Analysis of new brominated flame retardants in human serum and background air

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PÅ UPPDRAG AV
NATURVÅRDSVERKET

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Summary

As an assignment from the Swedish Environmental Protection Agency, a screening study of selected emerging brominated flame retardants (BFRs) has been carried out. The study build on an earlier screening study including most of the target analytes "Screening of Emerging Brominated Flame Retardants and Polybrominated dibenzofurans". In the cited study many of the analytes were not detected possibly due to low concentrations in relation to the instrumental detection limits.

In the current study a more sensitive mass spectrometric technique Gas Chromatography - High Resolution Mass Spectrometry (GC-HRMS) was used to improve the detection frequency. In addition, five more emerging BFRs that have been highlighted in a recent European Food Safety Authority report were also included.

The overall objective of this screening study was to determine the concentrations of selected BFRs and a group of well-known BFRs, polybrominated diphenyl ethers (PBDEs), in ambient air and in human serum, to highlight an important global transport pathway in the environment and the degree of human exposure, respectively.

Most of the emerging flame retardants occurred in all of the air samples. The mean concentration of several emerging flame retardants (TBECH, HBB, BEH-TEBP, BTBPE, DBDPE, and Dechlorane Plus) was between 10% and 60% of that of BDE-209, the most abundant PBDE.

The mean concentrations of the brominated phenols were generally higher than BDE-209. The concentrations of monobromo phenols and 2,4-dibromophenol were at least an order of magnitude higher than BDE-209, whilst 2,4,6-Tribromophenol was 4-fold higher than BDE-209.

The emerging FRs, brominated phenols and PBDEs all occurs at elevated concentrations during the summer period in Pallas in Northern Finland, which illustrates the potential for atmospheric long range transport and the positive influence of temperature on contaminant mobility.

The brominated phenols also showed a temporal trend at the Swedish West Coast site Råö, with elevated concentrations in the summer/autumn period, possible linked to increased natural production and emissions of these compounds during the summer period.

Three of the emerging BFR were detected in human sera. Bis(2,4,6-tribromophenoxy)-ethane (BTBPE) was found in all samples and at an average concentration higher than that of BDE-209. Pentabromoethylbenzene (PBEB) and 2-ethylhexyl 2,3,4,5-tetrabromo-benzoate (EH-TBB) were found in roughly half of the samples. The levels of brominated phenols was much higher than those of BDE-209, with 2,4,6-tribromophenol as the most abundant, likley due to high metabolic resistance.

Sammanfattning

På uppdrag av Naturvårdsverket har en screeningstudie av utvalda "nya" bromerade flamskyddsmedel (BFR) genomförts. Studien bygger på en tidigare studie inkluderande de flesta av flamskyddsmedlen "Screening av Emerging bromerade flamskyddsmedel och polybromerade dibensofuraner". I denna studie kunde många ämnen inte detekteras, möjligen på grund av låga koncentrationer i förhållande till de instrumentella detekteringsgränserna.

I den aktuella studien har en känsligare masspektrometrisk teknik gaskromatografi - högupplöst masspektrometri (GC-HRMS) använts för att förbättra detektionsfrekvensen. Dessutom har ytterligare fem nya BFR inkluderats, baserat på en nyligen publicerad rapport från Europeiska myndigheten för livsmedelssäkerhet.

Det övergripande målet för denna screeningundersökning var att bestämma halterna av de utvalda nya bromerade flamskyddsmedlen samt en grupp välkända flamskyddsmedel (polybromerade difenyletrar, PBDE) i luft från bakgrundsområden och i humant serum, vilket bör ge en bättre bild av den globala långväga lufttransporten samt en uppfattning av graden av människors exponering.

De flesta av de nya flamskyddsmedlen påträffades i samtliga luftprover. Medel-koncentrationen av flera nya flamskyddsmedel (TBECH, HBB, BEH-TEBP, BTBPE, DBDPE och Dechloran Plus) var relativt höga, mellan 10 % och 60 % av koncentrationen av dekabromdifenyleter (BDE-209), den PBDE som uppmättes i högst halt.

De genomsnittliga koncentrationerna av de bromerade fenolerna var i allmänhet högre än den för BDE-209. Koncentrationen av monobromfenoler och 2,4-dibromfenol var minst en storleksordning större än den för BDE-209, medan koncentrationen av 2,4,6-tribromfenol var fyra gånger högre.

Halterna av de nya flamskyddsmedlen, de bromerade fenolerna och PBDE var alla förhöjda under sommarperioden i Pallas i norra Finland, vilket visar på dess potential för atmosfärisk långväga spridning och att denna ökar med ökande temperatur.

De bromerade fenolerna visade också en tidstrend i luft från Råö på den svenska västkusten, med förhöjda halter under sommar och höst, eventuellt kopplade till ökad naturlig marin produktion och ökade emissioner av dessa föreningar under denna period.

Tre nya BFR detekterades i humant blod (sera). Bis(2,4,6-tribromfenoxy)etan (BTBPE) hittades i alla prover och med en genomsnittskoncentration högre än den för BDE-209. Pentabrometylbensen (PBEB) och 2-etylhexyl 2,3,4,5-tetrabrombensoat (EH-TBB) hittades i ungefär hälften av proverna.

De bromerade fenolerna påträffades också i sera och deras koncentrationer var mycket högre än den för BDE-209. 2,4,6-tribromfenol förekom i högst halt, troligen på grund av hög stabilitet mot metabolisk omvandling.

Contents

1 Introduction

As an assignment from the Swedish Environmental Protection Agency, a screening study of selected emerging pollutants, brominated flame retardants (BFRs), has been carried out. The established pollutants polybrominated diphenyl ethers (PBDEs) were also included for comparison purposes.

The study build on an earlier screening study including most of the target analytes "Screening of emerging brominated flame retardants and polybrominated dibenzofurans" (IVL Report B2110, 2013). In the cited study many of the analytes were not detected, possibly due to low concentrations in relation to the instrumental detection limits. In the current study a more sensitive mass spectrometric technique Gas Chromatography - High Resolution Mass Spectrometry (GC-HRMS) was used to improve the detection frequency. In addition, five more emerging BFRs that were highlighted in a recent European Food Safety Authority report were included.

This follow up study has been focused on air and human serum samples. Air samples were taken over a full year at two locations (Råö, Swedish West Coast and Pallas, Northern Finland) and the serum samples included 15 samples from Swedes of various age and sex. The study was designed to generate information about the temporal variability in BFR concentrations and how it is related to different source regions and, also, to give an estimate of the general populations exposure to new BFRs.

2 Background: Substances in the screening, properties, sources
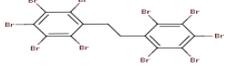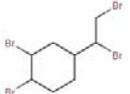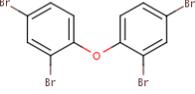
2.1 Brominated flame retardants (BFRs)

Brominated flame retardants (BFRs) are used to reduce the flammability in many products, including furniture, building materials and electronics. BFRs are expected to be emitted to the environment during the production or use-phase of goods and products.

Polybrominated diphenyl ethers (PBDEs) have previously been used in high volumes but due to their ubiquitous environmental presence and potential toxicities PentaBDE and OctaBDE have been banned in EU (EG 850/2004). All PBDEs have been banned in electronic equipment in EUs, RoHS directive. The phase out of PBDEs has led to an increasing number of alternative flame retardant chemicals.

Recently the occurrence of "new" brominated flame retardants (BFRs) in environmental samples from the Nordic countries has been investigated (Schlabach., 2011). The overall results of this Nordic screening showed that emerging brominated flame retardants were regularly found in many different sample matrices indicating a widespread use of these substances in the Nordic countries but there were geographical differences and differences in the environmental occurrence among substances and groups of substances.

Most BFRs selected for this screening were frequently found in biota in the previous Nordic and Swedish EPA screening studies. The substances included in the previous Swedish EPA screening are presented in **Table 1** with abbreviations, CAS-number and structure. The novel abbreviations recommend by Bergman *et al.*, 2012 are also included.

Table 1. Substances selected for the study based on a previous study (Name, CAS #, practical and structural abbreviation *(EFSA 2012)*, structure).

