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Serum levels of decabromodiphenyl ether (BDE-209) in women from different European countries and possible relationships with lifestyle and diet

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ABSTRACT

To determine possible effects of lifestyle, diet, housing and professional activities on differences in individual levels of decabromodiphenyl ether (BDE-209) in serum of women, 20 to 40 years of age, in The Netherlands, the United Kingdom, Norway and Spain.

BDE-209 was measured in serum of 145 female volunteers with no known occupational exposure from Norway, United Kingdom, The Netherlands and Spain. Blood levels of BDE-209 in a subgroup of 40 Dutch women were determined twice at a six months' interval. An extensive questionnaire was used to obtain detailed information about lifestyle factors that might contribute to BDE-209 exposure. Serum levels were used to determine margin of systemic exposure compared with a 28d rat toxicity study.

Median BDE-209 serum concentrations were highest in The Netherlands and United Kingdom, respectively 8.8 and 9.3 pg/g ww. or 2.6 and 2.8 ng/g lipid. Median levels in Spain and Norway were lower, respectively 7.4 and 5.2 pg/g ww. or 3.3 and 0.8 ng/g lipid. Maximum levels in individual women were higher by one order of magnitude than the mean or median. The country of residence was the only variable significantly associated with BDE-209 levels; we found that the differences between countries could not be explained by any of the investigated exposure variables, and that these did not explain differences between individuals either. No consistent relationships were determined between diets, household, clothes, number and duration of use of electronics and occupational activities for the whole study group.

We could not identify which of the multiple sources of exposure accounted for individual differences in blood levels. Although small differences in mean BDE-209 serum levels were recognized between countries, these differences are unlikely to cause a differential result with respect to risk assessment.

1. Introduction

In modern life, flame retardants have become part of efforts to protect society against injuries, death and economic damage due to fires. A wide range of chemicals have been developed as flame retardants, from which the polybrominated diphenyl ethers (PBDEs) have been commonly used for many decades. Various PBDE products have been in production and use for several decades, commercial PentaBDE, OctaBDE and DecaBDE mixtures comprising diphenyl ethers of varying bromination degree. Some PBDEs have physico-chemical properties that promote environmental persistence and accumulation in food chains and humans (Darnerud et al., 2001; de Wit, 2002; Frederiksen et al., 2009; Tanabe et al., 2008; Zhu et al., 2009). Certain lower brominated congeners have been reported to have long half-lives in humans, wild life and experimental animals, indicating a distinct role of bromine atoms in reducing metabolic rates of these compounds (Geyer

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et al., 2004; Gill et al., 2004; Toms et al., 2009b). As a result, levels of tetra- to heptabrominated BDEs in environmental biota and humans can equal those for PCBs in many industrialized countries (Haraguchi et al., 2009; Hites, 2004; Schecter et al., 2005).

In the European Union, the commercial Penta- and OctaBDE mixtures were taken off the market in 2005 because of adverse effects observed in experimental animals (Directive 2003/11/EC). In North America these commercial formulations were voluntarily withdrawn from the market by industry in 2004 (BSEF, 2009). Further, since May 2009, tetra- to heptabrominated diphenyl ethers have been listed in the UN Stockholm Convention on Persistent Organic Pollutants (http://www.pops.int). In contrast, commercial DecaBDE is still use as flame retardant for plastics and textiles when our study was done (BSEF, 2009; Harrad et al., 2008; Public Health England, 2009; 2013). The commercial mixture consists primarily of the fully brominated diphenyl ether (BDE-209) and smaller amounts of nonabrominated BDE (0.3–21.8%) and octabrominated BDE (0–0.04%). Although its use in electrical and electronic equipment had been banned in the EU in 2008 (BSEF, 2009) and the production and sales of commercial DecaBDE (c-DecaBDE) has been phased out in North America (BSEF, 2016), there is ongoing human exposure from dust in indoor environments (Harrad et al., 2006; Law et al., 2014) and from diet, particularly seafood (Shaw et al., 2009). Presently c-DecaBDE is still under consideration for restriction and elimination under EU's REACH regulation and UN's Stockholm Convention, respectively (http://chm.pops.int/Default.aspx?tabid=5171). In order to evaluate the result of these regulations in reducing human exposure, it is of great importance to establish good biomonitoring data for DecaBDE in particular.

Because of the adverse properties and effects of the lower brominated BDEs, commercial Penta- and OctaBDE have been phased out in European countries in the early 2000s and were globally banned by the UN Stockholm Convention in 2009. As a result, the increasing temporal trends of levels of tetra- to heptabrominated BDEs in human blood and milk have leveled off in the late 1990s in Europe and have declined since, this (Fängström et al., 2008; Thomsen et al., 2007), but is less distinct for North America (Law et al., 2014). Furthermore, an upward trend for decaBDE has been observed in the same time period (Law et al., 2014). It is well established that levels of lower brominated PBDEs in humans may vary strongly among geographical regions, e.g., mean total PBDE levels in North America are about one order of magnitude higher than in Europe (Frederiksen et al., 2009; Fromme et al., 2016; Hites, 2004). In non-occupational situations the relative contribution of decabromodiphenyl ether (BDE-209) in humans constitute a variable part of the total amount of PBDE body burden (Antignac et al., 2009; Frederiksen et al., 2009; Gomara et al., 2007; Thuresson et al., 2005). The geographical differences might partly be explained by different regional fire safety regulations and use of decaBDE containing flame-retardants in consumer products (Harrad et al., 2008). Also, within countries individual differences in PBDE levels can be quite substantial and may easily exceed more than one order of magnitude in human blood and milk (Frederiksen et al., 2009; Hites, 2004).

