest, *Chemosphere* 2007, *67*, 307 – 317.

[25] UNEP, Ridding the world of POPs: A guide to the Stockholm convention on persistant organic pollutants, 2002.

[26] Sudaryanto, A., Kajiwara, N., Tsydenova, O., Iwata, H., *et al*., Global contamination of PBDEs in human milk from Asia, *Organohalogen Compounds* 2005, *67*, 1315 – 1318.

[27] Fängström, B., Strid, A., Grandjean, P., Weihe, P., Bergman, Å., A retrospective study of PBDEs and PCBs in human milk from the Faroe Islands, *Environmental Health: A global Access science source*, 2005, *4*; http://www.ejournal.net/content/4/1/12.

[28] Lunder, S., Sharp, R., Mothers' milk. Record levels of toxic fire retardants found in American mothers' breast milk, *Environmental Working Group*, 2004.

[29] Fuerst, P., Dioxins, polychlorinated biphenyls and other organohalogen compounds in human milk, *Mol. Nutr. Food Res.* 2006, *50*, 922 – 933.

[30] Law, R. J., Kohler, M., Heeb, N. V., Gerecke, A. C., *et al*., Hexabromocyclododecane challenges scientists and regulators, *Environ. Sci. Technol.* 2005, *39*, 281A – 287A.

[31] Remberger, M., Sternbeck, J., Palm, A., Kaj, L., *et al*., The environmental occurrence of hexabromocyclododecane in Sweden, *Chemosphere* 2004, *54*, 9 – 21.

[32] Ballschmiter, K., Mennel, A., Buyten, J., Long chain alkylpolysiloxanes as non-polar stationary phases in capillary gas chromatography, *Fresenius J. Anal. Chem.* 1993, *346*, 396 – 402.

[33] Marsh, G., Hu, J., Jakobsson, E., Rahm, S., Bergman, Å., Synthesis and characterization of 32 polybrominated diphenyl ethers, *Environ. Sci. Technol.* 1999, *33*, 3033 – 3037.

[34] Hovander, L., Athanasiadou, M., Asplund, L., Jensen, S., Klasson Wehler, E., Extraction and cleanup methods for analysis of phenolic and neutral organohalogens in plasma, *J. Anal. Toxicol.* 2000, *24*, 696 – 703.

[35] Weiss, J., Päpke, O., Bignert, A., Jensen, S., *et al*., Concentrations of dioxins and other organochlorines (PCBs, DDTs, HCHs) in human milk from Seveso, Milan and a Lombardian rural area in Italy: a study performed 25 years after the heavy dioxin exposure in Seveso, *Acta Paediatr.* 2003, *92*, 467 – 472.

[36] Lignell, S., Glynn, A., Darnerud, P. O., Aune, M., *et al*., Regional differences in levels of persistent organic pollutants in breast milk from primapara women in Uppsala. Göteborg, Lund and Lycksele (Sweden), SLV Report, 2005.

[37] Covaci, A., Voorspoels, S., Ramos, L., Neels, H., Blust, R., Recent developments in the analysis of brominated flame retardants and brominated natural compounds, *J. Chromatogr. A* 2007, *1153*, 145 – 171.

[38] Covaci, A., Gerecke, A. C., Law, R. J., Voorspoels, S., *et al*., Hexabromocyclododecanes (HBCDs) in the environment and humans: A Review, *Environ. Sci. Technol.* 2006, *40*, 3679 – 3688.

[39] Petersen, M., Hamm, S., Schäfer, A., Esser, U., Comparative GC/MS and LC/MS detection of hexabromocyclododecane (HBCD) in soil and water samples, *Organohalogen Compounds* 2004, *66*, 226 – 233.

 

[40] Fängström, B., Hovander, L., Bignert, A., Athanassiadis, I., *et al*., Concentrations of polybrominated diphenyl ethers, polychlonnated biphenyls, and polychlorobiphenylols in serum from pregnant Faroese women and their children 7 years later, *Environ. Sci. Technol.* 2005, *39*, 9457 – 9463.

[41] Johnson-Restrepo, B., Kannan, K., Rapaport, D., Rodan, B., Polybrominated diphenyl ethers and polychlorinated biphenyls in human adipose tissue from New York, *Environ. Sci. Technol.* 2005, *39*, 5177 – 5182.

[42] Thomsen, C., Liane, V., Froshaug, M., Becher, G., Levels of brominated flame retardants in human samples from Norway through three decades, *Organohalogen Compounds* 2005, 658 – 661.

[43] Weiss, J., Meijer, L., Sauer, P., Linderholm, L., *et al*., PBDE and HBCDD levels in blood from Dutch mothers and infants – Analysis of a Dutch Groningen infant cohort, *Organohalogen Compounds* 2004, *66*, 2677 – 2682.

[44] Malmberg, T., Athanasiadou, M., Marsh, G., Brandt, I., Bergman, Å., Identification of hydroxylated polybrominated diphenyl ether metabolites in blood plasma from polybrominated diphenyl ether exposed rats, *Environ. Sci. Technol.* 2005, *39*, 5342 – 5348.

[45] Bergman, Å., Athanasiadou, M., Fäldt, E., Jakobsson, K., Hydroxylated PBDE metabolites in human blood, *Organohalogen Compounds* 2006, *68*, 635 – 638.

[46] Meironyté Guvenius, D., Aronsson, A., Ekman-Ordeberg, G., Bergman, Å., Norén, K., Human prenatal and postnatal exposure to polybrominated diphenyl ethers, polychlorinated biphenyls, polychlorobiphenylols and pentachlorophenol, *Environ. Health Perspect.* 2003, *111*, 1235 – 1241.

[47] Thomsen, C., Froshaug, M., Broadwell, S., Becher, G., Eggesbo, M., Levels of brominated flame retardants in milk from the Norwegian human milk study: HUMIS, *Organohalogen Compounds* 2005, 509 – 512.

[48] Schecter, A., Papke, O., Harris, T. R., Tung, K. C., Partitioning of polybrominated diphenyl ether (PBDE) congeners in human blood and milk, *Toxicol. Environ. Chem.* 2006, *88*, 319 – 324.

[49] Thuresson, K., Höglund, P., Hagmar, L., Sjödin, A., *et al*., Apparent half-lives of hepta- to decabrominated diphenyl ethers in humans as determined in occupationally exposed workers, *Environ. Health Perspect.* 2006, *114*, 176 – 181.

[50] Kierkegaard, A., Asplund, L., de Wit, C. A., McLachlan, M. S. *et al*., Fate of higher brominated PBDEs in lactating cows, *Environ. Sci. Technol.* 2007, *41*, 417 – 423.

[51] WHO, *Global strategy for infant and young child feeding*, 2003, pp. 1 – 30, ISBN 92 4 156221 8.

 