

## Polybrominated diphenyl ethers in UK human milk

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1       **Polybrominated diphenyl ethers in UK human milk; Implications for**  
2       **infantile exposure and relationship to external exposure**

3  
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23

24 **Abstract**

25 Fourteen tri-deca polybrominated diphenyl ethers (PBDEs) were investigated in 35 human  
26 milk samples from Birmingham, UK. While none of the hepta-nona BDEs (the main  
27 components of the OctaBDE technical mixture) were above the limit of quantitation (LOQ);  
28 BDE-47 (average concentration = 3.3 ng g<sup>-1</sup> lipid weight (lw)) was quantified in all samples  
29 contributing 34-74% to Σtri-hexa BDEs (the principal constituents of the PentaBDE  
30 commercial formulation). BDE-209 (the main congener in the DecaBDE formulation) was  
31 present above the LOQ in 69% of samples (average concentration = 0.31 ng g<sup>-1</sup> lw).  
32 Concentrations of Σtri-hexa BDEs ranged from 0.2-26 ng g<sup>-1</sup> lw with concentrations of BDE-  
33 47 > BDE-153 > BDE-99. While concentrations of Σtri-hexa BDEs in this study (average =  
34 5.95 ng g<sup>-1</sup> lw) were at the high end of those reported from other European countries,  
35 concentrations of BDE-209 were lower than those reported in human milk from other  
36 countries. The average exposure of a UK nursing infant to Σtri-hexa BDEs (35 ng (kg bw)<sup>-1</sup>  
37 day<sup>-1</sup>) via breast milk exceeded the upper-bound dietary intakes of both UK adults and  
38 toddlers. Using a simple one compartment pharmacokinetic model, PBDE intakes of UK  
39 adults via inhalation, diet and dust ingestion were converted to predicted body burdens.  
40 Predictions compared well with those observed for Σtri-hexa BDEs and BDE-209 in breast  
41 milk.

42 **Keywords:** PBDEs, human milk, infant exposure, BDE 209.

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## 50 **Introduction**

51 Polybrominated diphenyl ethers (PBDEs) have been extensively used as flame retardants for  
52 a wide range of consumer products including furniture, carpets, mattresses and casings for  
53 electronic equipment (BSEF 2013). Three technical PBDE formulations were commercially  
54 available: Penta (consisting primarily of BDE-47 and BDE-99 – 38-49% each, alongside  
55 smaller amounts of other tri- to hepta-BDEs), Octa (a mixture of hexa- to deca-BDEs – the  
56 exact congener composition varying substantially between the two principal formulations  
57 marketed) and Deca (92-97% decabromodiphenyl ether – BDE 209 – plus nona- (principally)  
58 and octa-BDEs) (La Guardia, et al. 2006). DecaBDE has dominated worldwide production  
59 with a global market demand of 56,100 tons in 2001, compared to 7,500 and 3,790 tons for  
60 PentaBDE and OctaBDE formulations respectively (BSEF 2013). Despite their utility, the  
61 persistence and bioaccumulative characters of these compounds have resulted in increasing  
62 concern over their potential adverse effects to human health (Frederiksen, et al. 2009; Harrad,  
63 et al. 2010). Animal studies have shown PBDEs to pose potential health risks including:  
64 endocrine disruption, neurodevelopmental and behavioural outcomes, hepatic abnormality  
65 and possibly cancer (Birnbaum and Staskal 2004; Darnerud 2008; Hakk 2010; Wikoff and  
66 Birnbaum 2011). The few data available from human epidemiological studies imply effects  
67 on: male reproductive hormones (Johnson, et al. 2013; Palace, et al. 2010), semen quality  
68 (Akutsu, et al. 2008), thyroid hormone homeostasis (Turyk, et al. 2008), cryptorchidism  
69 (Crump, et al. 2010), behavioral factors in pregnant women (Buttke, et al. 2013), as well as  
70 lower birth weight and length (Chao, et al. 2007; Lignell, et al. 2013). Such evidence has  
71 contributed to complete EU bans for Penta and OctaBDE, and restrictions on the use of  
72 DecaBDE in addition to other restrictions within several jurisdictions on the manufacture and  
73 new use of the three commercial PBDE formulations across the world (Harrad, et al. 2010).  
74 Moreover, PBDEs associated with Penta and OctaBDE have been listed under the UNEP

75 Stockholm Convention on POPs, while DecaBDE is currently under consideration for listing  
76 under Annexes A, B and/or C to the convention (Stockholm convention on POPs 2009).  
77 Despite such restrictions, human exposure to PBDEs is likely to continue for the foreseeable  
78 future, given their persistence and ubiquity of flame-retarded consumer materials (Harrad and  
79 Diamond 2006).

80 Several studies have reported different levels of PBDEs in various human tissues including  
81 serum, placenta, liver, adipose tissue and breast milk from different European, Asian and  
82 North American countries in the last few years (Cui, et al. 2012; Frederiksen, et al. 2009).  
83 These biomonitoring data provide a direct measurement of the human body burden of BFRs  
84 resulting from various external exposure pathways (e.g. inhalation, ingestion of dust, diet and  
85 water) and contribute to the risk assessment of such compounds. However, the only available  
86 information on BFRs in UK human samples is for tri- to hexa-BDEs (major components of  
87 the PentaBDE commercial product) where the median concentrations for  $\Sigma$ tri-to hexa-BDEs  
88 in human milk and serum samples collected in 2003 were 6.3 and 4.18 ng g<sup>-1</sup> lipid weight  
89 (lw) respectively (Kalantzi, et al. 2004). In addition, BDE-209 was detected in 11 out of 153  
90 serum samples at concentrations from 0.015-0.240 ng g<sup>-1</sup> lw) (Thomas, et al. 2006).

91 Current understanding is that non-occupational human exposure to PBDEs occurs mainly via  
92 a combination of diet, air and indoor dust (either via ingestion or dermal contact)  
93 (Frederiksen, et al. 2009; Lorber 2008; Trudel, et al. 2011). However, the extent to which the  
94 known contamination of indoor environments with PBDEs influences human body burdens  
95 remains unclear. While some studies have managed to establish significant positive  
96 correlations between the levels of PBDEs in food or indoor dust and their concentrations in  
97 human milk or serum (Dunn, et al. 2010; Thomsen, et al. 2008; Wu, et al. 2007); such  
98 correlations could not be established in other studies (Roosens, et al. 2009; Wang, et al.  
99 2013). An alternative approach involved application of a simple pharmacokinetic model to

100 predict the body burdens of PBDEs in American adults using intake data from different  
101 exposure pathways. The predicted body burdens were then compared to the reported levels of  
102 PBDEs in human matrices and the relationship between external and internal exposure of  
103 American adults to PBDEs was discussed (Lorber 2008).