Compound name, CAS # Practical abbreviation Structured abbreviation	Structure
Hexabromobenzene CAS 87-82-1 HBB HxBBz	
Pentabromotoluene CAS 87-83-2 PBT PeBT	
Pentabromoethylbenzene CAS 85-22-3 PBEB PeBEtBz	
Decabromodiphenyl ethane CAS 84852-53-9 DBDPE DBDPEiPhEt	
1,2-Dibromo-4-(1,2-dibromoethyl)cyclohexane CAS 3322-93-8 TBECH (BDE-DBCH)* DiBEt-DiBcH	
2,2´,4,4´-Tetrabromodiphenyl ether CAS 5436-43-1 BDE-47	
2,2′,4,4′,5-Pentabromodiphenyl ether CAS 32534-81-9 BDE-99	
2,2′,4,4′,6- Pentabromodiphenyl ether CAS 189084-64-8 BDE-100	
2,2′,4,4′,5′,5′-Hexabromodiphenyl ether CAS 68631-49-2 BDE-153	
Decabromobiphenyl ether CAS 1163-19-5 BDE-209 (decaBDE)	
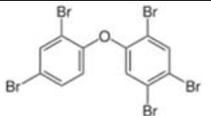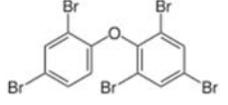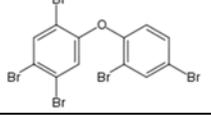
*The abbreviation BDE-DBCH is suggested by Bergman et al 2012; however TBECH is used in this report

In addition, five more emerging BFRs were included (**Table 2**) based on the European Food Safety Authority (EFSA) Scientific Opinion on Brominated Flame Retardants (BFRs) in Food: Brominated Phenols and their Derivatives (EFSA, 2012a) and Scientific Opinion on Emerging and Novel Brominated Flame Retardants (BFRs) in Food (EFSA, 2012b).

Table 2. Substances selected for the study based on European Food Safety Authority (EFSA) reports (Name, CAS #, practical and structural abbreviation *(EFSA 2012)*, structure).

Compound name, CAS # Practical abbreviation Structured abbreviation	Structure
2,4,6-tribromophenol CAS 118-79-6 TBP 2,4,6-TriBP	
Pentabromophenol CAS 608-71-9 PBP	
Bis(2-ethylhexyl) tetrabromophthalate CAS 26040-51-7 BEH-TEBP BEHTBP	
1,2-Bis(2,4,6-tribromophenoxy)ethane CAS 37853-59-1 BTBPE	
2-Ethylhexyl 2,3,4,5-tetrabromobenzoate CAS 183658-27-7 EH-TBB	
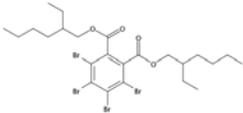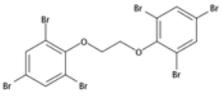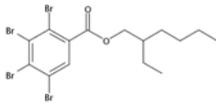
The standard mixtures used for quantification also contained syn- and anti-Dechlorane Plus, two polybrominated biphenyls (PBB-153 and PBB-209) and mono-and dibrom-phenols. Those were easily detected in the air samples and therefore also included in the quantification.

2.2 Properties, pathways and occurrence

In reports by Harju *et al.* (2008) and EFSA (2012a, 2012b) the emerging BFRs have been reviewed thoroughly. Basic physical and chemical properties are given in **Table 3**.

Hexabromobenzene (HBB), pentabromotoluene (PBT) and pentabromoethylbenzene (PBEB) have similar chemical structure and properties such as vapour pressure (Vp) and lipophilicity (log K_{ow}), **Table 3**. The low water solubility and vapour pressure and high log K_{ow} of HBB, PBT and PBEB give these chemicals a high affinity to particles in the environment. The reference substances BDE-47, BDE-99 have somewhat lower Vp and higher log K_{ow} compared to HBB, PBT and PBEB.

HBB is a fully aromatic perbrominated substance. It may undergo nucleophilic aromatic substitution with strong nucleophiles and reductive debromination under environmental conditions. PBT is a stable aromatic substance that may undergo reductive debromination in the environment. It may also be an environmental transformation product of tetrabromobisphenol A (TBBPA) and other BFRs, such as decabromodiphenylethane (DBDPE) (Møskeland, 2010). PBEB is regarded as persistent in the environment, although it may undergo reductive and photolytic debromination. In the OSPAR list of chemicals it is ranked as persistent, liable to be bioaccumulative and toxic (OSPAR, 2011).

Table 3. Properties of the BFRs included in the screening

Compound	Vapour pressure (Torr)	Water solubility (μg/L)	Log K_{ow}	Ref.
TBECH	2.2×10^{-5}	69	4.82	EFSA, 2012b
PBT	4.5×10^{-6}	0.94	6.25	EFSA, 2012b
PBEB	1.2×10^{-6}	47	6.76	EFSA, 2012b, OEHHA, 2008
HBB	8.5×10^{-7}	0.16	6.11	EFSA, 2012 (Vp, logKow) ChemIDPlus (Water sol.)
EH-TBB	2.78×10^{-9}	0.011	7.73	EFSA, 2012b, OEHHA, 2008
BEH-TEBP	1.16×10^{-13}		9.34	EFSA, 2012b
BTBPE	2.91×10^{-12}	200	8.31	EFSA, 2012b, OEHHA, 2008
DBDPE	6.0×10^{-15}	0.00021	11.1	EFSA, 2012b
TBP	1.50×10^{-3}	61 000	4.40	EFSA, 2012a, Kuramochi, 2003
PBP	1.91×10^{-5}	123	5.22	EFSA, 2012a, Kuramochi, 2003
BDE-47	1.9×10^{-6}	11	6.81	EPA (1)
BDE-99	3.8×10^{-7}	2.4	6.5-8.4	EPA (2)
BDE-209	3.5×10^{-8}	<0.1	6.3–12.6	EPA (3)

OHHA, 2008: http://oehha.ca.gov/multimedia/biomon/pdf/120408flamedoc.pdf
ChemIDPlus. http://chem.sis.nlm.nih.gov/chemidplus/
EPA (1) http://www.epa.gov/iris/toxreviews/1010tr.pdf
EPA (2) http://www.epa.gov/iris/toxreviews/1008tr.pdf
EPA (3) http://www.epa.gov/iris/toxreviews/0035tr.pdf

HBB, PBT and PBEB have frequently been found in different environmental matrices such as air, water, sediment, aquatic biota and wildlife as well as in indoor air, dust and in samples from waste water treatment plants (WWTPs) (Schlabach *et al.*, 2011, EFSA, 2012b). The highest ambient air concentrations occur close to source areas (urban areas) but these chemicals are also found in background air. Their occurrence at remote sites in the Arctic shows that they are stable enough to be transported over long distances and that the atmosphere can act as an important environmental pathway. Their occurrence in biota from background areas also indicates that these substances have bioaccumulation potential. HBB has also been detected in human milk (Fujii, *et al.*, 2012) and blood serum) (IVL Report B2110, 2013).

Decabromodiphenyl ethane (DBDPE) has experimentally been shown to undergo debromination and thermal transformations (Kierkegaard *et al.,* 2009). This substance is like

HBB, PBT and PBEB frequently found in several environmental media as well as in indoor air, dust and sludge samples. The occurrence in Swedish background air indicates that it will undergo atmospheric long range transport. DBDPE like BDE-209 exists in the atmosphere almost exclusively in the particle phase and their atmospheric transport will be determined by the transport behaviour of the particle they are attached to.

1,2-Dibromo-4-(1,2-di-bromo-ethyl)cyclohexane (TBECH) can exist as four pairs of enantiomers. Technical TBECH has a near 1:1 relationship between the α- and β-diastereomers (Tomy *et al.,* 2008). At temperatures above 120 ºC, some thermal conversion of the α- and the β- isomers can occur, resulting in formation of γ- and δ-isomers. TEBCH has been detected in different biota samples and it was also found in air in the Nordic screening study (Schlabach *et al.,* 2011).

The three additional neutral compounds in this study (BEH-TEBP, BTBPE and EH-TBB) have similar physic-chemical properties to the highly brominated PBDEs and are used in similar applications (replace PBDE formulations). All three has been detected in indoor air and dust, ambient air, sediment/sludge, and biota (Schlabach *et al.,* 2011; EFSA, 2012).

The last two compounds, TrBP and PBP, are both relatively small phenolic compounds. Consequently, these have higher volatility and water solubility and lower log K_{ow} values than the other compounds in the study.

