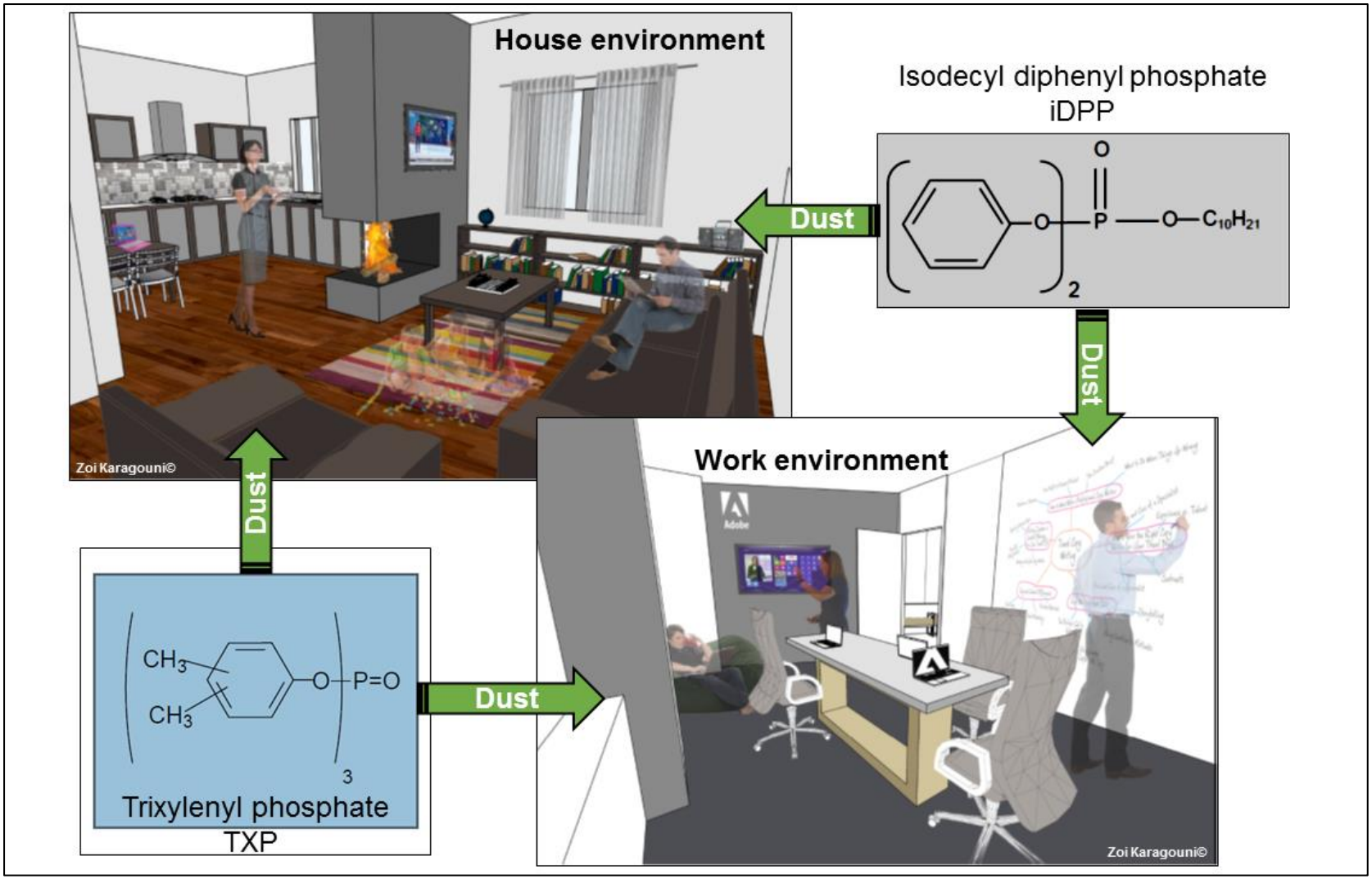
Legacy and alternative flame retardants in Norwegian and UK indoor environment: implications of human exposure via dust ingestion


House environment
Zoi Karagouni©
Isodecyl diphenyl phosphate
iDPP
Dust
Dust
Dust
Dust
Work environment
Zoi Karagouni©
Trixylenyl phosphate
TXP

Legacy and Alternative Flame Retardants in Norwegian and UK Indoor Environment: Implications of Human Exposure via Dust Ingestion

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Abstract

Indoor dust has been acknowledged as a major source of flame retardants (FRs) and dust ingestion is considered a major route of exposure for humans. In the present study, we investigated the presence of PBDEs and alternative FRs such as emerging halogenated FRs (EHFRs) and organophosphate flame retardants (PFRs) in indoor dust samples from British and Norwegian houses as well as British stores and offices. BDE209 was the most abundant PBDE congener with median concentrations of 4,700 ng g^{-1} and 3,400 ng g^{-1} in UK occupational and house dust, respectively, 30 and 20 fold higher than in Norwegian house dust. Monomeric PFRs (m-PFRs), including triphenyl phosphate (TPHP), tris(chloropropyl) phosphate (TCPP) and tris(2-chloroethyl) phosphate (TCEP) dominated all the studied environments. To the best of our knowledge, this is the first report of isodecyldiphenyl phosphate (iDPP) and trixylenyl phosphate (TXP) in indoor environments. iDPP was the most abundant oligomeric PFR (o-PFR) in all dust samples, with median concentrations one order of magnitude higher than TXP and bisphenol A bis(diphenyl phosphate (BDP). iDPP and TXP worst-case scenario exposures for British workers during an 8h exposure in the occupational environment were equal to 34 and 1.4 ng kg bw^{-1} day^{-1}, respectively. The worst-case scenario for BDE209 estimated exposure for British toddlers (820 ng kg bw^{-1} day^{-1}) did not exceeded the proposed reference dose (RfD) (7,000 ng kg bw^{-1} day^{-1}), while exposures for sum of m-PFRs (Σm-PFRs) in British toddlers and adults (17,900 and 785 ng kg bw^{-1} day^{-1} respectively) were an order of magnitude higher than for Norwegian toddlers and adults (1,600 and 70 ng kg bw^{-1} day^{-1}).