104 To address this paucity of UK human biomonitoring data for PBDEs, this study reports  
105 concentrations of  $\Sigma$ tri-hexa BDEs and *for the first time* BDE-209 in 35 human milk samples  
106 from Birmingham, UK. These data are then used to estimate the dietary exposure of UK  
107 nursing infants under different exposure scenarios. Finally, a simple, one-compartment  
108 pharmacokinetic model is applied to predict the body burdens of the studied PBDEs in UK  
109 adults (using indoor air and dust levels reported elsewhere by our research group for  
110 Birmingham, UK (Abdallah and Harrad 2010; Harrad and Abdallah 2011; Harrad, et al.  
111 2006; Harrad, et al. 2008a). The model predictions are then compared to the concentrations of  
112 target compounds measured in the analyzed human milk samples (used as indicator of adult  
113 female body burdens) for further understanding of the relationship between external and  
114 internal human exposure to PBDEs in UK adults.

## 115 **Materials and Methods**

### 116 *Sample collection*

117 Breast milk samples (each comprising ~50 mL) were obtained from 35 adult healthy  
118 primiparous volunteers via Birmingham Women's Hospital Milk Bank after the study  
119 protocol was approved by Warwickshire Research Ethics Committee and the R&D  
120 Department in Birmingham Women's NHS foundation trust. Informed consent was obtained  
121 from all the participants before sample collection. Samples collected in 2010 were kept in  
122 clean screw-capped glass containers and transferred from the Milk Bank to the laboratory in  
123 special ice boxes then stored at -20°C until the time of analysis. Due to ethical regulations,

124 the samples were collected in a completely anonymous fashion with all participant  
125 information kept strictly confidential. For the purpose of this study, only 1 milk sample was  
126 collected from each mother during her first 6 month of lactation.

### 127 *Sample extraction*

128 Accurately weighted aliquots of the freeze-dried samples (~ 2 g) were loaded into pre-  
129 cleaned 66 mL Accelerated Solvent Extraction (ASE 300, Dionex Inc., UK) cells containing  
130 1.5 g florisil, 3 g alumina, 5 g anhydrous Na<sub>2</sub>SO<sub>4</sub> and hydromatrix (Varian Inc., UK) to fill  
131 the void volume of the cells, spiked with 25 ng of each of <sup>13</sup>C-labelled BDE-47, BDE-99,  
132 BDE-153, BDE-183, BDE-209 as internal (surrogate) standards. The ASE cells were  
133 extracted with hexane:dichloromethane (1:9, v/v) at 90 °C and 1500 psi. The heating time was  
134 5 minutes, static time 4 min, purge time 90 s, flush volume 50%, with three static cycles. The  
135 lipid weight of the studied samples was determined gravimetrically on separate aliquots using  
136 a standard procedure (The European Standard EN 1528-2, 1996; see supplementary data for  
137 more details).

138

### 139 *Sample Clean-up*

140 The crude extracts were concentrated to 0.5 mL using a Zymark Turbovap® II (Hopkinton,  
141 MA, USA) then washed with 3 mL of 98% sulfuric acid. After phase separation, the hexane  
142 layer was transferred onto a florisil column topped with sodium sulfate and eluted with 25  
143 mL of hexane:dichloromethane (1:1, v/v). The eluate was evaporated to dryness under a  
144 gentle stream of N<sub>2</sub> and the dried extract reconstituted in 200 µL of <sup>13</sup>C-BDE-100 (25 pg µL<sup>-1</sup>  
145 in methanol) used as recovery determination (or syringe) standard to determine the recoveries  
146 of internal standards for QA/QC purposes.

147

148 *LC-APPI-MS/MS analysis*

149 Sample analysis was carried out using an LC-MS/MS system composed of a dual pump  
150 Shimadzu LC-20AB Prominence liquid chromatograph equipped with SIL-20A autosampler,  
151 a DGU-20A3 vacuum degasser coupled to a Sciex API 2000 triple quadrupole mass  
152 spectrometer. Details of the multi-residue analytical methodology used for separation and  
153 quantification of the studied PBDEs can be found elsewhere (Abdallah, et al. 2009). (A brief  
154 description is given in the supplementary data section).

155

156 *Comparison of PBDE intake to human body burdens.*

157 We have previously estimated UK adult intake of the target PBDEs via inhalation, dust  
158 ingestion and diet (Harrad and Abdallah 2011; Harrad, et al. 2006; Harrad, et al. 2008a;  
159 Harrad, et al. 2008b) (A summary of the assumptions on which these estimations are based is  
160 provided as supplementary data). To examine the relationship between these estimated  
161 intakes and the body burdens indicated via human milk samples, a simple one-compartment,  
162 first order pharmacokinetic (PK) model was used. The studied PBDEs were hypothesized to  
163 accumulate in lipids (the single compartment in the model). Therefore, the change in PBDE  
164 lipid concentration over time can be expressed by equation 1 (Lorber 2008).

165 
$$\frac{\delta C_{PBDE}}{\delta t} = \frac{I_{PBDE}(t) \times AF_{PBDE}}{BL(t) - K_{PBDE} \times C_{PBDE}(t)} \quad (1)$$

166 Where  $C_{PBDE}$  is the compound specific concentration in lipids ( $\text{ng g}^{-1} \text{lw}$ );  $I_{PBDE}$  is the daily  
167 intake of the target BFR ( $\text{ng day}^{-1}$ );  $AF_{PBDE}$  is the absorption fraction (unitless);  $BL$  is body  
168 lipid mass (g) and  $K_{PBDE}$  is the compound specific first order dissipation rate ( $\text{day}^{-1}$ ).



169 If  $K_{PBDE}$  is assumed to be constant over time then equation 1 can be solved into:

$$170 \quad C_{PBDE}(t) = C_{PBDE}(0) \times e^{(-K_{PBDE} \cdot t)} + \left[ \frac{(I_{PBDE}(t) \times AF_{PBDE})}{BL(t)} \right] \times \left[ \frac{(1 - e^{(-K_{PBDE} \cdot t)})}{K_{PBDE}} \right] \quad (2)$$

171 Where  $C_{PBDE}(0)$  is the studied PBDE body lipid concentration at time 0 (initial concentration  
172 before intake).

173 Assuming a constant dose over time at constant body lipid mass, the steady state PBDE lipid  
174 concentration can be calculated from equation 3. It is stressed that the assumption of steady  
175 state conditions is an inherent uncertainty with this approach.

$$176 \quad C_{PBDE} = \frac{(I_{PBDE} \times AF_{PBDE})}{BL \times K_{PBDE}} \quad (3)$$

#### 177 *Quality assurance/Quality control*

178 Good recoveries (68-106%) of the  $^{13}\text{C}$ -labelled internal standards were obtained for all the  
179 studied compounds (table SI-4). Further evaluation of the method extraction/clean up  
180 performance was achieved via spiking milk samples (n=6) with  $^{13}\text{C}$ -BDE-154 prior to freeze  
181 drying and excellent recoveries (>90%) were obtained (table SI-5).