2.3 Production and use

HBB, PBT, PBEB, DBDPE and TBECH are all used as additive flame retardants. PBT, PBEB and DBDPE are listed as LPV chemicals (low production volume) in the European Chemical Substances Information System (ESIS, 2012). (LPV: 10 - 1000 tonnes produced or imported annually).

HBB and PBT have generally been used as flame retardants in e.g. polymers, plastics, textiles, wood, and paper as well as in electronic devices (Xie *et al.,* 2011). The use of HBB in Japan between 1994 and 2001 has been reported to be 350 tons per. HBB is not reported to be produced in Europe (EFSA, 2012b). PBT is mainly used in unsaturated polyesters (OECD, 1995), polyethylene, polypropylene, polystyrene, SBR-latex, textile, rubbers and ABS with a global production volume estimated to between 1 000 and 5 000 tonnes annually.

PBEB has been reported to be used as an additive flame retardant in unsaturated polyesters, styrene butadiene copolymers and in other textiles but also in circuit boards, adhesives, wire and cable coatings and polyurethane foam (WHO/ICPS, 1997; Hoh *et al.,* 2005).

There is no information about the Swedish usage of HBB, PBT, and PBEB in chemical products (KemI-Stat, 2012).

DBDPE is an additive flame retardant which was introduced more than twenty years ago and that has similar applications as DecaBDE and it has been marketed as general purpose substitute for DecaBDE. It is used in applications such as plastics (including polyester and vinyl ester resins, rubber products and in different applications related to manufacture of textiles and leather. The compound is also used in polymers for electronic and electrical applications. DBDPE could also be used in adhesives and sealants. The use of DBDPE in chemical products in Sweden according to the Swedish Chemical product register was during 2006 and 2008-2013 between 5 and 40 tonnes annually (KemI-stat, 2012) (Figure 1). The information for other years is confidential. The number of chemical preparations has increased in recent years (**Figure 1**).
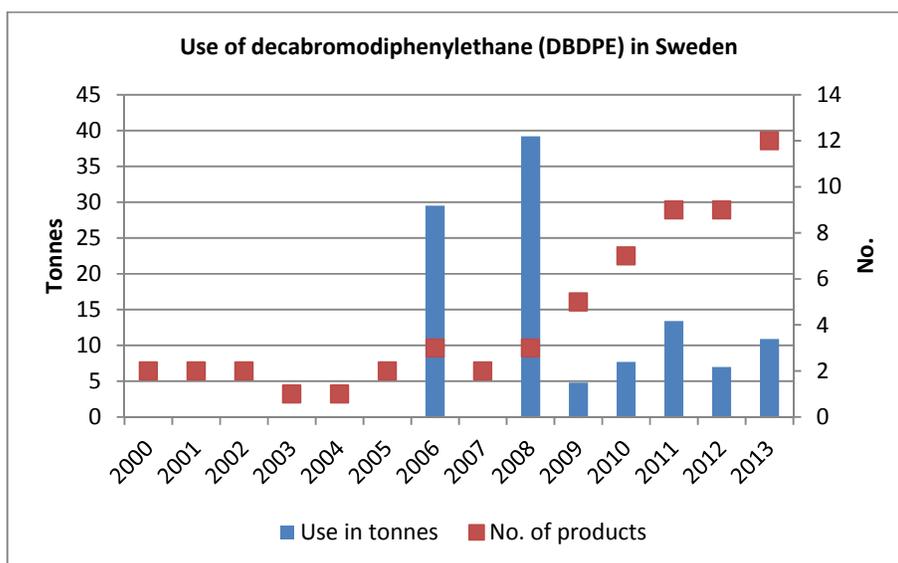
Figure 1. Use of decabromodifhenylethane (DBDPE) in number of chemical preparations and in tonnes (KemI-stat, 2013). Information on usage 2000-2005 and 2007 in Sweden is confidential.

TBECH (DBE-DBCH) is marketed as Saytex BCL-462. This material is primarily used as an additive flame retardant in expandable polystyrene beads, which are largely used to produce thermal insulation for housing. Concentrations of TBECH in these products are about 1% (Tomy *et al.,* 2008). TBECH is also used in polystyrene foam, in adhesive in fabric and vinyl lamination, electric cable coatings etc. There is no information about the use of TBECH in chemical products in Sweden (KemI-Stat, 2012).

BEH-TEBP and EH-TB are major constituents of Firemaster 550, used as a replacement for PentaBDE in polyurethane foam applications, and of Firemaster BZ-54 (EFSA, 2012). BEH-TEBP is used in Sweden, but in low quantities (up to 0.5tonnes) (KemI-Stat, 2013). BTBPE is used as a replacement for OctaBDE. It is classified as a low product volume chemical in EU (EFSA, 2012b) but there is no information about the current Swedish usage of BTBPE and EH-TB in chemical products (KemI-Stat, 2013).

TrBP and PBP are used as flame retardants but are also present as impurities in other BFR formulation. TrBP is also produced naturally in the marine environment.

3   **Sampling program**

Samples were selected based on the results of the previous Swedish EPA screening of new BFRs (IVL report B2110, 2013).

The measurements in air were undertaken to get background concentrations and to identify the importance of atmospheric long range transport. The air measurements were carried out at two background sites, Råö, an EMEP (co-operative programme for monitoring and evaluation of the long-range transmission of air pollutants in Europe) station at the Swedish West Coast, and Pallas, a remote station in northern Finland within AMAP (Arctic Monitoring Assessment Programme). The measurements were co-ordinated with the Swedish Monitoring Programme for Air Pollutants. In order study the seasonal variation in air concentrations, six monthly samples were taken over a year (Table 4).

Table 4. Sampling programme for BFRs in air

Number[a]	IVL no.	Sample	Start	Stopp	Volyme, m^3
1	Ra L 2013-11	Air, Råö	2013-10-28	2013-12-02	10335
2	Ra L 2014-01	Air, Råö	2013-12-28	2014-01-27	6999
3	Ra L 2014-02	Air, Råö	2014-01-27	2014-03-03	8455
4	Ra L 2014-04	Air, Råö	2014-03-31	2014-04-28	4999
5	Ra L 2014-06	Air, Råö	2014-05-26	2014-06-30	4060
6	Ra L 2014-08	Air, Råö	2014-07-28	2014-09-01	9351
7	PA L 2013-11	Air, Pallas	2013-10-28	2013-12-02	10340
8	PA L 2014-01	Air, Pallas	2013-12-30	2014-01-27	5968
9	PA L 2014-02	Air, Pallas	2014-01-27	2014-03-03	10191
10	PA L 2014-04	Air, Pallas	2014-03-31	2014-04-28	5110
11	PA L 2014-06	Air, Pallas	2014-05-26	2014-06-30	13527
12	PA L 2014-08	Air, Pallas	2014-07-28	2014-09-01	9924

[a] Umeå lab code 3671:xx.

Possible human exposure was investigated by reanalysing 15 human serum samples (Table 5).

Table 5. Sampling programme for BFRs in human serum

Number[a]	IVL no.	Site	Date	Stopp	Amount, g
13	1491	Human serum	Female, age 36	2012-06-12	8.505
14	1492	Human serum	Female, age 55	2012-06-12	7.482
15	1493	Human serum	Female, age 60	2012-06-12	7.511
16	1494	Human serum	Female, age 43	2012-06-12	7.897
17	1495	Human serum	Male, age 58	2012-06-12	5.692
18	1496	Human serum	Male, age 28	2012-06-12	6.464
19	1497	Human serum	Female, age 47	2012-06-12	8.038
20	1498	Human serum	Male, age 37	2012-06-12	7.319
21	1499	Human serum	Male, age 40	2012-06-12	7.684
22	1500	Human serum	Male, age 42	2012-06-12	6.771
23	1501	Human serum	Male, age 30	2012-06-12	6.204
24	1502	Human serum	Female, age 46	2012-06-12	4.428
25	1503	Human serum	Male, age 59	2012-06-12	6.896
26	1577	Human serum	Male, age 41	2012-06-28	6.389
27	1578	Human serum	Male, age 62	2012-06-28	5.603

[a] Umeå lab code 3671:xx.

4 **Methods**

4.1 Sampling

The outdoor air samples were collected using a high volume air sampler (HVS). A glass fibre filter (GFF) was used for trapping the particles followed by an adsorbent of polyurethane foam (PUF) for collecting compounds in the gas phase. The air sampling was carried out weekly and sample extracts were combined to represent longer time periods. The approximate air flow was 26 m^3/hour. All samples were stored at -18 ºC until analyses.

