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Indoor Contami n with Hexabromocyclododecanes, Polybrominated henyl Ethers, and Perfluoroalkyl Compounds: An ortant Exposure Pathway for People?

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This review underlines the importance of indoor contamination as a pathway of human exposure to hexabromocyclododecanes (HBCDs), polybrominated diphenyl ethers (PBDEs), and perfluoroalkyl compounds (PFCs). There is ample evidence of substantial contamination of indoor dust with these chemicals and that their concentrations in indoor air exceed substantially those outdoors. Studies examining the relationship between body burden and exposure via indoor dust are inconsistent; while some indicate a link between body burdens and PBDE and HBCD exposure via dust ingestion, others find no correlation. Likewise, while concentrations in indoor dust and human tissues are both highly skewed, this does not necessarily imply causality. Evidence suggests exposure via dust ingestion is higher for toddlers than adults. Research priorities include identifying means of reducing indoor concentrations and indoor monitoring methods that provide the most "biologically-relevant" measures of exposure as well as monitoring a wider range of microenvironment categories. Other gaps include studies to improve understanding of the following: emission rates and mechanisms via which these contaminants migrate from products into indoor air and dust; relationships between indoor exposures and human body burdens; relevant physicochemical properties; the gastrointestinal uptake by humans of these chemicals from indoor dust; and human dust ingestion rates.

Introduction

This paper stems from the recent growth in studies that monitor, elucidate sources of, and evaluate potential human health impacts of human exposure to both brominated flame retardants (BFRs) and perfluoroalkyl compounds (PFCs) (*1*–*5*). Initial thinking about sources, fate, and human exposure pathways for these chemicals was informed by organochlorines such as dioxins for which sources are essentially outdoor and exposure primarily dietary. Recent research has challenged this paradigm for persistent organic pollutants (POPs) with significant indoor uses. For these, extensive indoor deployment contaminates indoor air and dust compounded by the high proportion of time spent indoors - an estimated 22 h per day for U.K. adults (*6*). Furthermore, while considerable uncertainty surrounds

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human dust ingestion rates, the consensus is they are greater for young children (*7*).

While a wide range of POPs are present in indoor environments (*8*), this paper focuses on BFRs (polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecanes (HBCDs)) and PFCs (including perfluorocarboxylic acids/carboxylates (PFCAs, e.g. perfluorooctanoic acid (PFOA)), perfluoroalkylsulfonic acids/sulfonates (PFSAs, e.g. perfluorooctane sulfonate (PFOS)), and fluorotelomer alcohols (FTOHs)).

PBDEs are used in high impact polystyrene (HIPS) electronic housings, furniture foams, and fabrics at up to percent levels. The most recent figures for the three commercial formulations (Penta-BDE, Octa-BDE, and Deca-BDE) show their respective global production volumes in 2001 were 7500, 3790, and 56,100 t (*9*). Since PBDEs are blended physically within rather than bonded chemically to polymeric materials, they migrate into the environment where their persistence leads to contamination of humans (*10, 11*) that is of concern owing to their potential health risks (*12*−*16*). Such concerns have driven bans in several jurisdictions on manufacture and new use of all three formulations. Penta-BDE and Octa-BDE were listed recently under the Stockholm Convention on POPs (*17*) with some exposure guidelines proposed (*18, 19*).

Global production of HBCD in 2001 was 16,700 t (*9*). HBCD has found use as a flame retardant additive to expanded and extruded polystyrene foams for thermal insulation of buildings, back-coating of fabrics for furniture, and to a lesser extent in HIPS for electronic equipment like TVs (*3*). Like PBDEs, HBCD is not bound to polymeric products and is persistent and similarly ubiquitous in the environment and humans (*20, 21*). This has raised concerns because of its adverse health impacts in laboratory animals (*22*−*25*). Hence, while production continues, and no recognized health-based standard exists for HBCD, it is under active consideration for listing under the Stockholm Convention, and the European Chemicals Agency has declared it a priority substance under EU regulation that requires its associated risks to be controlled properly and its progressive replacement (*26*).

Industrial and consumer applications of PFCs are numerous owing to their unique properties (*27*). Examples include water-, soil-, and stain-resistant coatings for fabrics, oil-resistant coatings for paper products, fire fighting foams, paints, and floor polishes (*28*−*30*). Moreover, PFOA and other PFCAs are used as processing aids in production of fluoropolymers like polytetrafluoroethylene (*31*). Despite recent restrictions on production, they remain in humans (*32*), generating concerns about toxicity of some PFCs, with PFOS listed recently under the Stockholm Convention (*17*) and some exposure guidelines proposed (*33, 34*).

This paper addresses the following: strategies and methods for monitoring contamination and exposure; current evidence of contamination of indoor environments; source identification and attribution; causes of variability in contamination of indoor environments with BFRs and PFCs and the implications for source attribution and human exposure assessment and the contribution of indoor exposure to human body burdens.

The paper summarizes current knowledge, identifies gaps, and recommends research priorities.