182 No target compounds were detected in method blanks (n=5; consisting of 2 g pre-extracted  
183 anhydrous sodium sulfate treated exactly as a sample) or field blanks (n=5; consisting of ~2 g  
184 of broken pieces of the glass milk containers treated exactly as a sample). Therefore, there  
185 was no need for blank correction of concentrations and method limits of detection (LOD) and  
186 quantification (LOQ) were estimated based on 3:1 and 10:1 S:N ratios respectively.

187 The accuracy and precision of the analytical method applied for PBDE determination was  
188 assessed via replicate analysis (n=10) of NIST SRM 2585. The results obtained compared  
189 favourably with the reported reference values (table SI-6a).

## 190 **Results and discussion**

### 191 *Concentrations of $\Sigma$ tri-hexa BDEs in UK human milk*

192 While none of the investigated hepta- to nona-BDE congeners were above LOQ, BDE-47  
193 was quantified in all the analysed samples contributing 34-74% to  $\Sigma$ tri-hexa BDEs (Table 1).  
194 The predominant BDE congeners in the studied human milk were in the order BDE-47 >  
195 BDE-153 > BDE-99. These 3 congeners constituted an average of 85% of the quantified  $\Sigma$ tri-  
196 hexa BDEs in the studied samples. This is in agreement with previous reports of PBDEs in  
197 human milk from various countries (Frederiksen, et al. 2009). Interestingly, a higher average  
198 level of BDE-153 (1100 pg g<sup>-1</sup> lw) than that of BDE-99 (710 pg g<sup>-1</sup> lw) was observed (Table  
199 1). While this differs from the relative contribution of these 2 PBDE congeners in the  
200 commercial PentaBDE formulations (La Guardia, et al. 2006), several authors have reported  
201 higher levels of BDE-153 than BDE-99 in human milk (Ben Hassine, et al. 2012; Dunn, et al.  
202 2010; Frederiksen, et al. 2009). In addition, a recent study has reported BDE-153 as the  
203 dominant congener in 5 human breast milk samples from California (Park, et al. 2011).  
204 Furthermore, a study of PBDEs in human milk from the Faroe islands also reported  
205 predominance of BDE-153 (Fangstrom, et al. 2005). However, such high levels of BDE-153  
206 could not be associated with high consumption of seafood diet in the studied population,  
207 indicating that dietary exposure was not the reason for the elevated BDE-153 concentrations  
208 in breast milk. Therefore, we hypothesize that the relatively higher contribution of BDE-153  
209 to  $\Sigma$ tri-hexa BDEs in human milk samples than expected from the PentaBDE technical  
210 mixture may be attributed to 2 main factors:

211 First, the high bioaccumulation potential of BDE-153 in lipids (as evidenced by a half-life of  
212 6.5 years compared to 1.8 and 2.9 years for BDE-47 and BDE-99 respectively (Geyer, et al.  
213 2004)) which indicates that over time, BDE-153 will become the predominant congener in  
214 the body.

215 Second, the possible production of BDE-153 as a result of BDE-209 metabolic stepwise  
216 meta-meta debromination (Roberts, et al. 2011). This stepwise debromination was previously  
217 observed in peregrine falcon eggs from California, where BDE-153 was the dominant  
218 congener only in eggs with high levels of BDE-209 (Holden, et al. 2009). Interestingly, while  
219 concentrations of BDE-153 in this study were significantly ( $r = 0.443$ ;  $p < 0.01$ ) correlated  
220 with those of BDE-209, no other statistically significant ( $p < 0.05$ ) correlation was observed  
221 between BDE-209 levels and any of the PBDE congeners or  $\Sigma$ tri-hexa BDEs in the analyzed  
222 samples. This further supports the hypothesis that metabolic degradation of BDE-209 yields  
223 the highly bioaccumulative BDE-153 resulting in elevated concentrations of the latter in  
224 human milk.

225 While the levels of  $\Sigma$ tri-hexa BDEs in this study (Table 1) are slightly lower than those  
226 reported in UK human milk samples collected in 2003 ( $n=54$ , average =  $6.3 \text{ ng g}^{-1} \text{ lw}$ ), these  
227 concentrations are still at the high end of those reported from other European, Asian, African  
228 and Australasian countries (Table 2). On the other hand,  $\Sigma$ tri-hexa BDEs in UK human milk  
229 are substantially lower than those reported from USA and Canada (Table 2) which is in  
230 agreement with the far more extensive production and use of the PentaBDE technical  
231 formulation in North America than elsewhere (BSEF 2013).

232

### 233 *Concentrations of BDE-209 in UK human milk*

234 BDE-209 was above LOQ in 69% of the studied milk samples ranging from  $<0.06$ - $0.92 \text{ ng g}^{-1}$   
235  $\text{ lw}$  (Table 1). To the authors' knowledge, this paper is the first to report concentrations of

236 BDE-209 in UK human milk. Interestingly, these levels are at the lower end of BDE-209  
237 concentrations reported in human milk from other European countries (Table 2) despite the  
238 substantially higher levels of this BFR reported in UK indoor dust compared to the rest of  
239 Europe (Harrad, et al. 2010) and the reported higher usage of BDE 209 in the UK than other  
240 EU countries (EU Risk Assessment Report 2002). This may indicate that while indoor dust  
241 ingestion is the major pathway of external human exposure to BDE-209 (Harrad, et al. 2008a;  
242 Lorber 2008), the high levels of this compound in indoor dust do not significantly contribute  
243 to human body burdens. Our research group have recently reported on the very low  
244 bioaccessibility (~14%) of BDE-209 in indoor dust across the human gastrointestinal tract  
245 (GIT) following oral ingestion (Abdallah, et al. 2012), consistent with animal studies  
246 reporting low bioavailability (4-26%) of BDE-209 (Huwe and Smith 2007; Sandholm, et al.  
247 2003). Such poor uptake of BDE-209 from the GIT, combined with its very short human  
248 half-life ( $t_{0.5} = 7$  days, (Geyer, et al. 2004) and its preferential partitioning to serum rather  
249 than milk fat (Mannetje, et al. 2012) may result in the apparently low influence of BDE-209  
250 concentrations in indoor dust on UK adult body burdens.

251

252 *Nursing infants' dietary intake of PBDEs via breast milk:*

253 Breast milk is a recognized medium for direct transfer of POPs to nursing infants. To  
254 estimate the nursing infants' dietary intake of the studied BFRs via breast milk, equation 4  
255 was used.

256 
$$Di = \frac{C_{PBDE} \times F_{lipid}}{Bw} \dots\dots\dots(4)$$

257 Where  $Di$  is the estimated dietary intake ( $\text{ng kg}^{-1} \text{bw day}^{-1}$ );  $C_{PBDE}$  is the concentration of  
258 target PBDE in milk ( $\text{ng g}^{-1} \text{lw}$ );  $F_{lipid}$  is the daily lipid intake via breast milk ( $\text{g day}^{-1}$ ) and  $Bw$   
259 is the body weight (4.14 kg) (U.S. EPA 2002.). The infant's daily lipid intake via breast milk

260 ( $F_{lipid}$ ) was calculated based using U.S. EPA guidelines (U.S. EPA 2002.) which suggest an  
261 average intake of 702 mL milk per day for a 1 month old infant weighing 4.14 kg. The  
262 median lipid content of the analyzed milk samples was 3.47 g lipid per 100 mL of breast milk  
263 resulting in a daily lipid intake of 24.4 g lipid day<sup>-1</sup>.