Venous blood was sampled from healthy volunteers using evacuated tubes containing acrylic gel and a spray-dried trombin based clot activator coating (Vacutainer 368498, BD Diagnostics). After centrifugation the serum was stored in polypropylene tubes in freezer.

4.2 Analysis of BFRs

4.2.1 Chemicals and materials

The reference compounds and ^{13}C-labelled internal standards were obtained from Cambridge Isotope Laboratories (CIL) and Wellington Laboratories. GFF were burned at 400°C for 8 h and PUF adsorbents were pre-extracted in a Soxhlet apparatus before use.

4.2.2 Sample extraction

Air samples were extracted in accordance with the methods used in the monitoring program for air pollutants. The samples (PUF-plugs and filters) were Soxhlet extracted with acetone for 24±2 hours. Extracts from the adsorbent and filter were combined and divided for determination of the different substance groups. The final extract was spiked with an internal standard mixture.

Human serum samples were spiked with internal standards and homogenized in a vortex mixer. The extraction was the performed according to Hovander *et. al.* (2000).

4.2.3 Sample cleanup

The extracts were split 75:25 for analysis of neutral and phenolic compounds, respectively. The neutral compounds were fractionated on silica gel as described by Sahlström *et al.* (2012). Non-polar compounds were recovered in the first fraction eluted with *n*-hexane and moderately polar compounds in the second, eluted with 5% ethyl ether (DEE) in *n*-hexane. The first fraction was used for non-polar compounds and the second for moderately polar compounds (EH-TBB, BEH-TEBP and BTBPE). The phenolic fraction was partitioned with NaOH solution, acetylated with acetic acid anhydride, acidified with HCl, and back-partitioned to *n*-hexane (Liljelind *et al.*, 2003). Before instrumental analysis the extracts were concentrated to between 100 and 500 µl.

4.2.4 Instrumental analysis

Analyis were performed using gas chromatography – high resolution (≥10 000) mass spectrometry (GC-HRMS) with electron ionization and selected ion recording (SIR). A long GC column was used for most compounds to obtain good separation (Agilent DB5-MS; 60 m x 0.25 mm i.d., 0.25 µm film). However, a short GC column (DB5-MS; 15 m x 0.25 mm i.d., 0.1 µm film) was used to elute high boiling BFRs in a reasonable time and to avoid thermal decomposition.

The injection was made in pulsed splitless mode at 250°C. Helium was used as carrier gas at a flow rate of 1.2 mL/min. The transfer line was held at 280°C.

The instrument linearity was checked with a six point calibration curve. Once linearity was demonstrated, quantifications were done using a single-point calibration. Quantifications were performed by the isotope dilution technique, using ^{13}C-labelled internal standards.

4.2.5 Quality control

When performing environmental screening all steps in the study such as selection of sampling site, sampling frequency, time of sampling, performing of sampling, transport and storage of samples, chemical analysis and data treatment are generating some degree of uncertainty. To quantitatively estimate the contribution of all steps is an extremely difficult task or not possible at all. However, we will discuss the relevance of key contributors in a qualitative way.

One important question is whether a sample is representative for a given time period or a given region. Many of the selected compounds are intermittently emitted to the environment and a constant concentration of these compounds in the environment is not expected. To increase the representativeness of the air samples were time-integrated over long periods.

The uncertainty of the chemical analysis is governed by loss during extraction and clean-up, interference from other compounds, trueness of analytical standards, instrumental parameters, and contamination. Blanks were run in paralell to samples to estimate the degree of field and laboratory background. The background was generally low and no background correction was made. There was however a relatively high background of HBB, which had to be corrected for the air samples (and prevented reliable quantification of serum samples).

The following quality criteria were used to ensure correct identification and quantification of the target compounds: (a) the retention times should match those of the standard compounds within ± 0.05 min., (b) the intensity ratios of the selected SIR ions should be within ± 15 % of that observed for the standard compounds (c) the signal-to-noise ratios should be greater than 3:1.

4.2.6 Air tracectories

Trajectory plots from NILU (http://www.nilu.no/projects/ccc/trajectories/[1]) were used to evaluate the travel path of air masses with the arrival at Pallas and Råö. Trajectory plots were made four times a day (0:00, 6:00, 12:00 and 18:00) for each location. Each trajectory spans 1 week. Separate trajectories were generated for three different heights at arrival site (500, 1000 and 1500 m above sea level (asl)). In this project trajectories with a span of 72 hours back in time were generated for Råö and Pallas; to minimise the uncertainties of the origin of the air masses. The longer time span the more uncertain origin of the air masses. Example of trajectory plots from Råö and Pallas are given in **Figure 2.**

Air mass trajectories are calculated using the Flextra model developed by NILU in cooperation with Institute of Meteorology and Geophysics, Wienna and using meteorological data provided from ECMWF (European Centre for Medium Range Weather Forcast).
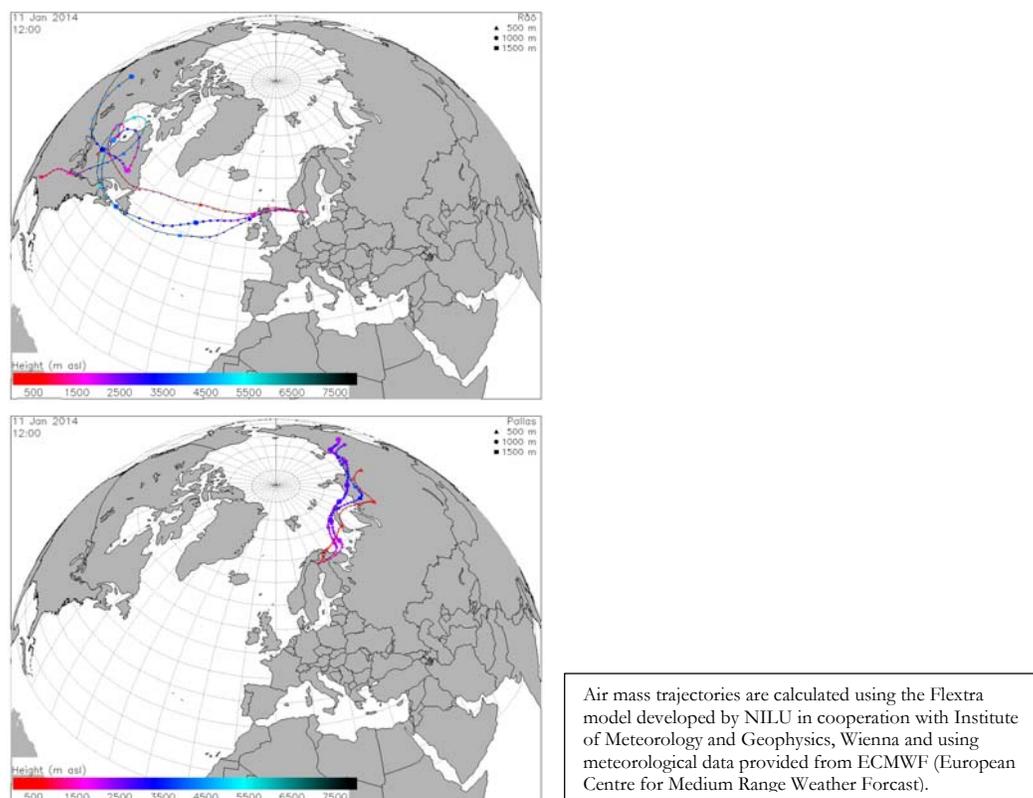
Figure 2. Examples of trajectory plot, Råö (left) and Pallas (right) 2014-01-11 (nilu.no)

The trajectory analyses generated approximately 110-140 plots for each sampling period and site. The origin of the air masses and theirs travel path for each period were divided in eight sectors arrange by the sectors of the compass (N, NE, E, SE, S, SW, W and NW). For each sector, the origin of the air masses were compiled showing the total amount of occasions with air mass transport from a specific sector at height of 500, 1000 and 1500 m asl at the arrival site and presented in form of radar chart plots. The radar chart plots for each sampling period were then used to summarize the prevailing wind patterns for each of the six sampling periods.

5 Results

An overview of the detection frequencies, *i.e.* the fraction of samples where a substance was found in a concentration above the limit of detection (LOD) for air and serum matrices are given in **Table 6**.

Table 6. Detection frequencies (%) of individual FRs in air and serum samples.