Keywords: PBDEs; alternative flame retardants; UK; Norway; indoor dust; human exposure

Highlights

- PBDEs, EHFRs and PFRs were analysed in Norwegian and UK house, store & office dust
- First report of iDPP and TXP in indoor dust with several o-PFRs also detected
- m-PFRs dominated all indoor environments, followed by EHFRs, PBDEs, and o-PFRs
- BDE209 levels were significantly higher in British than Norwegian house dust
-
- o-PFR estimated intakes for employees in Britain were higher than stay-home adults

Abbreviations

EHFRs: emerging halogenated flame retardants

m-PFRs: monomeric PFRs

o-PFRs: oligomeric PFRs

1. Introduction

Flame retardants (FRs) are widely used in everyday consumer products including carpets, electronic appliances, clothing and textiles, thermal insulation and cable coatings. Since the 1970s, polybrominated diphenyl ethers (PBDEs) have been widely used in consumer products as FRs (Alaee et al., 2003). Various human health effects are associated with PBDEs exposure such as disruption of the endocrine and thyroid homeostasis (Legler and Brouwer, 2003) and neurodevelopmental growth of children (Costa and Giordano, 2007). The commercial mixtures Penta-BDE and Octa-BDE have been listed as persistent organic pollutants (POPs) for elimination under the Stockholm Convention (Stockholm Convention, 2009a, 2009b), while the Deca-BDE mixture is currently under review. The use of Deca-BDE was banned in Norway in 2008 (EBFRIP, 2008), while it was included by the EU in the amended Annex XVII of REACH (EC No 1907/2006), banning its production, use and marketing in the EU (European Commission, 2016). As a result of the REACH amendment, furniture and fire safety regulations in the UK are currently under review by the national competent authorities (UK Department for Business, Energy & Industrial Strategy, 2016). Due to legislative restrictions on their commercial use, PBDEs have been replaced with alternatives, known as "emerging" halogenated flame retardants (EHFRs) including 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (EH-TBB; Penta-BDE replacement), bis(2-ethylhexyl)-3,4,5,6-tetrabromophthalate (BEH-TEBP; Penta-BDE replacement), 1,2-bis(2,4,6-tribromophenoxy) ethane (BTBPE; Octa-BDE replacement), decabromodiphenyl ethane (DBDPE; Deca-BDE replacement) and Dechlorane Plus (DPs; Deca-BDE replacement) (Stapleton et al., 2008; Wang et al., 2011) and organophosphate flame retardants (PFRs) such as tris(2-chloroethyl) phosphate (TCEP) and tris(chloropropyl)phosphate (TCPP) (van der Veen and de Boer, 2012).

Several studies have indicated that also EHFRs and PFRs may pose potential risks to humans. EH-TBB and BEH-TEBP, major components in the commercial product Firemaster 550®, have been proven to act as endocrine disruptors and obesogens when orally administered to rats (Patisaul et al., 2013) and can bind and activate the transcription of peroxisome proliferator-activated receptor γ (PPAR γ) ligands, while triphenyl phosphate (TPHP)-induced *in vitro* adipocyte differentiation and diverted osteogenic differentiation towards lipid accumulation has been reported (Pillai et al., 2014). DPs, EH-TBB, BEH-TEBP and PFRs, such as TCEP and tris(1,3-dichloro-2-propyl) phosphate (TDCIPP) have been detected in human breast milk and blood in Asian populations (Ben et al., 2013; Kim et al., 2014), as well as in blood, hair and nails in USA residents (Liu et al., 2016). TDCIPP has been linked with reduction in free thyroxine and increase in prolactin secretion in US men, while TPHP was associated with weakening sperm quality (Meeker and Stapleton, 2010). An *in vitro* estrogenic and anti-androgenic potency of TDCIPP, tris(2-butoxyethyl) phosphate (TBOEP), and TPHP on human osteosarcoma (U2OS) cell line exposed to indoor dust extracts has also been reported (Suzuki et al., 2013). In the EU, restrictions on

the use of chlorinated PFRs, such as TDCIPP and TCPP, have been issued based on toxicological concerns related to their carcinogenic potency (ECHA, 2008a, 2008b).

Monomeric PFR (m-PFRs), including TDCIPP, TCPP and TCEP, are routinely used as FRs in flexible polyurethane foams (PUFs) and textiles (Ali et al., 2012; Cao et al., 2014b). TPHP can be used as a plasticiser and a FR in PVC, thermoplastics and synthetic polymers, while TBOEP is exclusively used as a plasticiser in floor polish and rubber products (Marklund et al., 2003; Stapleton et al., 2009; van der Veen and de Boer, 2012). The use of EHFRs and m-PFRs in consumer products has thus increased and this is reflected by their high abundance in indoor dust in the UK (Brommer and Harrad, 2015), China (Cao et al., 2014a), Japan (Tajima et al., 2014), Sweden (Newton et al., 2015) and Norway (Cequier et al., 2014). PFRs such as TCPP, TCEP and TBOEP dominate house, office and hotel environments, with levels in hotel dust six fold higher than office dust from China (Cao et al., 2014b). A few studies have reported oligomeric PFRs (o-PFRs) in considerable amounts in dust, such as tetraekis(2-chlorethyl)-dichloroisopentyl diphosphate (V6), an alternative of Penta-BDE, TCPP and TDCIPP (ECHA, 2008c), along with resorcinol bis(diphenyl phosphate (RDP) and bisphenol A bis(diphenyl phosphate (BDP) as Deca-BDE alternatives in electronic and plastic consumer products (Ballesteros-Gómez et al., 2014; Brandsma et al., 2013; Matsukami et al., 2015). Since house dust acts as a repository sink for EHFRs and PFRs, dust originating from indoor environments (e.g. houses, offices, stores) is considered as a major source of human exposure to FRs (Alves et al., 2014; Jones-Otazo et al., 2005).

In April 2016, the Washington State House Bill 2545 (Toxic-free Kids and Families Act) was approved to ban children's products and residential upholstered furniture from the market containing more than 0.1% of TCEP, TDCIPP, Deca-BDE, hexabromocyclododecane (HBCD) and tetrabromobisphenol A (TBBPA) with an effective date set for June 2016. Additional six FRs, including TPHP, TCPP, V6, EH-TBB, BEH-TEBP, and isopropylated triphenyl phosphate (IPTPHP) will be evaluated and recommended to the Legislature for possible restriction in consumer products (State of Washington, 2016). The implementation of this bill may potentially trigger the phasing out PBDE alternatives, thus initiate the development and use of newer FRs. Therefore, the continuous and rigorous assessment of

legacy and alternative FRs, especially oligomeric PFRs (o-PFRs), in the indoor environment is essential due to their potential adverse effects on human health.

To bridge this knowledge gap, the main objectives of the present study are:

a) To assess the presence of legacy and alternative FRs in three different indoor environments from two European countries (the UK and Norway)

b) To estimate and compare human intakes to a wide range of FRs via dust ingestion using the same dust samples for non-working adults and toddlers in Norwegian and British houses, as well as for working adults in British stores and offices.

2. Materials and Methods

2.1 Sampling

Ten indoor dust samples were collected from pre-existing vacuum cleaner bags (houses) in Norway (Oslo) as a part of the A-TEAM cohort sampling during November 2013 – April 2014 (Papadopoulou et al., 2016). Twenty-two indoor dust samples from pre-existing vacuum cleaner bags (10 houses, 6 stores and 6 offices; Table SI-1) were collected in Reading (UK) during August – December 2013. The UK house dust samples were collected from the homes of University of Reading employees, while UK office and store vacuum cleaner bags were collected in Reading with respect to the participant's approval and willingness to cooperate in the present study. All dust samples were sieved to <250 μm using a methanol-washed metallic sieve; this size fraction of dust is likely to be ingested according to (Yu et al., 2012). Oven-baked Na_2SO_4 (granular) was also sieved as field blank. All dust samples were kept in hexane-washed amber glass bottles and stored at 4°C till analysis.