264 Table 3 shows the estimated dietary intake of target PBDEs via breast milk using different  
265 exposure scenarios (in which exposure factors (e.g. dust ingestion rate) were held constant  
266 but using different PBDE concentrations (e.g. 25<sup>th</sup> percentile) derived from our breast milk  
267 data). While the estimated average UK infant exposure to  $\Sigma$ tri-hexa BDEs is much lower than  
268 that in North America (Park, et al. 2011), a 1 month-old infant in the UK is still more  
269 exposed to  $\Sigma$ tri-hexa BDEs than in several other European countries via breast milk  
270 (Roosens, et al. 2010). Interestingly, the average exposure of a nursing infant to  $\Sigma$ tri-hexa  
271 BDEs via breast milk exceeded upper-bound dietary intakes of UK adults and toddlers (UK  
272 Food Standards Agency 2006) (Figure 1), while for BDE-209, dietary exposure was the most  
273 significant exposure pathway for toddlers.

274 The low concentrations of BDE-209 in the studied milk samples resulted in much lower  
275 exposure of UK nursing infants to this contaminant than the USEPA reference daily dose  
276 (RfD) of 7  $\mu$ g kg bw<sup>-1</sup> day<sup>-1</sup>. Similarly, our estimated UK infant daily intakes (Table 3) are  
277 lower than the USEPA reference doses for BDE-47 (100 ng kg bw<sup>-1</sup> day<sup>-1</sup> for  
278 neurodevelopmental toxicity) and  $\Sigma$ tri-hexa BDEs (2000 ng kg bw<sup>-1</sup> day<sup>-1</sup> for liver toxicity)  
279 (U.S.EPA 2008). However, the median level of  $\Sigma$ tri-hexa BDEs in this study (4.98 ng kg<sup>-1</sup>  
280 lw) is slightly higher than that associated with congenital cryptorchidism (4.16 ng kg<sup>-1</sup> lw;  
281  $p < 0.01$ ) in Danish-Finnish newborn boys (Crump, et al. 2010) and generally in line with  
282 levels associated with irregular menstruation periods in a Taiwanese population (Chao, et al.  
283 2010). While this does not provide solid evidence on the potential health effects associated  
284 with the reported levels of PBDEs in human milk due to the lack of relevant studies in the

285 UK, our results certainly raise concerns about potential adverse effects resulting from  
286 exposure of infants and mothers to PBDEs. Although breastfeeding mothers should be  
287 encouraged and supported due to the well-documented beneficial effects of breast feeding,  
288 scientific studies ought to characterize and measure the contaminants in breast milk so that  
289 protective measures may be provided, if necessary, to avoid any potential harmful effects on  
290 the mother or the newborn.

291

### 292 *Comparison of PBDEs intake to human body burdens*

293 To convert daily adult intakes of BFRs via different exposure pathways to expected body  
294 burdens, the bioaccessible fractions of each target compound (Abdallah, et al. 2012) were  
295 used in equation 3 to substitute for  $AF_{PBDE}$  in case of exposure via dust ingestion or diet,  
296 while the inhalable fraction was assumed to be 100% bioavailable. The body lipid mass was  
297 estimated based on a 25% body fat for an average adult weighing 70 kg (U.S. EPA 1997).  
298 Finally,  $K_{PBDE}$  was calculated as  $0.693/t_{0.5}$ ; where  $t_{0.5}$  is the half-life of the studied BFR in the  
299 body lipid compartment (Geyer, et al. 2004).

300 In general, good agreement was observed between the predicted and the observed body  
301 burdens of main target PBDEs (table 4) given the simplicity of the model used (e.g. only one  
302 body compartment was studied), the dearth of information regarding the half-lives of  
303 different PBDE congeners in various compartments of the human body, and the uncertainty  
304 about the bioavailability of the studied compounds from different exposure routes.

305 In addition, the PK model used here does not estimate human exposure via routes such as  
306 dermal contact and water intake. This is due to the high uncertainty and complete absence of  
307 experimental data on the extent of BFR absorption via dermal contact by humans coupled  
308 with the expected minimal contribution of water intake to the overall daily exposure to BFRs  
309 based on the very low aqueous solubility of PBDEs.

310 Nevertheless, the good agreement between the predicted and observed results indicates that  
311 the studied exposure routes are the main pathways driving UK adult body burdens of PBDEs.  
312 This is in line with the findings of Lorber (Lorber 2008) who studied the exposure of  
313 Americans to PBDEs and reported indoor dust ingestion as the main route of exposure  
314 followed by diet and inhalation. However, more research is required for assessment of the  
315 bioavailability of various PBDEs via different exposure routes and determination of  $t_{0.5}$  of  
316 PBDEs in various human tissues.

317

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320 bank (Heather Barrow, Jenny Harris and Anne Hemming). We also thank Kelly Hard (R & D  
321 manager at Birmingham Women's Hospital) for helping with the ethical issues for this  
322 project.

323

### 324 **Supplementary data**

325 Specific details of analytical methodology, exposure estimation, QA/QC measurements and  
326 concentrations of target BFRs in each sample are available as supplementary data.