Matrix	Air	Serum
No of samples:	*12*	*15*
TBECH	100%	ND (1)
PBT	100%	ND (1)
PBEB	100%	41%
HBB	100%	NQ
EH-TBB	100%	35%
BEH-TEBP	92%	ND (5)
BTBPE	100%	100%
DBDPE	83%	ND (20)
TBP	100%	100%
PBP	100%	100%
syn-DP	100%	NA
anti-DP	100%	NA
BDE-28	100%	100%
BDE-47	100%	100%
BDE-99	100%*	100%
PBE-100	100%*	100%
BDE-153	100%	100%
BDE-154	100%	100%
BDE-183	100%	87%
BDE-196	100%	100%
BDE-206	100%	100%
BDE-209	100%	100%
PBB-153	100%	NA
PBB-209	100%	NA

* Not quantified in 5 samples due to interferences.
ND (x): Below the limit of detection (x pg/g). NQ: Not quantified. NA: Not analyzed.

All analytes were found with high detection frequencies in the ambient air samples. BEH-TEBP and DBDPE were below the limits of detection (LOD) in one and two samples, respectively. In five samples BDE-99 and BDE-100 were detected, but not possible to quantify; due to interferences in the chemical analysis.

The PBDEs and brominated phenols were also found in almost all human serum samples. The sole exception was BDE-183 that was detected in all samples but two. PBEB and EH-TEBP was detected in little less than half of the samples. The other emerging BFRs were either below the LOD or could not be quantified due to elevated blank levels (HBB).

In the following, the concentrations found are presented in more detail.

5.1 Air samples

5.1.1 Concentrations

The geometrical mean concentrations of the target analytes are summarized in **Figure 2** and the individual values are given in Tables 7-9.

BDE-209 was the most abundant PBDE in the ambient air samples, followed by BDE-47 and BDE-99. The levels of PBDEs at Råö and Pallas were normal during these sampling occasions when compared to data in the monitoring program (www.ivl.se).

The mean concentration (fg/m^3) of many of the neutral emerging FRs (TBECH, HBB, BEH-TEBP, BTBPE, DBDPE, and syn/anti-DP) was within one order of magnitude of that of BDE-209. DBDPE was closest in concentration (89 fg/m^3) to that of BDE-209 (153 fg/m^3), followed by α-TBECH, BTBPE, and β-TBECH at 59 fg/m^3, 51 fg/m^3, and 43 fg/m^3. The mean concentrations of the monocyclic aromatic BFRs were relatively low (3-9 fg/m^3), with the exception for HBB (40 fg/m^3).

DBDPE and BDE-209 have previously been measured in Swedish ambient air by Egebäck *et al.* (2012) and who found concentration of DBDPE and BDE-209 in the ranges 77-7900 and 93-1800 fg/m^3, respectively. The mean concentrations detected in air in the current study falls within these ranges.

In a recent study, Newton *et al.* (2015) reported Stockholm air concentrations of emerging and established BFRs. The geometric mean concentrations were as follows: Total TBECH 480 fg/m^3, PBT 160 fg/m^3, HBB 62 fg/m^3, EH-TBB 120 fg/m^3, BTBPE 130 fg/m^3, DBDPE 150 fg/m^3, and BDE-209 140 fg/m^3. Those emerging BFR concentrations are higher than the concentrations found in the current study, from 1.5-fold (HBB) to 33-fold (PBT), which is to expect for an urban area.

The concentrations of the brominated phenols were all relatively high. The monobromo-phenols and 2,4-dibromophenol were all at least an order of magnitude higher than BDE-209. 2,4,6-Tribromophenol was 4-fold higher than BDE-209. PBP was not found above the LOD in any of the samples.

A few of the new BFRs and BPs were detected in two Råö air samples in the Nordic screening study (Schlabach, 2011). Air from January 2010 contained the most compounds: BTBPE (810 fg/m^3), EH-TBB (140 fg/m^3), 2,4-DBP (9.7 pg/m^3) and 2,4,6-TrBP (20 pg/m^3). These levels are higher than the once detected in the current study and also higher than the levels found in urban air from Oslo and Stockholm in the Nordic screening, which indicates that the samples may have been taken during an air pollution event.

Generally, the between sample variability was of the same magnitude as the mean concentrations. This variability may be related to both the spatial and temporal variability in air concentrations, which will be discussed further in the coming section.
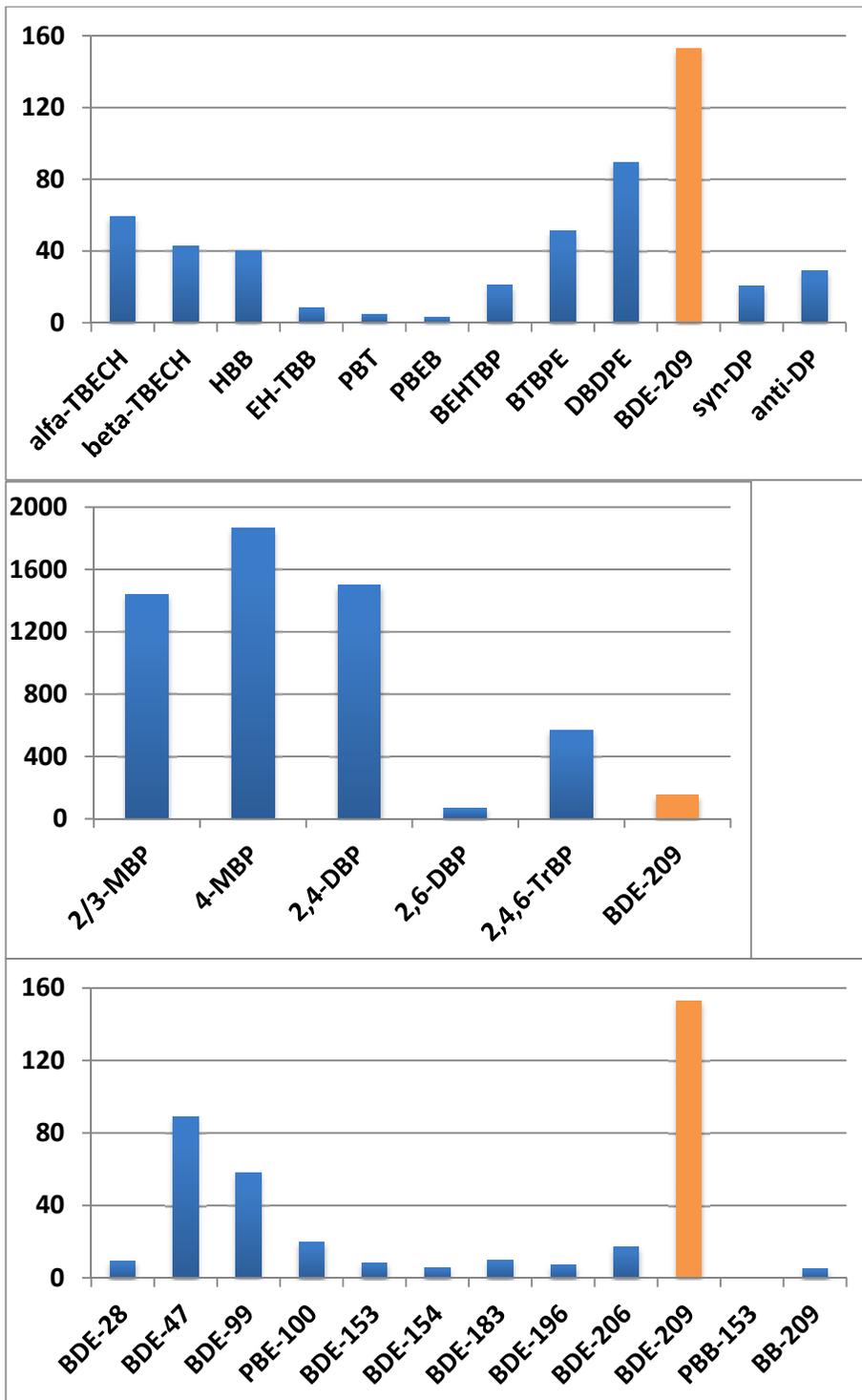
Figure 2. Geometric mean concentrations (fg/m^3) of emerging halogenated FRs (top panel), brominated phenols (middle panel) and established BFRs (PBDEs and PBBs) in ambient air.