2.2 Extraction and clean-up

The method was based on a previous study (Van den Eede et al., 2012a) with some modifications. Briefly, 30 mg of dust was extracted with 2.5 mL hexane:acetone (3:1) using ultra-sonication extraction for 10 min and vortexing for 1 min three times. The combined extract was concentrated on aminopropyl (NH_2) silica cartridges (500 mg, 3 mL, Agilent, USA) and further fractionated with 10 mL hexane (F1) and 12 mL of ethyl acetate (F2). F1 was further concentrated, following a clean-up on an acidified silica cartridge (5%, 1 g, 6 mL) and elution with 12 mL dichloromethane. F2 was equally aliquoted into two portions, F2a and F2b. Then, F1, F2a and F2b were evaporated, reconstituted with 100 μL of iso-octane (F1 & F2a) and methanol (F2b), respectively, and then filtered. Finally, the extracts were transferred to injection vials and analyzed on GC-ECNI-MS (F1, for PBDEs and EHFRs), GC-EI-MS (F2a, for m-

PFRs, except TXP) and LC-QqQ-MS (F2b, for o-PFRs and TXP). More details about sample preparation and instrumental analysis are found in SI.

2.3 QA/QC and Data Analysis

Overall, 28 and 31 compounds (out of 33) were detected in house and occupational dust samples, respectively (Tables SI-2, SI-3, SI-4, and SI-5). SRM 2585 (n=2, NIST, USA) was used for QC testing and the results were in line with the literature (Table SI-6). Four Na_2SO_4 samples (30mg) were used as field blanks for background checking and results were blank corrected for all analytes by subtraction of the mean field blank values from the raw FR values (expressed in ng/g) according to (Abdallah and Covaci, 2014). Method limits of detection (mLOD) were calculated as three times the standard deviation of the field blanks. For non-detected analytes, mLOD was calculated based on signal-to-noise-ratio 3:1 (Table SI-7). GraphPad Prism® version 7.00 for Windows, (GraphPad Software, La Jolla CA, USA) was used for statistical analysis. Compounds with detection frequencies (DF) lower than 40% were excluded from statistical analysis. Where needed, non-detections were replaced by half of mLOD for statistical analysis. All data were checked for normality using the D'agostino and Pearson tests, data that failed the normality test were log-transformed and checked for normality again. Not all data were normally distributed after log-transformation. Ordinary two-way ANOVA (Uncorrected Fisher's test, $p<0.05$) was performed to assess statistically significant differences of FRs between UK house and occupational concentrations and between UK and Norwegian houses. Due to some data failing to pass normality tests, Spearman's correlation ($p<0.05$) was employed to assess statistical dependence and correlation between FRs in the three different dust categories.

3. Results and discussion

This study reports concentrations of four groups of FRs in dust from UK stores and offices (n=6 offices and n=6 stores), UK houses (n=10) and Norwegian houses (n=10). Studied chemicals included nine PBDE congeners, eight EHFRs, ten monomeric PFRs, and six oligomeric PFRs (Tables S1-8, SI-9, SI-10, SI-11, SI-12, and SI-13). Overall, the UK occupational dust samples had the highest FR contamination, followed by UK and Norwegian house dust. In an attempt to define newly identified PFRs, this group is divided in monomeric (m-PFRs), including TPHP, TnBP, TCPP, TDCIPP etc., and oligomeric (o-PFRs), including V6, BDP and RDP, using the abbreviation nomenclature as suggested by (Matsukami et al., 2015). In our study, monomeric PFRs presented the highest levels in total, followed by EHFRs, PBDEs and oligomeric PFRs.

3.1 PBDEs

Most PBDEs were frequently detected in UK houses and occupational dust with DF>50%, unlike in the Norwegian house dusts (Fig. 1A, B, C; Table SI-8, SI-10, and SI-12). BDE28 to BDE183 levels were

relatively lower compared to BDE209, probably because of the global phase out of Penta- and Octa-BDE commercial mixtures (Dodson et al., 2012). Similar to indoor dust samples from Belgium, China and Sweden (Ali et al., 2011; Newton et al., 2015; Zheng et al., 2011) median level of BDE47 was four-fold higher in UK (12 ng g^{-1}) than in Norwegian house dust samples. Median concentrations of BDE47 (9.1 ng g^{-1}) and BDE183 (11 ng g^{-1}) in occupational dust were within the concentration range of studies from Belgium and Germany (Ali et al., 2011; Brommer et al., 2012), but lower than the USA (Michigan) and China (Batterman et al., 2010; Cao et al., 2014b). BDE209 , the most abundant PBDE congener, was detected in all samples, with median concentrations of 4,700 ng g^{-1} and 3,400 ng g^{-1} in UK occupational and house dust, respectively, which is much higher than a recent study of Norwegian classroom dust (507 ng g^{-1}) (Cequier et al., 2014) and also in the Norwegian house dust samples from the present study (160 ng g^{-1}) (Fig 1A). A statistically significant difference of BDE209 concentrations was observed between UK and Norwegian house dust ($p=0.014$). Since DBDPE acts a major replacement of BDE209, the BDE209/DBDPE ratio is indicative of the progress of phasing out Deca-BDE. The median BDE209 /DBDPE ratio was <1 for Norwegian house dust while it was >3 in UK house dust. Such findings can be possibly attributed to low Deca-BDE usage in Norway and its unilateral ban since 2008 (EBFRIP, 2008), contrary to the EU where Deca-BDE was added to the candidate list of substances of very high concern for authorisation under the REACH regulation in 2012 with its use in consumer products eventually banned within the REACH framework earlier in 2016 (ECHA, 2012; European Commission, 2016). Unlike the Nordic indoor environment where hard-surfaced wooden flooring is more frequently applied (Roos and Hugosson, 2008), an evident preference towards carpet flooring in UK houses could potentially contribute to the higher BDE209 levels, hence the high BDE209/DBDPE median ratio in UK house dust (Jonsson, 2005). However, the median BDE209 /DBDPE ratio in the UK occupational dust was <1, probably due to the replacement of Deca-BDE in newer products in stores and offices compared to house environment.