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336 **References**

- 337 Abdallah, M.A.-E.; Tilston, E.; Harrad, S.; Collins, C. In vitro assessment of the bioaccessibility of  
338 brominated flame retardants in indoor dust using a colon extended model of the human  
339 gastrointestinal tract. *J Environ Monitor.* 14:3276-3283; 2012
- 340 Abdallah, M.A.; Harrad, S. Modification and calibration of a passive air sampler for monitoring vapor  
341 and particulate phase brominated flame retardants in indoor air: application to car interiors.  
342 *Environ Sci Technol.* 44:3059-3065; 2010
- 343 Abdallah, M.A.; Harrad, S.; Covaci, A. Isotope dilution method for determination of polybrominated  
344 diphenyl ethers using liquid chromatography coupled to negative ionization atmospheric pressure  
345 photoionization tandem mass spectrometry: validation and application to house dust. *Anal Chem.*  
346 81:7460-7467; 2009
- 347 Akutsu, K.; Takatori, S.; Nozawa, S.; Yoshiike, M.; Nakazawa, H.; Hayakawa, K., et al.  
348 Polybrominated diphenyl ethers in human serum and sperm quality. *B Environ Contam Tox.*  
349 80:345-350; 2008
- 350 Alivernini, S.; Battistelli, C.L.; Turrio-Baldassarri, L. Human Milk as a Vector and an Indicator of  
351 Exposure to PCBs and PBDEs: Temporal Trend of Samples Collected in Rome. *B Environ*  
352 *Contam Tox.* 87:21-25; 2011
- 353 Antignac, J.P.; Cariou, R.; Zalko, D.; Berrebi, A.; Cravedi, J.P.; Maume, D., et al. Exposure  
354 assessment of French women and their newborn to brominated flame retardants: Determination of  
355 tri- to deca- polybromodiphenylethers (PBDE) in maternal adipose tissue, serum, breast milk and  
356 cord serum. *Environ Pollut.* 157:164-173; 2009
- 357 Ben Hassine, S.; Ben Ameer, W.; Gandoura, N.; Driss, M.R. Determination of chlorinated pesticides,  
358 polychlorinated biphenyls, and polybrominated diphenyl ethers in human milk from Bizerte  
359 (Tunisia) in 2010. *Chemosphere.* 89:369-377; 2012
- 360 Birnbaum, L.S.; Staskal, D.F. Brominated flame retardants: cause for concern? *Environ Health*  
361 *Perspect.* 112:9-17; 2004
- 362 BSEF. Bromine Science and Environmental Forum. [www.bsef.com](http://www.bsef.com) (accessed 17-15-2013); 2013
- 363 Buttko, D.E.; Wolkin, A.; Stapleton, H.M.; Miranda, M.L. Associations between serum levels of  
364 polybrominated diphenyl ether (PBDE) flame retardants and environmental and behavioral factors  
365 in pregnant women. *J Expo Sci Env Epid.* 23:176-182; 2013
- 366 Chao, H.-R.; Shy, C.-G.; Wang, S.-L.; Chen, S.C.-C.; Koh, T.-W.; Chen, F.-A., et al. Impact of non-  
367 occupational exposure to polybrominated diphenyl ethers on menstruation characteristics of  
368 reproductive-age females. *Environ Int.* 36:728-735; 2010
- 369 Chao, H.R.; Wang, S.L.; Lee, W.J.; Wang, Y.F.; Papke, O. Levels of polybrominated diphenyl ethers  
370 (PBDEs) in breast milk from central Taiwan and their relation to infant birth outcome and maternal  
371 menstruation effects. *Environ Int.* 33:239-245; 2007
- 372 Crump, D.; Egloff, C.; Chiu, S.; Letcher, R.J.; Chu, S.; Kennedy, S.W. Pipping Success, Isomer-  
373 Specific Accumulation, and Hepatic mRNA Expression in Chicken Embryos Exposed to HBCD.  
374 *Toxicol Sci.* 115:492-500; 2010
- 375 Cui, C.; Tian, Y.; Zhang, L.; Gao, Y.; Jin, J.; Wang, P., et al. Polybrominated diphenyl ethers  
376 exposure in breast milk in Shanghai, China: levels, influencing factors and potential health risk for  
377 infants. *Sci Total Environ.* 433:331-335; 2012
- 378 Currado, G.M.; Harrad, S. Comparison of polychlorinated biphenyl concentrations in indoor and  
379 outdoor air and the potential significance of inhalation as a human exposure pathway. *Environ Sci*  
380 *Technol.* 32:3043-3047; 1998
- 381 Darnerud, P.O. Brominated flame retardants as possible endocrine disrupters. *Int J Androl.* 31:152-  
382 160; 2008
- 383 Devanathan, G.; Subramanian, A.; Sudaryanto, A.; Takahashi, S.; Isobe, T.; Tanabe, S. Brominated  
384 flame retardants and polychlorinated biphenyls in human breast milk from several locations in  
385 India: Potential contaminant sources in a municipal dumping site. *Environ Int.* 39:87-95; 2012
- 386 Dunn, R.L.; Huwe, J.K.; Carey, G.B. Biomonitoring polybrominated diphenyl ethers in human milk  
387 as a function of environment, dietary intake, and demographics in New Hampshire. *Chemosphere.*  
388 80:1175-1182; 2010



389 EU Risk Assessment Report. European Union Risk Assessment Report on  
390 BIS(PENTABROMOPHENYL) ETHER. European Commission, Joint Research Centre,  
391 European Chemicals Bureau, EUR20402EN, 2002. Vol. 17; 2002

392 Fangstrom, B.; Strid, A.; Grandjean, P.; Weihe, P.; Bergman, A. A retrospective study of PBDEs and  
393 PCBs in human milk from the Faroe Islands. *Environ Health*. 4:12-21; 2005

394 Frederiksen, M.; Vorkamp, K.; Thomsen, M.; Knudsen, L.E. Human internal and external exposure to  
395 PBDEs--a review of levels and sources. *Int J Hyg Environ Health*. 212:109-134; 2009

396 Geyer, H.J.; Schramm, K.W.; Darnerud, P.O.; Aune, M.; Feicht, E.A.; Fried, K.W., et al. Terminal  
397 elimination half-lives of the brominated flame retardants TBBPA, HBCD, and lower brominated  
398 PBDEs in humans. *Organohalogen Compounds*. 66:3867-3872; 2004

399 Gomara, B.; Herrero, L.; Pacepavicius, G.; Ohta, S.; Alaei, M.; Gonzalez, M.J. Occurrence of co-  
400 planar polybrominated/chlorinated biphenyls (PXBs), polybrominated diphenyl ethers (PBDEs)  
401 and polychlorinated biphenyls (PCBs) in breast milk of women from Spain. *Chemosphere*. 83:799-  
402 805; 2011

403 Hakk, H. Different HBCD stereoisomers are metabolized differently. *Toxicol Lett*. 196:S33-S34;  
404 2010

405 Harrad, S.; Abdallah, M.A. Brominated flame retardants in dust from UK cars - within-vehicle spatial  
406 variability, evidence for degradation and exposure implications. *Chemosphere*. 82:1240-1245;  
407 2011

408 Harrad, S.; de Wit, C.A.; Abdallah, M.A.; Bergh, C.; Bjorklund, J.A.; Covaci, A., et al. Indoor  
409 contamination with hexabromocyclododecanes, polybrominated diphenyl ethers, and  
410 perfluoroalkyl compounds: an important exposure pathway for people? *Environ Sci Technol*.  
411 44:3221-3231; 2010

412 Harrad, S.; Diamond, M. New directions: Exposure to polybrominated diphenyl ethers (PBDEs) and  
413 polychlorinated biphenyls (PCBs): Current and future scenarios. *Atmos Environ*. 40:1187-1188;  
414 2006

415 Harrad, S.; Hazrati, S.; Ibarra, C. Concentrations of polychlorinated biphenyls in indoor air and  
416 polybrominated diphenyl ethers in indoor air and dust in Birmingham, United Kingdom:  
417 Implications for human exposure. *Environ Sci Technol*. 40:4633-4638; 2006

418 Harrad, S.; Ibarra, C.; Abdallah, M.A.; Boon, R.; Neels, H.; Covaci, A. Concentrations of brominated  
419 flame retardants in dust from United Kingdom cars, homes, and offices: causes of variability and  
420 implications for human exposure. *Environ Int*. 34:1170-1175; 2008a