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Table 7. Concentrations (fg/m^3) of emerging BFRs and Dechlorane Plus (DP) in ambient air.

Sample no	Site	Date	α-TBECH	β-TBECH	PBT	PBEB	HBB	EH-TBB	BEHTBP	BTBPE	DBDPE	syn-DP	anti-DP
1	Råö	Nov-13	412	89	8.4	8.0	25	11	22	Interf.	127	31	42
2	Råö	Jan-14	504	141	9.0	4.9	17	36	87	Interf.	47	68	46
3	Råö	Feb-14	64	48	3.4	2.2	88	14	25	105	30	19	37
4	Råö	Apr-14	92	81	7.9	5.1	26	7.9	49	89	124	30	64
5	Råö	Jun-14	142	126	9.7	4.5	36	6.7	18	60	93	25	41
6	Råö	Aug-14	87	98	6.2	3.0	19	6.7	15	395	42	18	27
7	Pallas	Nov-13	24	23	2.4	1.3	40	3.8	24	11	ND (20)	9.3	33
8	Pallas	Jan-14	41	37	3.7	1.8	80	3.2	27	29	41	14	12
9	Pallas	Feb-14	77	76	4.0	1.7	42	4.0	6.0	33	46	20	41
10	Pallas	Apr-14	40	35	6.4	4.2	64	23	18	50	470	29	29
11	Pallas	Jun-14	17	14	4.1	4.2	37	8.3	7.4	34	423	14	9.6
12	Pallas	Aug-14	21	10	1.9	2.9	91	8.3	ND (5)	28	ND (20)	9.0	15
Mean			59	43	4.9	3.2	40	8.5	21	51	89	21	29
Standard deviation			152	43	2.7	1.9	27	9.5	23	113	163	16	16

Table 8. Concentrations (fg/m^3) of brominated phenols (BPs) in ambient air.

Sample no	Site	Date	2/3-MBP	4-MBP	2,4-DBP	2,6-DBP	2,4,6-TrBP
1	Råö	Nov-13	1879	3851	4160	70	690
2	Råö	Jan-14	1383	1303	1388	54	475
3	Råö	Feb-14	1387	1268	1170	62	573
4	Råö	Apr-14	573	1108	1990	53	888
5	Råö	Jun-14	1014	4094	3716	67	1626
6	Råö	Aug-14	543	4121	13315	50	1321
7	Pallas	Nov-13	1406	798	209	32	145
8	Pallas	Jan-14	3330	2233	403	74	310
9	Pallas	Feb-14	620	210	247	31	231
10	Pallas	Apr-14	9278	6825	860	138	309
11	Pallas	Jun-14	5164	7908	3560	271	761
12	Pallas	Aug-14	495	730	3027	60	1283
Mean			1438	1863	1499	66	568
Standard deviation			2600	2510	3590	66	478

Table 9. Concentrations (fg/m^3) of PBDEs and PBBs in ambient air.

Sample no	Site	Date	BDE-28	BDE-47	BDE-99	PBE-100	BDE-153	BDE-154	BDE-183	BDE-196	BDE-206	BDE-209	PBB-153	BB-209
1	Råö	Nov-13	8.6	74	57	21	17	9.5	20	16	30	173	0.43	3.8
2	Råö	Jan-14	9.8	87	81	28	46	27	59	32	45	337	0.53	9.1
3	Råö	Feb-14	4.8	44	42	16	17	9.3	21	14	20	150	0.65	10
4	Råö	Apr-14	6.2	57	34	21	10	6.7	18	14	30	225	0.85	10
5	Råö	Jun-14	7.5	49	30	20	4.0	3.3	4.6	5.5	16	132	0.77	4.4
6	Råö	Aug-14	7.3	42	20	12	2.9	2.4	5.4	4.1	9.1	110	0.41	3.1
7	Pallas	Nov-13	7.0	69	42	13	3.1	2.4	3.6	2.6	11	110	0.29	2.0
8	Pallas	Jan-14	6.8	61	35	15	3.9	2.9	5.3	3.7	9.2	84	0.55	3.1
9	Pallas	Feb-14	7.2	71	56	21	12	8.5	14	9.5	22	207	0.39	6.7
10	Pallas	Apr-14	26	344	255	37	23	8.7	29	14	44	584	1.31	6.3
11	Pallas	Jun-14	21	286	157	23	7.7	4.2	5.5	3.0	9.5	91	0.98	3.1
12	Pallas	Aug-14	17	248	112	23	3.7	2.5	3.0	2.6	6.2	58	0.84	6.0
Mean			9.3	89	58	20	8.5	5.4	10	7.3	17	153	0.61	5.0
Standard deviation			6.8	108	68	6.9	12	6.9	16	8.6	14	146	0.30	2.8

5.1.2 Spatial and temporal variability

The maximum concentrations of the three BFR groups in samples from Råö at the Swedish West Coast and Pallas in Northern Finland are very similar (**Figures 3 and 4**), which shows their potential for atmospheric long range transport. There is however some differences in the temporal trends and the contaminant patterns.

There do not seem to be any clear seasonal trend in the emerging BFR or established BFR concentrations in air from Råö (**Figure 3**), but there are some BFRs clearly deviating in their absolute and relative abundances from the average values. TBECH was elevated in samples from November 2013 and January 2014, BDE-209 was elevated in January 2014, and BTBPE was elevated in August 2014.
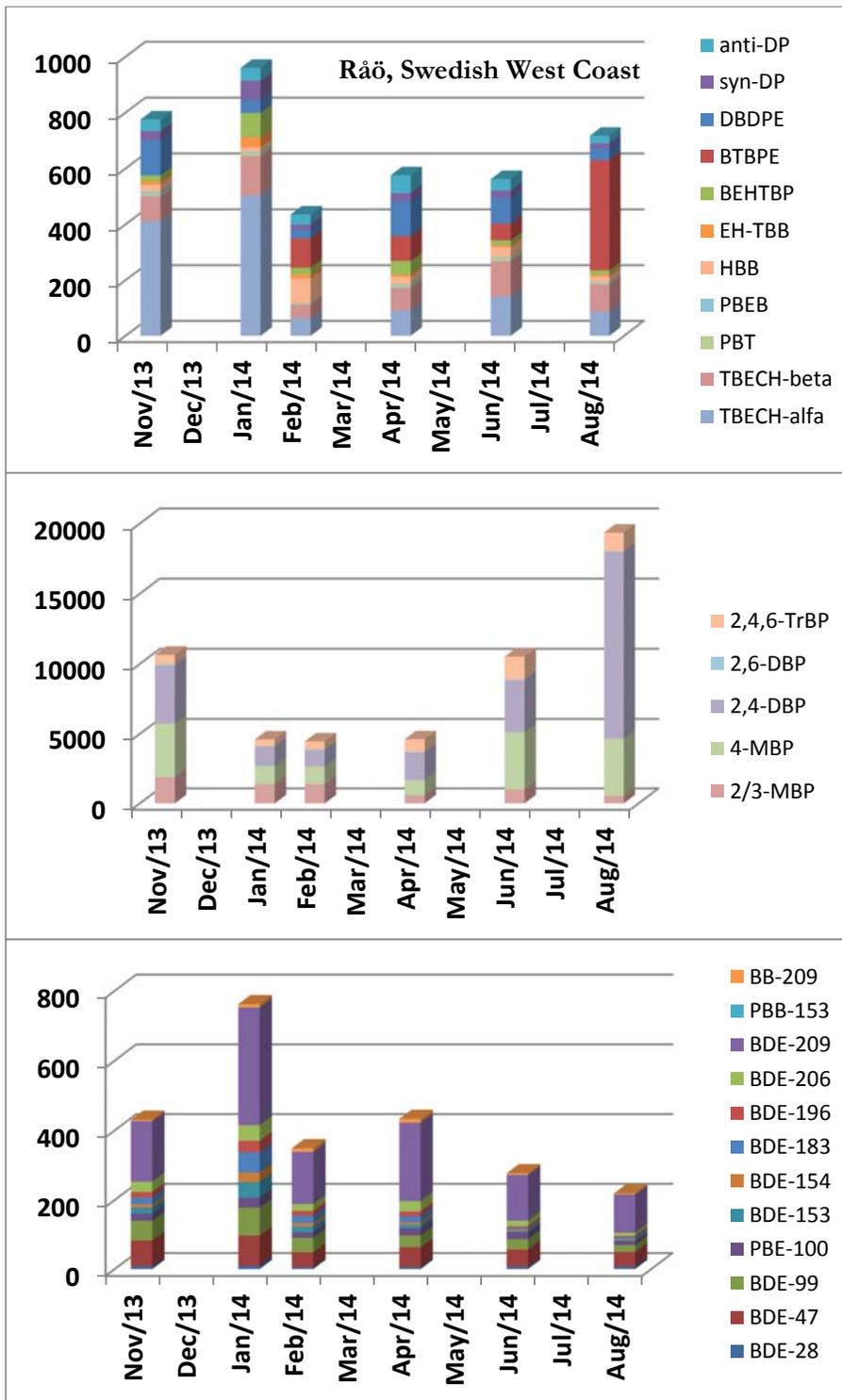
The brominated phenol concentrations, especially 2,4-DBP, in air from Råö do however exhibit a seasonal trend, with elevated concentrations in the summer/autumn period. This indicates a considerable contribution from natural sources. Marine organisms are well known to produce BPs, in particular 2,4-DBP and 2,4,6-TrBP (WHO, 2005).