At present, the cause for this strong variability in human levels is unclear, but lifestyle factors have been suggested as a contributing factor. Although, food is an important pathway for human exposure to PBDEs (Fromme et al., 2009; Meng et al., 2007; Schecter et al., 2006, 2008; Voorspoels et al., 2007; Wu et al., 2007), the ingestion of house dust is also considered to be an important exposure pathway, especially for BDE-209 (Harrad et al., 2006, 2008; Jones-Otazo et al., 2005; Sjodin et al., 2008; Toms et al., 2009a).

Many in vivo toxicokinetic and toxicological studies with PBDEs with different degrees of bromination were done over the last decade to support risk assessment for humans and wildlife (Birnbaum and Cohen Hubal, 2006; Darnerud, 2003; Staskal et al., 2008). As a result, multiple toxic and biological effects have been identified (Darnerud, 2003; He et al., 2009; Kuriyama et al., 2005), which show similarities between the lower brominated PBDEs and decaBDE (Dingemans et al., 2016). These include interactions with the pregnane X (PXR) and sex steroid receptors (Dang et al., 2007; Fery et al., 2009; Mercado-Feliciano and Bigsby, 2008; Pacyniak et al., 2007), steroidogenesis (Canton et al., 2006; Canton et al., 2008) and thyroid hormone homeostasis (Lema et al., 2008; Talsness et al., 2008). In addition, effects on neurodevelopment and behavior in mammalian test systems have been observed for these compounds, including BDE-209 (Viberg et al., 2003, 2006, 2008, 2009a, 2009b); these effects bear similarity with non-dioxin-like PCBs (Eriksson et al., 2006; He et al., 2009). With respect to mechanism of action involvement of metabolites has also been determined for various endpoints such as sex steroid hormone receptors, steroidogenesis (Canton et al., 2006, 2008; He et al., 2008) and regulation and interference with calcium homeostasis in neuronal cells (Alm et al., 2006; Bocio et al., 2003; Dingemans et al., 2008). There is also emerging evidence that exposure to PBDEs in early human life stage can influence endocrine and neurobehavioral development (Sagiv et al., 2015; Harley et al., 2017; Zota et al., 2011). Recently, it has been argued that risk assessment for PBDEs and non-dioxin PCBs should be combined (Dingemans et al., 2016) Earlier studies suggested that PBDEs can have a dioxin-like mechanism of action, but this is now attributed to contamination of commercial PBDE mixtures with brominated dibenzo-*p*-dioxins and dibenzofurans (Luthe et al., 2008; Peters et al., 2004, 2006; Van den Berg et al., 2006).

Many lower brominated PBDEs bioaccumulate in the aquatic and human food chain and in the past, bioaccumulation of BDE-209 was assumed to be low due to the large molecular size, extreme hydrophobicity and low bioavailability (Darnerud et al., 2001; Debruyn et al., 2009; Drouillard et al., 2007; Hardy et al., 2009; Huwe et al., 2008b; Kelly et al., 2008; Shaw et al., 2008). However, recent results from both aquatic and terrestrial food web studies demonstrate that BDE-209 bioaccumulates, i.e., bioaccumulation factors and trophic magnification factors above 1 (Chen et al., 2007, 2008; Law et al., 2006; UNEP, 2015). Further, environmental levels of BDE-209 can be up to lower ppm levels in abiotic compartments like sediment and house dust (Harrad et al., 2008; Song et al., 2005a, 2005b; Xiang et al., 2007; Zegers et al., 2003). Thus, risk assessment of PBDEs is complicated by significant differences among congeners with respect to toxicokinetics, toxicology as well as differences between species, including humans (Birnbaum and Cohen Hubal, 2006). Our present study was conducted to determine systemic exposure via blood of BDE-209 in women in four different European countries (The Netherlands, United Kingdom, Norway and Spain) and to study factors influencing those levels, for example differences in life style and fire safety regulations. So far, there are few systematic studies that have focused on systemic exposure of DecaBDE in residents and their households. Blood samples were collected from a group of volunteers, women 20 to 40 years of age. In view of the uncertainties in human exposure to c-DecaBDE, a questionnaire was designed to obtain broad and specific information regarding possible sources of exposure, including lifestyle, use of electrical and electronic devices, diet and country of residence. This questionnaire was compiled based on the information by the BSEF or EU on the (possible) use of DecaBDE in household products (cf EFSA, 2011). The combined information might explain any individual differences in levels of BDE-209 in serum and elicit the possible manner in which human exposure to c-DecaBDE occurs in non-occupational situations. The present report describes the results of a first study of an originally planned 10-year human monitoring program in Europe that would provide the authorities with insight into the long term serum levels of BDE-209 in humans and possible causal relationships with specific exposure scenarios.

2. Materials and methods

2.1. Blood sampling and data collection

In view of different European dietary and lifestyle factors Norway, Spain and The Netherlands were selected from the Nordic,