3.2 Emerging halogenated FRs

Nearly all EHFRs were frequently detected (DF>50%) in all three types of dust (Fig. 1A, B, C, Table SI-8, SI-10, SI-12). DBDPE and BEH-TEBP were the most abundant EHFRs (DF>80%). In house dust, DBDPE median concentration was two-fold higher in UK (1,100 ng g^{-1}) than Norway (686 ng g^{-1}) (Fig 1A&B), which was in agreement with a previous Norwegian study (Cequier et al., 2014) and considerably higher than DBDPE levels in dust from Belgium and Sweden (Ali et al., 2011; Newton et al., 2015). The median concentration of BEH-TEBP in UK house dust **(**110 ng g^{-1}) was equivalent to recent studies from USA and Sweden (Dodson et al., 2012; Newton et al., 2015). However, BEH-TEBP median in our Norwegian dust samples was lower than a previous Norwegian study (Cequier et al., 2014)**.** The small sample size of the Norwegian dust collection analysed in the present study (n=10) may act as a limiting factor. Our dust samples were collected from pre-existing vacuum cleaner bags, whereas

in (Cequier et al., 2014) dust samples (n=48) were collected using forensic filters. In UK occupational dust, DBDPE had the highest median concentration (5,400 ng g^{-1}), followed by BEH-TEBP (250 ng g^{-1}), both of which were higher than previous studies on Belgian and German office dust (Ali et al., 2011; Brommer et al., 2012), but lower than a recent Chinese study (Cao et al., 2014b). EH-TBB was several folds lower than BEH-TEBP in all three types of dust. Additional sources of BEH-TEBP in consumer products other than Firemaster 550® (EH-TBB/BEH-TEBP ratio 4:1 in commercial mixture (Stapleton et al., 2008) are suspected to be Great Lakes DP-45™ and Firemaster® BZ-54 (Chemtura Inc., USA), (Bearr et al., 2012; Zheng et al., 2015). A statistically significant difference between UK house and occupational dust concentrations was found for two Deca-BDE alternatives, DBDPE ($p<0.05$) and *anti*-DP ($p<0.05$) (Stapleton et al., 2008; Zhu et al., 2007). *Anti*-DP (median: UK occupational 43.1 ng g^{-1}; UK house 6.8 ng g^{-1}; Norwegian house 4.5 ng g^{-1}) was the predominant DP isomer compared to *syn*-DP (median: UK occupational 15.2 ng g^{-1}; UK house 4.6 ng g^{-1}; Norway 2.6 ng g^{-1}), in agreement with other studies (Cequier et al., 2014; Newton et al., 2015; Zheng et al., 2015). TBECH isomers were less frequently detected (DF<60%), with concentrations of α-TBECH consistently higher than β-TBECH, although the β-TBECH isomer was not detected in Norwegian house dust samples. This may be attributed to β-TBECH being less volatile compared to α-TBECH, leading to lower β-TBECH levels in indoor dust, unlike the 50:50 α/β TBECH isomer ratio in the commercial mixture. (Tao et al., 2016; Wong et al., 2015).

3.3 Monomeric PFRs

All m-PFRs were frequently detected (DF>50%) in all three types of samples, apart from TnPP which was found <mLOD in all samples (Fig. 1 D, E, F; Table SI-9, SI-11 & SI-13). The median concentration of sum of 10 m-PFRs (Σ_{10}m-PFRs) (88,000 ng g^{-1}) in UK occupational dust was similar to UK house dust (79,000 ng g^{-1}), but four-fold higher than in Norwegian house dust (23,000 ng g^{-1}). Individual PFR levels in our UK house dust samples were in agreement with a recent study of UK house dust (Brommer and Harrad, 2015). TCPP and TBOEP presented the highest median concentrations in UK houses (65,000 ng g^{-1} and 8,100 ng g^{-1}, respectively) (Fig.1E), with TCPP median in UK houses two-fold higher than house dust from Japan (30,900 ng g^{-1}) and considerably lower from another Japanese house study (1,570,000 ng g^{-1}) (Kanazawa et al., 2010). In Norwegian houses, TBOEP ranked first (18,000 ng g^{-1}), nearly two-fold higher than previously reported data from USA house dust (11,000 ng g^{-1}) (Dodson et al., 2012) and in agreement with (Cequier et al., 2014). TBOEP (median 33,000 ng g^{-1}) and TCPP (median 25,000 ng g^{-1}) were also two predominant m-PFRs in UK occupational dust. Used as a plasticiser in flexible PVC, thermoplastics and food packaging, EHDPHP median concentration (20,000 ng g^{-1}) ranked as the third highest m-PFR in occupational dust, one to two orders of magnitude higher than its median in UK house dust. This may suggest that EHDPHP usage in the UK occupational environment and its application in new consumer products are steadily increasing. EHDPHP median concentration in UK house dust (2,400 ng g^{-1}) was 12-fold higher than in the Norwegian house dust, yet

marginally lower than recently reported UK house dust concentrations (Brommer and Harrad, 2015). No statistically significant difference was observed between UK and Norwegian house dust concentrations (p=0.07) or between UK house and occupational dust samples (p=0.055) for EHDPHP.

TCPP median concentration in UK houses from our study was 30 times higher compared to Norwegian house median concentration, while TCPP in Norwegian house dust was lower than levels from Belgium and another Norwegian house dust study (Cequier et al., 2014; Van den Eede et al., 2011). A statistically significant difference was found for TCPP (p=0.016) when comparing UK and Norwegian house dust concentrations. This may be possibly attributed to higher TCPP usage in the UK where TCPP is a TCEP replacement, while TCPP production and use in Norway have decreased during the past decade (ECHA, 2008a; van der Veen and de Boer, 2012). Median concentrations of TPHP and TDCIPP in UK house dust were two-fold higher (1,500 and 750 ng g^{-1}, respectively) than in Norwegian houses (830 and 340 ng g^{-1}, respectively), but lower than TPHP and TDCIPP levels reported from the USA (Betts, 2013; Stapleton et al., 2009). TMPP and TEHP were marginally different between house dusts in the two countries, while the median concentration of TnBP was two-fold higher in Norwegian house dust compared to UK house dust. Concentrations of m-PFRs have recently been reported in floor and surface dust, sampled with dust collection filters, from the same Norwegian population group (n=61) (Xu et al., 2016). The range of m-PFRs levels in floor and surface dust (collected from the living room) from Xu et al (2016) is of the same order as the vacuum cleaner dust in the present study (n=10, Norwegian house dust). TBOEP dominated the Norwegian house environment both in our study and in Xu et al (2016). The TBOEP concentration range in the present study (1300-48,000 ng g^{-1}) was within the range of floor (727-311,000 ng g^{-1}) and settled dust (<mLOD-540,000 ng/g) from Xu et al (2016), yet with higher median concentrations (our study: 18,000 ng g^{-1}; Xu floor dust: 8,100 ng g^{-1}; Xu settled dust: 6,800 ng g^{-1}). Such results may be attributed to: a) differences in sample size; b) vacuum cleaner dust was sieved, but floor and settled were not; the large particles, like sand and hair, might dilute the contamination in dust sample; c) vacuum cleaner dust is representative of the entire house, while Xu et al (2016) only studied the living room; d) vacuum cleaner dust represents long term indoor contamination, while floor and settled dust represent short term contamination. This suggests that the sampling strategy factors such as collection season, area, tools and population selection, could potentially influence the study outcome. Therefore, researchers are advised to choose a sampling strategy firmly based on the aim and scope of their study.