All classes of compounds exhibit at seasonal trend in air from Pallas, with elevated concentrations in the summer period (**Figure 4**). The concentration of DBDPE was highly elevated in April 2014 and June 2014, BDE-209 was highly elevated in April 2014, and BDE-47 and BDE-99 was highly elevated during the second half of 2014. These are all high molecular weight semi-volatile chemicals, which possibly becomes more mobile during the warmer summer period (**Table 10**). In addition, there results may suggest that air from Europe (southwest) carry more of these pollutants than air from Artic regions or Russia. On the contrary, the volatile α- and β-TBECH was elevated during the winter periods, which is counterintuitive and may suggest contributions from a local source.

Table 10. The average temperatures and dominating origin of the air masses with arrival at Råö and Pallas for each sampling period. More information is also given in Appendix 1.

Sampling period	Råö °C	Råö wind direction	Pallas °C	Pallas wind direction
November 2013	6.5	From west	-5.2	From southwest to north
January 2014	0.6	From southwest to west and from east	-12	From northeast to southwest
February 2014	3.2	From southwest to west	-5.5	From southeast to southwest
April 2014	8.7	From southwest to west and from east	-0.6	From southwest to north
June 2014	16	From southwest to northeast	9.2	From northwest to east/southeast
August 2014	18	From southwest to north	12	From north to west

The bromophenol patterns show an interesting trend in air from Pallas. From November 2013 to April 2014 the lighter monobromo homologues dominates completely, whilst the di- and tribromo homologues increases later in 2014. In August 2014 the di- and tribromo homologues dominates over the monobromo homologues. That pattern bear striking similarities with the patterns observed in air from Råö at the Swedish West Coast. This may indicate a wind pattern dominated by winds that have passed over the Atlantic. The radar plots (summarized in Table 10) provide some support for this idea as they suggest that the sampled air from this time period partially originates from northwest, i.e. from the N. Atlantic.

Figure 3. Concentrations (fg/m^3) of emerging halogenated FRs (top panel), brominated phenols (middle panel) and established BFRs (PBDEs and PBBs) in air from Råö, Swedish West Coast.
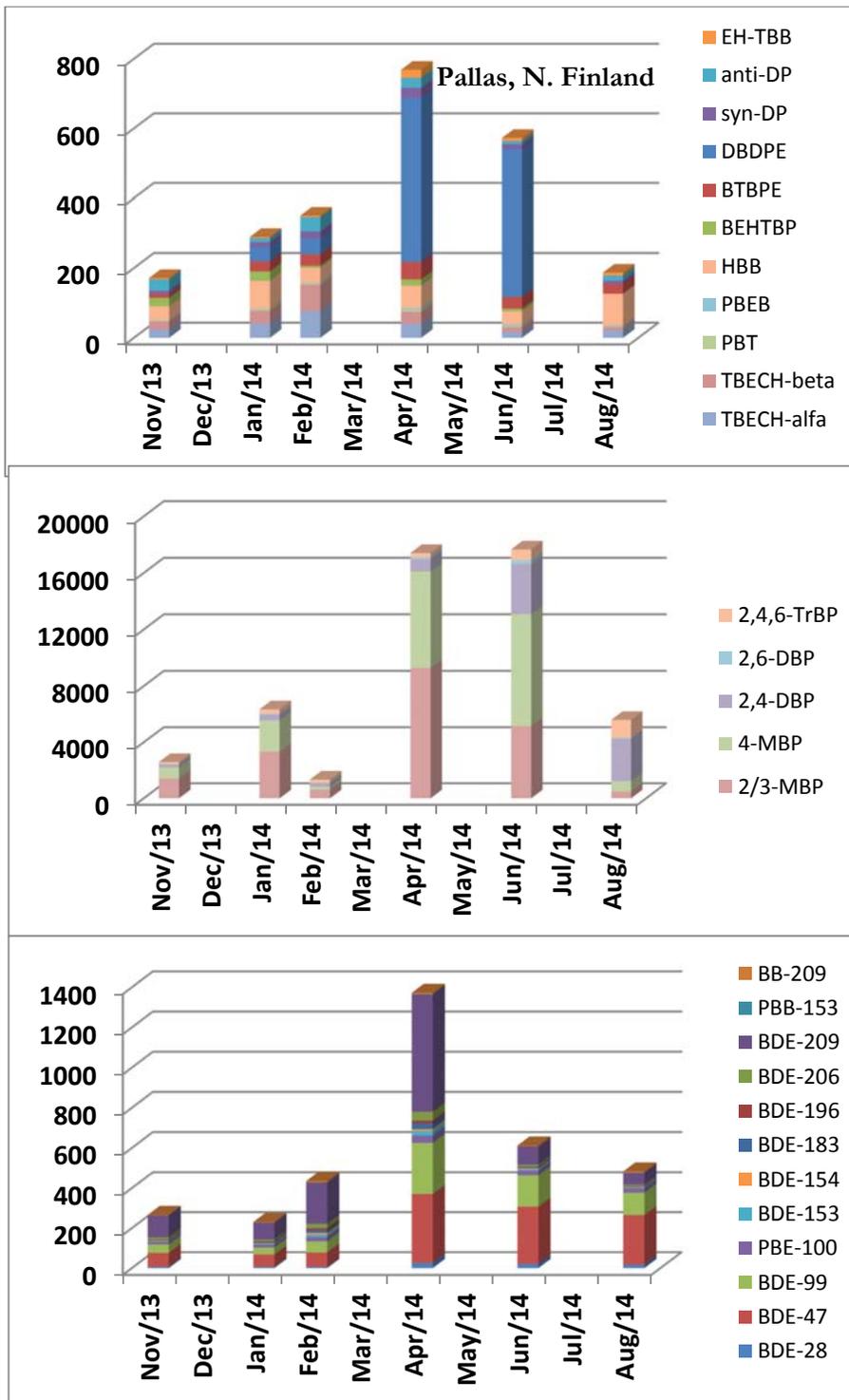
Figure 4. Concentrations (fg/m^3) of emerging halogenated FRs (top panel), brominated phenols (middle panel) and established BFRs (PBDEs and PBBs) in air from Pallas, Northern Finland.

5.2 Human samples

In human blood sera from 15 individuals the PBDEs, BTBPE and the bromophenols were found in all samples, PBEB was found in seven samples, and EH-TBB was found in six samples. The geometric mean concentrations are given in **Figure 5**.

PBT (0.1 pg/g), TBECH (<1 pg/g), BEH-TEBP (<5 pg/g), and DBDPE (<20 pg/g) was not found. HBB was found but could not be quantified due to high blank levels (10 pg/g).

The concentrations of BTBPE was generally comparable with those of BDE-209. One sample (no. 24) had much higher BTBPE concentration (779 pg/g) than BDE-209 concentration (5.8 pg/g). The concentrations of EH-TBB and PBEB was about 25% and 2%, respectively, of that of BDE-209. This sample also had the highest concentrations of EH-TBB (5.5 pg/g) and PBEB (1.4 pg/g).

The mean BDE-209 concentration (1.8 ng/g lipid, assuming a typical 0.40% lipids) were close to the BDE-209 concentration (1.3 ng/g lipid) found by the Swedish Food Agency in a study of serum collected from first-time mothers during 1996 to 2010 (Danerud, 20015).