421 Harrad, S.; Ibarra, C.; Diamond, M.; Melymuk, L.; Robson, M.; Douwes, J., et al. Polybrominated  
422 diphenyl ethers in domestic indoor dust from Canada, New Zealand, United Kingdom and United  
423 States. *Environ Int*. 34:232-238; 2008b

424 Holden, A.; Park, J.S.; Chu, V.; Kim, M.; Choi, G.; Shi, Y., et al. Unusual Hepta- and Octa-  
425 Brominated Diphenyl Ethers and Nona-Brominated Diphenyl Ether Profile in California, USA,  
426 Peregrine Falcons (*Falco peregrinus*): More Evidence for Brominated Diphenyl Ether-209  
427 Debromination. *Environ Toxicol Chem*:1; 2009

428 Huwe, J.K.; Smith, D.J. Accumulation, whole-body depletion, and debromination of  
429 decabromodiphenyl ether in male sprague-dawley rats following dietary exposure. *Environ Sci*  
430 *Technol*. 41:2371-2377; 2007

431 Johnson, P.I.; Stapleton, H.M.; Mukherjee, B.; Hauser, R.; Meeker, J.D. Associations between  
432 brominated flame retardants in house dust and hormone levels in men. *Sci Total Environ*. 445:177-  
433 184; 2013

434 Jones-Otazo, H.A.; Clarke, J.P.; Diamond, M.L.; Archbold, J.A.; Ferguson, G.; Harner, T., et al. Is  
435 house dust the missing exposure pathway for PBDEs? An analysis of the urban fate and human  
436 exposure to PBDEs. *Environ Sci Technol*. 39:5121-5130; 2005

437 Kalantzi, O.L.; Martin, F.L.; Thomas, G.O.; Alcock, R.E.; Tang, H.R.; Drury, S.C., et al. Different  
438 levels of polybrominated diphenyl ethers (PBDEs) and chlorinated compounds in breast milk from  
439 two UK regions. *Environ Health Persp*. 112:1085-1091; 2004

440 Kim, U.J.; Lee, I.S.; Kim, H.S.; Oh, J.E. Monitoring of PBDEs concentration in umbilical cord blood  
441 and breast milk from Korean population and estimating the effects of various parameters on  
442 accumulation in humans. *Chemosphere*. 85:487-493; 2011

443 La Guardia, M.J.; Hale, R.C.; Harvey, E. Detailed polybrominated diphenyl ether (PBDE) congener  
444 composition of the widely used penta-, octa-, and deca-PBDE technical flame-retardant mixtures.  
445 *Environ Sci Technol.* 40:6247-6254; 2006

446 Lignell, S.; Aune, M.; Darnerud, P.O.; Hanberg, A.; Larsson, S.C.; Glynn, A. Prenatal exposure to  
447 polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) may influence  
448 birth weight among infants in a Swedish cohort with background exposure: a cross-sectional study.  
449 *Environ Health-Glob.* 12; 2013

450 Lignell, S.; Aune, M.; Darnerud, P.O.; Soeria-Atmadja, D.; Hanberg, A.; Larsson, S., et al. Large  
451 variation in breast milk levels of organohalogenated compounds is dependent on mother's age,  
452 changes in body composition and exposures early in life. *J Environ Monitor.* 13:1607-1616; 2011

453 Lorber, M. Exposure of Americans to polybrominated diphenyl ethers. *J Expo Sci Env Epid.* 18:2-19;  
454 2008

455 Mannelje, A.t.; Coakley, J.; Mueller, J.F.; Harden, F.; Toms, L.-M.; Douwes, J. Partitioning of  
456 persistent organic pollutants (POPs) between human serum and breast milk: a literature review.  
457 *Chemosphere.* 89:911-918; 2012

458 Palace, V.; Park, B.; Pleskach, K.; Gemmill, B.; Tomy, G. Altered thyroxine metabolism in rainbow  
459 trout (*Oncorhynchus mykiss*) exposed to hexabromocyclododecane (HBCD). *Chemosphere.*  
460 80:165-169; 2010

461 Park, J.S.; She, J.W.; Holden, A.; Sharp, M.; Gephartg, R.; Souders-Mason, G., et al. High Postnatal  
462 Exposures to Polybrominated Diphenyl Ethers (PBDEs) and Polychlorinated Biphenyls (PCBs) via  
463 Breast Milk in California: Does BDE-209 Transfer to Breast Milk? *Environ Sci Technol.* 45:4579-  
464 4585; 2011

465 Roberts, S.C.; Noyes, P.D.; Gallagher, E.P.; Stapleton, H.M. Species-Specific Differences and  
466 Structure-Activity Relationships in the Debromination of PBDE Congeners in Three Fish Species.  
467 *Environ Sci Technol.* 45:1999-2005; 2011

468 Roosens, L.; Abdallah, M.A.; Harrad, S.; Neels, H.; Covaci, A. Factors influencing concentrations of  
469 polybrominated diphenyl ethers (PBDEs) in students from Antwerp, Belgium. *Environ Sci*  
470 *Technol.* 43:3535-3541; 2009

471 Roosens, L.; D'Hollander, W.; Bervoets, L.; Reynders, H.; Van Campenhout, K.; Cornelis, C., et al.  
472 Brominated flame retardants and perfluorinated chemicals, two groups of persistent contaminants  
473 in Belgian human blood and milk. *Environ Pollut.* 158:2546-2552; 2010

474 Sandholm, A.; Emanuelsson, B.M.; Wehler, E.K. Bioavailability and half-life of decabromodiphenyl  
475 ether (BDE-209) in rat. *Xenobiotica.* 33:1149-1158; 2003

476 Schecter, A.; Pavuk, M.; Papke, O.; Ryan, J.J.; Birnbaum, L.; Rosen, R. Polybrominated diphenyl  
477 ethers (PBDEs) in US mothers' milk. *Environ Health Persp.* 111:1723-1729; 2003

478 She, J.W.; Holden, A.; Sharp, M.; Tanner, M.; Williams-Derry, C.; Hooper, K. Polybrominated  
479 diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) in breast milk from the Pacific  
480 Northwest. *Chemosphere.* 67:S307-S317; 2007

481 Stapleton, H.M.; Kelly, S.M.; Pei, R.; Letcher, R.J.; Gunsch, C. Metabolism of Polybrominated  
482 Diphenyl Ethers (PBDEs) by Human Hepatocytes in Vitro. *Environ Health Persp.* 117:197-202;  
483 2009

484 Stockholm convention on POPs. Governments unite to step-up reduction on global DDT reliance and  
485 add nine new chemicals under international treaty.  
486 [http://chmpopsint/Convention/Pressrelease/COP4Geneva8May2009/tabid/542/language/en-](http://chmpopsint/Convention/Pressrelease/COP4Geneva8May2009/tabid/542/language/en-US/Default.aspx)  
487 [US/Default.aspx](http://chmpopsint/Convention/Pressrelease/COP4Geneva8May2009/tabid/542/language/en-US/Default.aspx) (accessed 5-6-2009); 2009