3.4 Oligomeric and monomeric PFRs

Although TXP and TDBPP are considered as monomeric PFRs (Table SI-5), we will discuss them together with oligomeric PFRs (o-PFRs) due to the novel character of their environmental emissions and their usage in similar FR products (Matsukami et al., 2015). To the best of our knowledge, this is the first report of iDPP and TXP in the indoor environment. Most o-PFRs were detected in all three

types of dust (DF>80%) (Fig.1 D, E, F; Table SI-9, SI-11, and SI-13), apart from RDP (no detection in Norwegian house dust) and TDBPP (DF<50% in UK and Norwegian house dust samples). All o-PFRs were frequently detected in occupational dust samples with substantially higher concentrations compared to the house dust samples. iDPP was the most abundant o-PFR in our dust samples, ranging from 600-145,000 ng g^{-1}, 110-1,700 ng g^{-1} and 6-260 ng g^{-1} in UK occupational dust, UK house dust and Norwegian house dust, respectively. Also, median concentrations of BDP (UK occupational dust 480 ng g^{-1}; UK house dust 66 ng g^{-1}; Norwegian house 35 ng g^{-1}), TXP (UK occupational dust 240 ng g^{-1}; UK house dust 26 ng g^{-1}; Norwegian house dust 9.1 ng g^{-1}) and V6 (UK occupational dust 40 ng g^{-1}; UK house dust 17 ng g^{-1}; Norwegian house dust 4 ng g^{-1}) were relatively higher than RDP and TDBPP, which were in general close to the mLOD. Maximum values for iDPP and BDP were close to 145,000 ng g^{-1} and 6,000 ng g^{-1}, respectively, both found in dust from a toy store. In a personal computer (PC) store, the maximum concentration of TXP was near 6,000 ng g^{-1}. iDPP concentrations of UK house and occupational dusts were statistically significantly different (p=0.019). We can assume that this is a result of the faster replacement rates of consumer products in the occupational environment compared to UK houses. No significant difference was found for TXP and BDP (p=0.07), possibly as a result of the small sample size analysed in the present study (10 UK houses and 12 stores).

A few studies have reported the presence of oligomeric PFRs in indoor dust and SRM 2585. RDP and BDP have been identified in our dust samples, but not in SRM2585 (Table SI-6). (Brandsma et al., 2013) reported higher concentrations of BDP and RDP in house dust when collected on/around electric items than in distance. Although it has been reported in baby products and car dust since 2011, V6 may have been used in consumer products since the early 1990s considering that SRM 2585 was prepared using a pool of samples collected during mid to late 1990s (Fang et al., 2013; Stapleton et al., 2011). An average concentration of 117 ± 6 ng g^{-1} for V6 was reported by (Fang et al., 2013) in SRM2585 with LC-APCI-MS/MS, two-fold higher than our result (47 ± 23 ng g^{-1}) where LC-ESI-MS/MS was employed for instrumental analysis. Since TDBPP, iDPP, and TXP were also present in SRM 2585 with very low levels (Table SI-6), we can assume their commercial use has been ongoing earlier than has been generally perceived or that such compounds may be impurities of PFRs, such as TPHP, TMPP and EHDPHP (Derouet et al., 1996; UK Environment Agency, 2009a).

3.5 iDPP and TXP commercial mixtures

According to the UK Environment Agency (2009), iDPP, an alkyl diaryl phosphate ester, is manufactured in the UK and distributed by Ferro UK Ltd. and ICL-IP Europe B.V. in unknown amounts so far and is used as a FR plasticiser in flexible PVC, synthetic rubber, textiles and pigment products. The registered trademarks for iDPP available in Europe are Phosflex® 390 and Santicizer® 148 with the commercial mixture composition set as 90% iDPP and <5% TPHP as a technical mixture impurity (UK Environment Agency, 2009b). Newer PFRs such as iDPP have a general impurity due to their

manufacture process which potentially causes a diverse contamination profile indoors with similarly structured PFRs, e.g. iDPP with EHDPHP. In the present study, iDPP highest concentrations were found in British-based toys (145,000 ng g^{-1}) and kitchenware stores (15,000 ng g^{-1}). Extensive use of laminated wooden flooring, plasticised vinyl polymer products and displays was observed in the two stores. As legislation on the use of PBDEs and their alternatives in consumer products gets stricter, higher levels of "newer" FR are likely to be observed in the indoor environment, including iDPP. TCEP and TDCIPP will be partly restricted to 0.1% by weight in children's products from 2017 by Washington State (USA) (State of Washington, 2016), which might pave the way for replacement of earlier PBDE alternatives with newer FRs in consumer products. We may also assume that low levels of iDPP in Norwegian house dust could be due to limited commercial availability of iDPP in consumer products in the Norwegian market by comparison with the UK.

Trixylenyl phosphate (TXP) is a triaryl phosphate ester currently manufactured by Chemtura Inc. (formerly Great Lakes Chemical Corp., USA) under the registered trademark Kronitex® TXP (Chemtura Corp, 2013) and by ICL-IP Ltd. (Israel) as Syn-O-Ad® 8475 (ICL IP Inc., 2008) with an estimated usage in Europe between 100 – 1000 tonnes/year (ECHA, 2015). In 2013, the European Chemicals Agency (ECHA) indicated the use of TXP as a tricresyl phosphate (TCP) substitute and formally listed it as a "substance of very high concern" because of its potential reproductive toxicity (ECHA, 2013). Xylenols such as TXP are naturally derived alcohols with recommended application in wire and cable insulation, fire resistant lubricants and PVC applications where low volatility and high resistance products are essential (Harper, 2003). In our study, TXP maximum concentration (5,800 ng g^{-1}) was reported in a dust sample collected from a computer store. The store's interior design was covered with PVC and carpet flooring, numerous computer displays and repair rooms where cables and wires are frequently found.