Similarly, the mean BTBPE concentration (3.0 ng/g lipid) was within the range (<0.2-8 ng/g lipid) reported by Ali *et al.* (2013) for 85 human serum samples from Pakistan.

The levels of brominated phenols were an order of magnitude higher than those of BDE-209, with 2,4,6-TrBP as the most abundant. This isomer should be the most persistent to metabolism, due to the lack of vicinal hydrogen positions prone to Cyp-P450 mediated oxidation. The observed TrBP concentrations (mean 106 pg/g serum, 26 ng/g lipids) are similar to those found by Thomsen *et al.* (2002) in Norway (0.08-26 ng/g lipids).

Table 10. Concentrations (pg/g) of emerging BFRs, brominated phenols and PBDEs in human serum.

Sample no	Sex	Age	PBEB	EH-TBB	BTBPE	2/3-MBP	4-MBP	2,4-DBP	2,6-DBP	2,4,6-TrBP	Sum PBDE
13	F	36	ND (0.2)	2.6	15	64	82	48	25	137	85
14	F	55	0.11	2.9	6.0	74	100	76	26	79	44
15	F	60	0.49	2.8	4.3	170	56	21	29	69	48
16	F	43	0.24	5.4	3.4	51	31	20	20	79	62
17	M	58	0.33	ND (1)	33	70	31	30	27	49	94
18	M	28	ND (0.2)	ND (1)	16	185	155	50	22	85	44
19	F	47	ND (0.2)	ND (1)	4.5	63	50	16	23	154	37
20	M	37	0.25	ND (1)	4.5	52	64	35	26	269	64
21	M	40	ND (0.2)	ND (1)	4.8	75	72	37	28	106	59
22	M	42	ND (0.2)	ND (1)	12	104	140	53	24	133	29
23	M	30	ND (0.2)	ND (1)	12	54	51	23	24	92	41
24	F	46	1.4	5.5	779	34	40	19	29	119	32
25	M	59	ND (0.2)	2.7	13	135	67	26	34	51	41
26	M	41	ND (0.2)	ND (1)	8.2	86	43	36	47	263	85
27	M	62	0.14	ND (1)	11	96	73	27	44	116	68
Mean			0.30	3.5	12	79	63	31	28	106	52
SD			0.45	1.4	199	44	37	16	7.7	67	20

ND (x): Below the limit of detection (x pg/g).
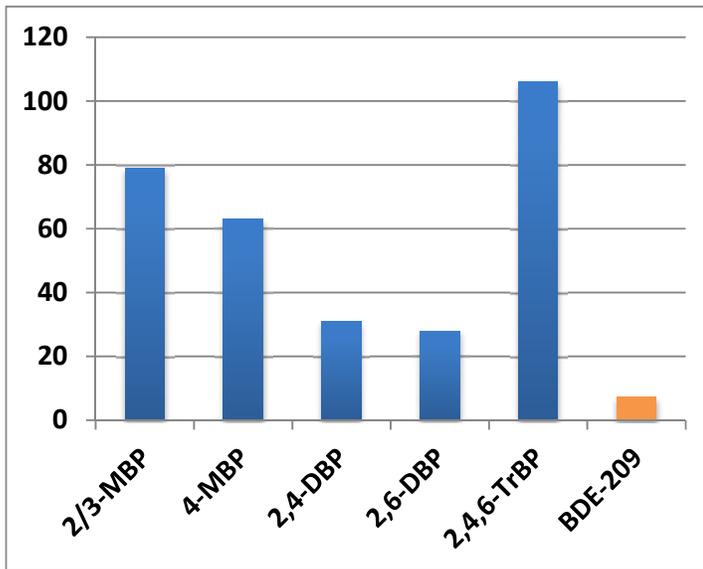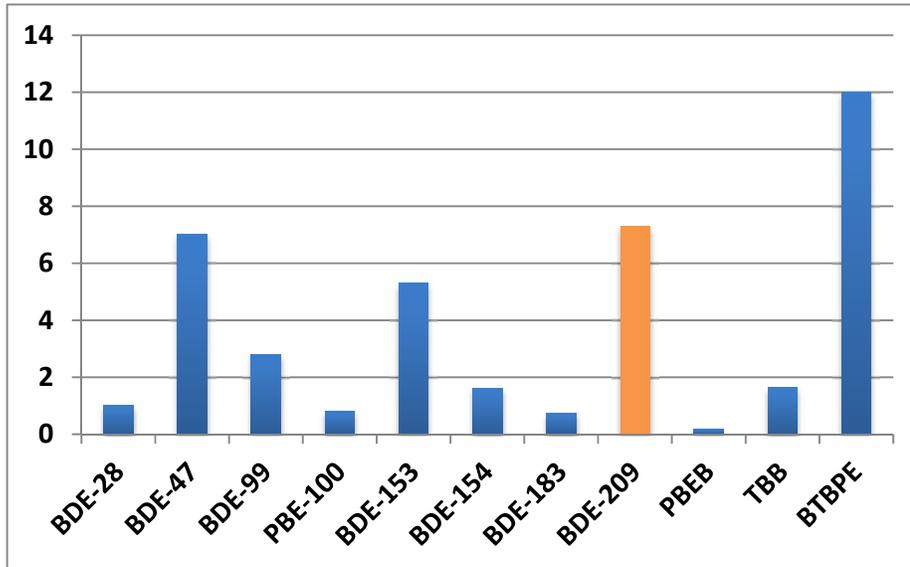
Figure 5. Geometric mean concentrations (pg/g) of established BFRs (top, left) and emerging BFRs (top, right), and brominated phenols (lower panel) in human blood sera (n=15).

5.3 Potential biological effects

There is a lack of toxicity information on the emerging BFRs detected in human serum. No particular studies are reported for BTBPE, PBEB and EH-TBB in human (Covaci, 2012).

BTBPE has low accumulation, rapid excretion and low toxicity in laboroatry animals (Hakk, 2003; Covaci, 2012). Considering the relatively low uptake and relatively high concentrations detected in serum, the human exposure to BTBPE is likely high.

Further, animal studies using rats suggest that prenatal exposure to Firemaster 550 (containing EH-TBB and TBPE) in relatively high doses (3 mg/kg/day) may alter metabolism and cause weight gain (Patisaul, 2013). The syptoms were consistent with the hallmark features of human metabolic syndrome (Prasad, 2012).

2,4,6-TBP is rapidly absorbed from the gastrointestinal tract in mammals and also rapidly excreted via urine and faeces. A combined repeated-dose oral toxicity study on 2,4,6-TBP in rats showed, at 1000 mg/kg body weight per day, reduced body weight gain, increases in absolute and relative liver weights in both sexes, and increases in protein levels in blood in male rats. The no observable adverse effect level (NOAEL) was considered to be 100 mg/kg body weight per day in rats of both sexes. No information was available on the absorption, distribution, elimination and toxicity of other brominated phenols in laboratory animals and no studies have been identified on the effects of brominated phenols on human health. (WHO, 2005).

6   Summary and conclusions

Most of the emerging FRs occurred in all of the air samples. The mean concentration of several emerging FRs (TBECH, HBB, BEH-TEBP, BTBPE, DBDPE, and syn/anti-DP) was between 10% and 60% of that of BDE-209, the most abundant PBDE.

The mean concentrations of the brominated phenols were generally higher than those of BDE-209. The concentrations of monobromophenols and 2,4-dibromophenol were at least an order of magnitude higher than those of BDE-209, whilst 2,4,6-tribromophenol was 4-fold higher.

The emerging FRs, brominated phenols and PBDEs all occurs at elevated concentrations during the summer period in air from Pallas in Northern Finland, which illustrates their potential for atmospheric long range transport.

The brominated phenols also showed a temporal trend at the Swedish West Coast site Råö, with elevated concentrations in the summer/autumn period, possible linked to increased natural production and emissions of these compounds during the highly productive summer period.

Three of the emerging BFR were detected in human sera. BTBPE was found in all samples and at an average concentration higher than that of BDE-209. PBEB and EH-TBB were found in roughly half of the samples.

The levels of brominated phenols are more than 10-fold higher than those of BDE-209, with 2,4,6-TrBP as the most abundant, likley due to a relatively high metabolic resistance.

Based on the results from the current screening we propose that the human intake of BTBPE, PBEB and EH-TBB should be assessed.

BTBPE and DBDPE could also be candidates for inclusion in the national environmental monitoring programs, e.g. for air, biota and sewage sludge.

7   **Acknowledgement**

8   **References**

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