488 Sudaryanto, A.; Kajiwara, N.; Tsydenova, O.V.; Isobe, T.; Yu, H.X.; Takahashi, S., et al. Levels and  
489 congener specific profiles of PBDEs in human breast milk from China: Implication on exposure  
490 sources and pathways. *Chemosphere.* 73:1661-1668; 2008

491 Thomas, G.O.; Wilkinson, M.; Hodson, S.; Jones, K.C. Organohalogen chemicals in human blood  
492 from the United Kingdom. *Environ Pollut.* 141:30-41; 2006

493 Thomsen, C.; Knutsen, H.K.; Liane, V.H.; Froshaug, M.; Kvale, H.E.; Haugen, M., et al.  
494 Consumption of fish from a contaminated lake strongly affects the concentrations of  
495 polybrominated diphenyl ethers and hexabromocyclododecane in serum. *Mol Nutr Food Res.*  
496 52:228-237; 2008

497 Thomsen, C.; Stigum, H.; Froshaug, M.; Broadwell, S.L.; Becher, G.; Eggesbo, M. Determinants of  
498 brominated flame retardants in breast milk from a large scale Norwegian study. *Environ Int.* 36:68-  
499 74; 2010

500 Toms, L.M.; Hearn, L.; Kennedy, K.; Harden, F.; Bartkow, M.; Temme, C., et al. Concentrations of  
501 polybrominated diphenyl ethers (PBDEs) in matched samples of human milk, dust and indoor air.  
502 *Environ Int*; 2009

503 Trudel, D.; Scheringer, M.; von Goetz, N.; Hungerbuhler, K. Total consumer exposure to  
504 polybrominated diphenyl ethers in North America and Europe. *Environ Sci Technol.* 45:2391-  
505 2397; 2011

506 Turyk, M.E.; Persky, V.W.; Imm, P.; Knobeloch, L.; Chatterton, R.; Anderson, H.A. Hormone  
507 Disruption by PBDEs in Adult Male Sport Fish Consumers. *Environ Health Persp.* 116:1635-1641;  
508 2008

509 U.S. EPA. Exposure Factors Handbook, Vol. 1 - General Factors. EPA/ 600/P-95/002; US  
510 Government Printing Office: Washington, DC; 1997

511 U.S. EPA. Child-Specific Exposure Factors Handbook. EPA-600-P-00-002B; National Center for  
512 Environmental Assessment: Washington, DC; 2002.

513 U.S.EPA. 2,2',4,4'-Tetrabromodiphenyl ether (BDE-47) (CASRN 5436-43-1) Integrated Risk  
514 Information System US Environmental Protection Agency.  
515 <http://www.epa.gov/iris/toxreviews/1010tr.pdf> (accessed 14-7-2013); 2008

516 UK Food Standards Agency. Brominated chemicals: UK dietary intakes.  
517 <http://www.food.gov.uk/multimedia/pdfs/fsis1006pdf> (accessed 15/12/2008); 2006

518 Wang, T.; Han, S.L.; Ruan, T.; Wang, Y.W.; Feng, J.Y.; Jiang, G.B. Spatial distribution and inter-  
519 year variation of hexabromocyclododecane (HBCD) and tris-(2,3-dibromopropyl) isocyanurate  
520 (TBC) in farm soils at a peri-urban region. *Chemosphere.* 90:182-187; 2013

521 Wikoff, D.S.; Birnbaum, L. Human Health Effects of Brominated Flame Retardants. In: Eljarrat E,  
522 Barcelo D, eds. Brominated Flame Retardants; 2011

523 Wu, N.; Herrmann, T.; Paepke, O.; Tickner, J.; Hale, R.; Harvey, E., et al. Human exposure to  
524 PBDEs: Associations of PBDE body burdens with food consumption and house dust  
525 concentrations. *Environ Sci Technol.* 41:1584-1589; 2007

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539 **Tables**

540 **Table1: Statistical summary of PBDE concentrations (ng g<sup>-1</sup> lw) in human milk samples**  
541 **(n=35) from Birmingham, UK.**

	<b>BDE-47</b>	<b>BDE-49</b>	<b>BDE-85</b>	<b>BDE-99</b>	<b>BDE-100</b>	<b>BDE-153</b>	<b>BDE-154</b>	<b>∑tri-hexa</b>	<b>BDE-209</b>
<b>Average</b>	3.30	<0.05	0.08	0.71	0.45	1.10	0.30	5.95	0.31
<b>SD*</b>	3.25	0.08	0.15	0.67	0.39	1.05	0.30	5.35	0.30
<b>Median</b>	2.80	<0.05	<0.05	0.69	0.38	0.91	0.21	5.00	0.25
<b>DF** (%)</b>	100	20	46	94	89	97	77	100	69
<b>LOQ</b>	0.043	0.045	0.051	0.055	0.053	0.058	0.059	N/A <sup>#</sup>	0.062
<b>Minimum</b>	0.17	<0.05	<0.05	<0.06	<0.05	<0.06	<0.06	0.2	<0.06
<b>25<sup>th</sup> %ile</b>	0.78	<0.05	<0.05	0.20	0.12	0.35	0.07	1.70	<0.06
<b>75<sup>th</sup> %ile</b>	5.15	<0.05	0.09	0.85	0.70	1.43	0.55	9.55	0.58
<b>Maximum</b>	14.65	0.45	0.83	3.43	1.86	4.57	11.10	26.10	0.92

542 \* Standard deviation.

543 \*\* Detection frequency.

544 <sup>#</sup> Not applicable.

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552 **Table 2: Average concentrations of PBDEs (ng g<sup>-1</sup> lw) in human milk samples from**  
 553 **different countries.**

<b>Location</b>	<b>year</b>	<b>number</b>	<b>∑tri-hexa BDEs</b>	<b>BDE- 209</b>	<b>Reference</b>
<b>UK</b>	2009-10	35	5.9	0.3	(this study)
<b>UK</b>	2001-03	54	6.3	N/A*	(Kalantzi, et al. 2004)
<b>Norway</b>	2003-09	393	2.7	0.6	(Thomsen, et al. 2010)
<b>Sweden</b>	1996-2006	276	3.4	N/A	(Lignell, et al. 2011)
<b>France</b>	2004-06	93	2.5	1.6	(Antignac, et al. 2009)
<b>Spain</b>	2005	9	2.1	2.5	(Gomara, et al. 2011)
<b>Belgium</b>	2006	22	3.0	5.9	(Roosens, et al. 2010)
<b>Italy</b>	2005-07	13	1.3	N/A	(Alivernini, et al. 2011)
<b>USA</b>	2002	47	34.0	0.9	(Schechter, et al. 2003)
<b>Canada</b>	2003	10	50.4	0.4	(She, et al. 2007)
<b>Australia</b>	2007	10	7.6	0.3	(Toms, et al. 2009)
<b>China</b>	2004	19	2.5	3.0	(Sudaryanto, et al. 2008)
<b>India</b>	2009	45	1.1	0.4	(Devanathan, et al. 2012)
<b>Korea</b>	2008-09	21	2.7	N/A	(Kim, et al. 2011)
<b>Tunisia</b>	2010	36	8.3	N/A	(Ben Hassine, et al. 2012)