3.6 Correlation between FRs present in dust from different environments

Spearman's correlation revealed significant and positive correlations among low brominated PBDEs in all environments (Fig.2) in agreement with (Cequier et al., 2014) as they formulate a group of compounds with similar structural and physico-chemical characteristics and are present in the same commercial mixtures. In the occupational environment, where oligomeric PFRs were more abundant than PBDEs and EHFRs, iDPP, RDP and BDP were strongly correlated between each other, EHDPHP and TPHP ($\rho>0.9$; $p<0.01$) and TnBP, TCEP and TBOEP ($0.6<\rho<0.8$; $p<0.01$) also occurred together probably due to their application as plasticisers and FRs in similar consumer products and RDP being used as TCEP substitute due to its low release to the environment (van der Veen and de Boer, 2012). Also, TPHP is present in the indoor environment either as an individual FR or as an impurity in the BDP and RDP technical mixtures (Mihajlović, 2015; UK Environment Agency, 2009c; van der Veen and de Boer, 2012). In the UK house environment, V6 was highly correlated with TCEP ($\rho>0.7$; $p<0.01$)

probably due to TCEP impurity in V6 formulation, while no significant correlation was achieved for Norway, where TCEP use has significantly decreased since 2003 (van der Veen and de Boer, 2012). In UK houses, oligomeric PFRs including RDP and BDP, were strongly correlated with each other ($\rho>0.9$; $p<0.01$), while only BDP was correlated with BDE-209 ($\rho>0.79$; $p<0.01$), although they are both proposed as Deca-BDE alternatives in electronics (Ballesteros-Gómez et al., 2014). In Norwegian houses, TXP was moderately to highly correlated with Tetra-BDEs, Hepta-BDEs, and BDE-209 ($0.6>\rho>0.7$; $p<0.01$), with *anti*-DP and TCEP ($\rho>0.7$; $p<0.01$) and with TDCIPP ($\rho>0.7$; $p<0.05$). Alpha- and β-TBECH isomers were highly correlated with each other and BDE-28 ($\rho>0.9$; $p<0.01$) in all environments and with BEH-TEBP in the occupational environment ($\rho>0.7$; $p<0.01$) may be caused by the banned Tri-BDE formulations and parallel Firemaster 550® or Great Lakes DP-45™ and Firemaster® BZ-54 applications in electronic products.

3.7 Human exposure assessment

Different scenarios of human exposure via dust ingestion have been estimated for oligomeric PFRs in the present study (Table-1, Tables SI-15, SI-16, and SI-17). More information on equations and parameters used for exposure estimates are presented at SI Table 14. To the best of our knowledge, this is the first study providing multi-scenario exposure assessment for this wide variety of FRs based on the same samples from two different countries. However, we recognise that the small number and representativeness of samples analysed in the present study represents a major uncertainty in these intake calculations.

In all scenarios (Tables SI-15, SI-16, and SI-17), much higher intakes from dust ingestion have been calculated for m-PFRs than for PBDEs, EHFRs and o-PFRs. Toddlers were found to have much higher estimated exposure to all FR than adults, due to higher dust ingestion rates (average exposure scenario 20 and 50 mg per 24 h, for adults and toddlers, respectively; high exposure scenario, 50 and 200 mg per 24 h for adults and toddlers, respectively) and lower body weight (12.3 kg for toddlers and 70 kg for adults). Close-to-floor activity and more frequent hand-mouth-contact are rationales behind using higher dust ingestion rates for toddlers. In the worst case scenario, estimated exposure of British toddlers from dust ingestion were 890, 17,900, and 650 ng kg bw^{-1} day^{-1} for ΣPBDEs, Σm-PFRs and ΣEHFRs, respectively; while the estimated exposures for Norwegian toddlers were equal to 60, 1,600, and 40 ng kg bw^{-1} day^{-1} for ΣPBDEs, Σm-PFRs and ΣEHFRs, respectively. Contrary to the exposure of Norwegian toddlers, the estimated exposure of BDE209 for British toddlers in the worst case scenario was equal to 820 ng kg bw^{-1} day^{-1}, about 12% of the daily reference dose (RfD) (7,000 ng kg bw^{-1} day^{-1}) (Table SI-17). Based on our assessment, Norwegian stay-home adults and toddlers, have one order of magnitude lower exposure of ΣPBDEs and Σm-PFRs from average dust ingestion (50 mg) than British adults and toddlers. For TBOEP exposure with average dust intake rate, Norwegian stay-home adults (median 5.3 ng kg bw^{-1} day^{-1}) and toddlers (median 75 ng kg bw^{-1} day^{-1}) were two-fold higher compared to British

counter parts (2.3 and 33 ng kg bw^{-1} day^{-1} respectively). However, Norwegian adults and toddlers were found to have lower exposure for other m-PFRs and o-PFRs, such as TPHP and BDP, set below the proposed RfD values (Table SI-16&17). (Ali et al., 2013) reported slightly higher exposure to ΣPBDEs for both adult and toddler via house dust ingestion in Kuwait compared to Norway, but lower than our British non-workers. For Σm-PFRs and ΣEHFRs, the calculated intake for adults and toddlers from Kuwait and Pakistan were lower compared to our study for Norwegians and British non-workers. In another study from Norway, slightly higher median exposure of ΣPBDEs (female 0.4 ng kg bw^{-1} day^{-1}, children 1 ng kg bw^{-1} day^{-1}) and Σm-PFRs (female 16 ng kg bw^{-1} day^{-1}, children 133 ng kg bw^{-1} day^{-1}) were reported compared to our assessment for Norwegians (Cequier et al., 2014), but lower than our British stay-home adult.

With 8 h of exposure (50 mg day^{-1} dust intake rate), the estimated exposures of British workers for ΣPBDEs, Σm-PFRs and ΣEHFRs were higher than Norwegian non-workers (Table SI-15&16). Estimated exposure for British workers to ΣEHFRs was nearly two-fold higher (median 0.55 ng kg bw^{-1} day^{-1}) than British stay-home adults (median 0.36 ng kg bw^{-1} day^{-1}), unlike ΣPBDEs and Σm-PFRs exposures in these population groups. Given the small sample size in our study from UK stores and offices, we present here FR estimated intakes for the two dust sample groups combined as a general exposure scenario for British employees with 8h exposure duration. A more elaborate view on estimated intakes for all FRs for individual offices and stores is available in SI. Briefly, in average and high dust ingestion rate scenarios, exposure for ΣPBDEs, Σm-PFRs and ΣEHFRs between UK office employees (SI Table 18) and UK stores employees (SI Table 19) were found to be within a comparable range. In worst case scenario, estimated intakes for British-based toys store employees were 14-fold lower for EHDPHP than TBOEP, reaching 30 and 434 ng kg bw^{-1} day^{-1}, respectively. The second highest estimated intake for TBOEP was found for employees in a British-based store selling office supplies, electronics and furniture equal to 147 and 368 ng kg bw^{-1} day^{-1} in average and high dust ingestion rates, respectively. The two cases of store employees (in toys store and office supplies store) did not exceed the proposed RfD for TBOEP ($1.5x10^4$ ng kg bw^{-1} day^{-1}) in both dust ingestion rate scenarios and 8h of exposure. Human exposure via dust ingestion has never been estimated for most o-PFRs, except BDP and RDP (Brandsma et al., 2013). Among all o-PFRs, in most scenarios, the highest intakes via dust ingestion were calculated for iDPP, followed by BDP or TXP (Table 1). Considering 8h of exposure during a workday, British employees were found to have higher estimated exposure of individual o-PFRs than British and Norwegian stay-home adults (24 h) (Table 1). The worst-case scenario for iDPP was estimated for employees in a British-based toy store, where the estimated exposure was 34.6 ng kg bw^{-1} day^{-1}, nearly three-fold higher than the average dust intake scenario, set considerably below the proposed LOAEL (Table 1). In the worst case scenario for toddlers, Norwegian toddlers may have an exposure of equal to 11.3 ng kg bw^{-1} day^{-1} for BDP, while British toddlers have TXP exposure equal to 8.7 ng kg bw^{-1} day^{-1}. In contrast, for Dutch and Greek toddlers (worst case scenario), higher BDP

exposures were reported equal to 1,100 ng kg bw^{-1} day^{-1} and 750 ng kg bw^{-1} day^{-1}, respectively; while their RDP exposure were also thousand-fold higher than our assessment (Brandsma et al., 2013). Based on findings in this study, exposure to TDBPP does not seem to raise major toxicological concerns for humans, as TDBPP was rarely detected in our dust samples or other environmental samples (Lopez et al., 2011).

4. Conclusions

Our study reports levels of legacy and alternative FRs in house dust samples from Norway and the UK, as well as from British stores and offices. The median levels of m-PFRs were found to be considerably higher in all environments compared to EHFRs, PBDEs and o-PFRs. Due to higher FR concentrations in British house dust samples, the estimated human intakes for FRs for toddlers in Britain were found to be higher than toddlers in Norway. However, the small number and representativeness of samples analysed in the present study should be carefully considered as it represents a major uncertainty in these intake calculations. In the worst case scenario, BDE209 estimated intake for British toddlers did not exceed the proposed RfD, yet it was considerably higher than for Norwegian toddlers, thus setting British toddlers more prone to potentially adverse health effects related to BDE209 exposure compared to Norwegian ones. This is the first study reporting human exposure via dust ingestion for most o-PFRs. Toddler estimated intakes for o-PFRs were found to be higher than stay-home adults in both countries. In the worst case scenario, iDPP estimated intake for employees in a British-based toy store was considerably higher than for other o-PFRs, together with TDBPP and TXP. This is the first study reporting considerable concentrations of iDPP and TXP in the indoor environment of Norway and the UK. iDPP and TXP together with other halogen-free alternatives such as EHDPHP, are likely to be considered in the future as substances of high toxicological interest for two reasons: a) their potential for human exposure via dust ingestion is considerable and b) their toxicological potency to humans remains unresolved. TXP reproductive toxicity to humans has been reported (ECHA, 2013; Latendresse et al., 1994), while signs of teratogenic alterations have been observed when iDPP and EHDPHP were orally administered in rodents (Robinson et al., 1986) . Also, inhalation has been proposed as a significant route of exposure for several m-PFRs (Cequier et al., 2015; Schreder et al., 2016). Therefore, future research should be considered on the possible adverse health effects of o-PFRs in humans and potential alternative routes of exposure such as inhalation and dermal uptake, as well as measuring their levels in the indoor environment.

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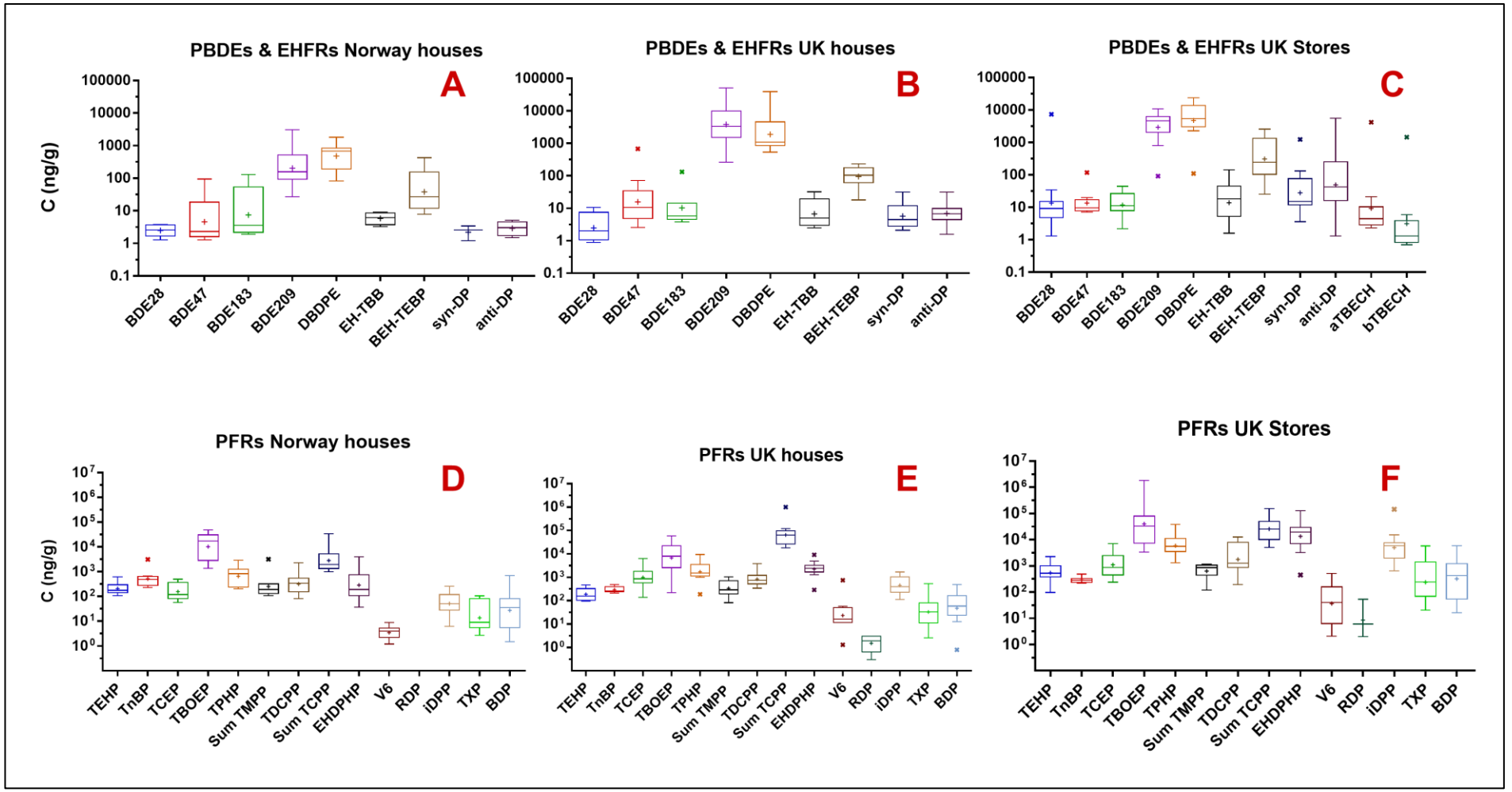

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720 Figure 1 - Boxplots of indoor dust concentrations for selected PBDEs, EHFRs and PFRs from Norwegian houses (A&D) (N=10), UK houses (B&E) (N=10) and
721 UK stores and offices (C&F) (N=12). Shown in the whiskers are 25th and 75th percentiles, median (central line), mean (+ symbol) and outlier (x symbol) values.
722 All data shown are log transformed. Please note the linear scale for concertation (ng g^{-1}) on y axis.