554 \* N/A not analyzed

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562 **Table 3: Estimated exposure\* (ng (kg bw)<sup>-1</sup> day<sup>-1</sup>) of a 1 month old infant to the target**  
563 **BFRs via breast milk under different scenarios\*\*.**

	<b>25<sup>th</sup> %ile</b>	<b>Average</b>	<b>Median</b>	<b>75<sup>th</sup> %ile</b>
<b>BDE-47</b>	4.6	19.3	16.3	30.3
<b>BDE-99</b>	1.2	4.2	4.0	5.1
<b>BDE-100</b>	0.7	2.7	2.2	4.2
<b>BDE-153</b>	2.1	6.5	5.3	8.4
<b>BDE-154</b>	0.4	1.7	1.3	3.2
<b>Σtri-hexa BDEs</b>	10.0	34.9	29.4	56.4
<b>BDE-209</b>	<0.1	1.8	1.2	3.4

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565 \* Values below LOQ were assumed to be 1/2 LOQ.

566 \*\* Based on an average body weight of 4.14 kg and a daily lipid intake of 24.4 g lipid day<sup>-1</sup>

567 (U.S. EPA 2002.).

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575 **Table 4: Comparison of predicted adult body burdens arising from average and median**  
 576 **daily exposures<sup>#</sup> to major target PBDEs with observed levels in human milk samples.**

	<b>BDE-47</b>	<b>BDE-99</b>	<b>BDE-100</b>	<b>BDE-153</b>	<b>BDE-154</b>	<b>Σ<sub>5</sub>BDEs</b>	<b>BDE-209</b>
<i>Average intake* (ng day<sup>-1</sup>)</i>							
<b>Dust<sup>a</sup></b>	1.10	1.80	0.24	0.31	0.17	3.70	4270
<b>Diet<sup>b</sup></b>	35	30	5.60	7.00	2.80	80	310
<b>Air<sup>c</sup></b>	0.90	0.60	0.14	0.05	0.03	1.70	9.40
<i>Median intake* (ng day<sup>-1</sup>)</i>							
<b>Dust<sup>a</sup></b>	0.29	0.67	0.08	0.12	0.01	1.20	2975
<b>Diet<sup>b</sup></b>	35	30	5.60	7.00	2.80	80	310
<b>Air<sup>c</sup></b>	0.20	0.30	0.04	0.01	0.01	0.55	7.40
<i>Average predicted body burdens (ng g<sup>-1</sup> lw)</i>							
<b>Dust</b>	0.06	0.05	0.01	0.02	0.01	0.14	0.34
<b>Diet</b>	3.33	1.39	0.38	1.15	0.16	6.40	0.03
<b>Air</b>	0.11	0.05	0.01	0.01	0.01	0.20	0.01
<b>Sum</b>	3.49	1.49	0.40	1.19	0.18	6.74	0.38
<i>Median predicted body burdens (ng g<sup>-1</sup> lw)</i>							
<b>Dust</b>	0.01	0.02	0.00	0.01	0.00	0.04	0.24
<b>Diet</b>	3.33	1.44	0.38	1.15	0.16	6.45	0.03
<b>Air</b>	0.03	0.03	0.00	0.00	0.00	0.06	0.00
<b>Sum</b>	3.36	1.48	0.39	1.16	0.16	6.55	0.27
<i>Observed body burdens (ng g<sup>-1</sup> lw)</i>							
<b>Average</b>	3.28	0.71	0.45	1.09	0.28	5.92	0.31
<b>Median</b>	2.77	0.68	0.38	0.9	0.21	4.98	0.24

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578 <sup>#</sup> Values below LOQ were assumed to be 1/2 LOQ.

579 \* Based on average adult dust ingestion rate of 20 mg day<sup>-1</sup> (Jones-Otazo, et al. 2005),  
 580 average inhalation rate of 20 m<sup>3</sup> day<sup>-1</sup> (Currado and Harrad 1998) and average adult weight  
 581 of 70 kg.

582 <sup>a</sup> Estimated from reference (Harrad, et al. 2008a); <sup>b</sup> Estimated from reference (UK Food  
 583 Standards Agency 2006); <sup>c</sup> Estimated from references (Harrad, et al. 2006; Stapleton, et al.  
 584 2009).

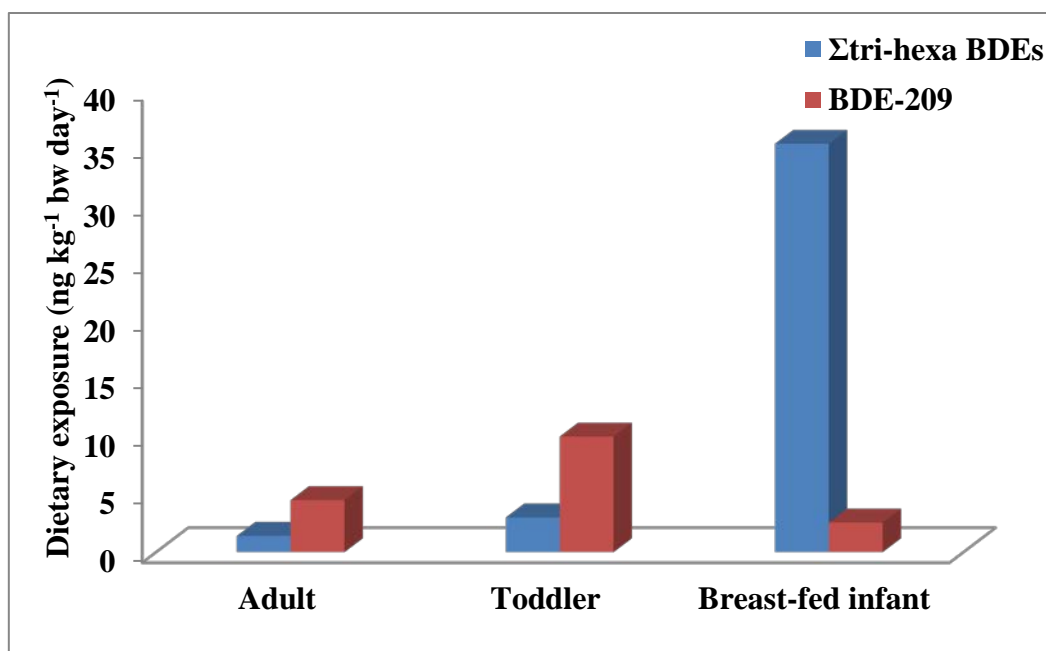
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589 **Figure 1: Average estimates of dietary exposure ( $\text{ng (kg bw)}^{-1} \text{ day}^{-1}$ ) of UK adults\*,**  
590 **toddlers\* and breast-fed infants\*\* to PBDEs.**



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592 \* From reference (UK Food Standards Agency 2006); \*\* This study.

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