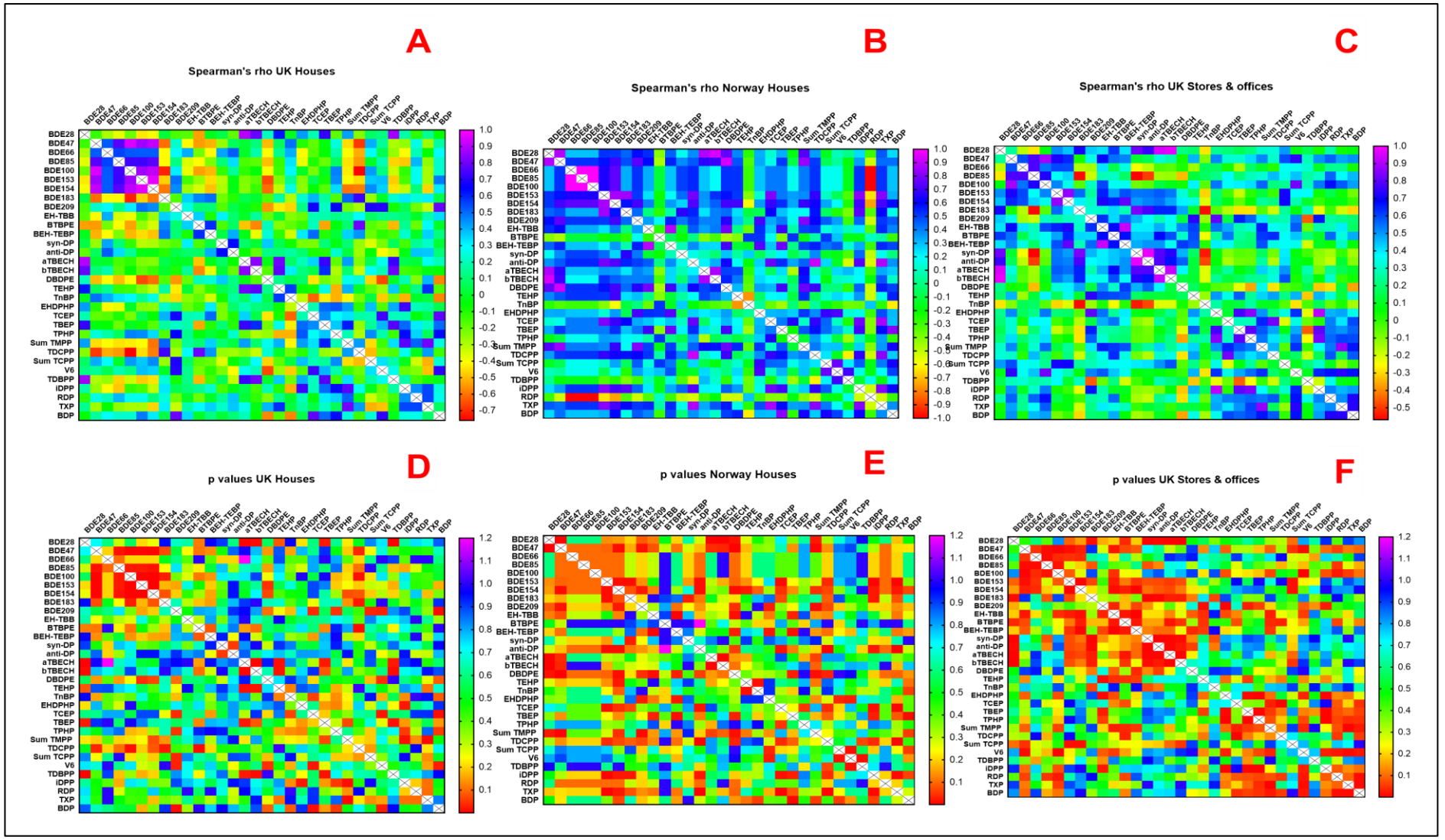

Figure 2 - Heat maps presenting Spearman's rank correlation (ρ) and p-values for all FRs in UK houses (2A&D),) Norwegian houses (2B&E) and UK stores nd offices (2C&F).

Table 1 - The estimated daily human intake (median and maximum) to selected PFRs in different scenario (ng kg bw^{-1} day^{-1}).

Human exposure assessment for selected PFRs (ng kg bw^{-1} day^{-1})											
	Compound	Stay-home toddler (t=24h)				Stay-home adult (t=24h)				Adult at work (t=8h)	
		UK houses		Norway houses		UK houses		Norway houses		UK offices and Stores	
		Median	Maximum	Median	Maximum	Median	Maximum	Median	Maximum	Median	Maximum
Normal exposure scenario (dust intake 50 mg/d)	**V6**	0.067	3.073	0.016	0.036	0.005	0.216	0.001	0.003	0.004	0.049
	TDBPP	0.002	0.002	0.002	0.003	<0.001	<0.001	<0.001	<0.001	<0.001	0.001
	iDPP	1.63	6.858	0.209	1.065	0.115	0.482	0.015	0.075	0.562	13.853
	RDP	0.008	0.013	0.007	0.007	0.001	0.001	0.001	0.001	0.001	0.005
	TXP	0.108	2.183	0.037	0.427	0.008	0.153	0.003	0.03	0.023	0.554
	BDP	0.272	1.972	0.144	2.833	0.019	0.139	0.01	0.199	0.046	0.565
High exposure scenario (dust intake 200 mg/d)	**V6**	0.27	12.293	0.066	0.143	0.012	0.54	0.003	0.006	0.010	0.122
	TDBPP	0.008	0.008	0.01	0.011	<0.001	<0.001	<0.001	0.001	0.001	0.004
	iDPP	6.52	27.431	0.834	4.26	0.286	1.205	0.037	0.187	1.404	34.632
	RDP	0.031	0.05	0.029	0.029	0.001	0.002	0.001	0.001	0.001	0.013
	TXP	0.431	8.732	0.148	1.707	0.019	0.384	0.007	0.075	0.058	1.386
	BDP	1.086	7.886	0.576	11.333	0.048	0.346	0.025	0.498	0.115	1.412

***** Normal scenario was considered for dust intake of 20 mg and 50 mg per 24 h, for adults and toddlers, respectively; while for high exposure scenario, 50 mg and 200 mg per 24 h, respectively, dust exposures were considered for stay-home adults and toddlers. Daily exposure for working adults in UK stores and offices has been estimated as well using the same parameters (median, maximum, ingestion rate), but for 8h exposure duration. Body weights, 70 kg for adults and 12.3 kg for toddlers, were applied for the estimation