Strategies for Monitoring BFRs and PFCs in Indoor Environments. *Indoor Air.* Sampling indoor air for BFRs, PFCs, and related POPs like polychlorinated biphenyls (PCBs) has been conducted via three approaches: (a) high-volume active sampling (*35*), (b) low-volume active sampling (*36*), and (c) passive air sampling (*37*−*40*). Each has benefits and disadvantages, but the principal concern is the comparability of data generated by different methods. High volume active air samplers underestimate concentrations if the volume of the microenvironment sampled is exceeded during sampling (*35*). This may also occur when deploying low volume active air samplers for extended periods in confined spaces like vehicles. Passive air samplers - the most common use polyurethane foam (PUF) disks (impregnated with XAD resin for PFCs (*41*)) as the sampling medium - avoid such problems, but semiquantitatively sample the vapor phase and a small but variable fraction of particulate-bound chemical. This is a significant limitation, as it precludes monitoring particulate-bound chemicals like BDE-209. Provided filter and vapor phase sorbents are used, this does not apply to active sampling. However, artifacts like volatilization of compounds from filter-collected particles, sorption of gas-phase compounds onto the filter, and reactions with oxidants during sampling may bias particle/gas partitioning estimates (*42*). Reports (*43*) of modified PUF disk-based samplers that sample quantitatively both particulate and vapor phases are thus timely. Moreover, notwithstanding a report of PBDE concentrations in different particle size fractions of outdoor air (*44*); given that finer airborne particles may more easily penetrate the lower respiratory tract, a potentially important data gap is the lack of knowledge regarding particle size distribution of BFRs and PFCs in indoor air.

The influence of sampling method is highlighted by a study where PBDE concentrations experienced by participants in their homes were significantly higher when using low volume active samplers worn by the participant (personal sampling), than when using low volume active samplers located at fixed points (static sampling) (*36*). Incremental exposure was greatest for congeners associated primarily with the particulate phase like BDE-209 and attributed to personal samplers capturing PBDEs associated with the "personal cloud" of particulates generated by participants.

Given elevated BFR concentrations in vehicle air, the location of samplers within the car is pertinent. Of the studies reporting airborne PBDEs in cars; while one deployed samplers in the trunk (*38*), the other sampled cabin air (*45*). The extent to which the former may fail to reflect accurately exposure of vehicle occupants is unknown, with studies required to establish whether significant differences exist in BFR contamination between the trunk and cabin. Moreover, such monitoring should ideally only be conducted during vehicle occupancy, reflecting only air to which occupants are exposed. This is especially pertinent in cars as the high in-vehicle temperatures and minimal ventilation that can occur during vehicle nonoccupancy can generate elevated BFR concentrations to which occupants are exposed only briefly.

Indoor Dust. A variety of approaches to sampling indoor dust exist. We stress the overriding objective of a sampling method in this context is to procure samples that reflect accurately the BFRs and PFCs to which an individual is exposed. Herein, we refer to such samples as "biologically-relevant" (*46*). With respect to "dust", we refer to settled dust for which exposure is presumed to occur via ingestion (usually accidental, but for some, particularly toddlers, deliberate). This is distinct from suspended dust, for which exposure occurs via inhalation. One approach is to take the contents of vacuum cleaners donated by householders (*38, 47*). Advantages are it provides an integrated measure of contamination and potential exposure from all rooms in which it is deployed. It is cost-effective and enhances donor compliance as it does not require the researcher to enter the home. However, such samples will not reflect accurately varying levels of contamination between different rooms. This may reduce the accuracy of exposure assessments if such between-room contamination differences are substantial. It seems unlikely that vacuum cleaners are used proportionally to the time spent—or more importantly, exposure—in each room. Other issues with participant-

provided vacuum cleaner contents are as follows: variable vacuum cleaner sampling rates, the cleaner may be used in environments not frequented by the donor (e.g., lent to a friend), multiple uses of the same bag, and potential for post and during sampling contamination. Such issues introduce measurement error that will generally hide relationships to indicators of internal exposure.

A generally favored alternative is systematic procurement of samples by the research team using standardized procedures and equipment (*46, 48*−*54*). While possibly hindering donor compliance, this facilitates comparability between samples. Moreover, if pre-extracted sample receptacles (e.g., "socks"/Soxhlet thimbles) placed within the "sampling train" (furniture attachment) are used (*50, 54*), analyte loss and sample contamination (particularly from the vacuum cleaner) is minimized and sampling consistency maximized. The receptacles are replaced before taking each sample.

Even for researcher-procured samples, appreciable differences exist. While one approach samples the entire room surface until a sufficient mass of dust is collected (15−30 min) (*53*), another samples a standardized floor area for a standardized time period (*48*−*52*). Within-room variations exist in dust contamination with BFRs (*51, 52*). These mean vacuuming the entire room may oversample less-frequented parts; equally that sampling one specific area may not assess completely contamination within the room. This latter approach may afford a more biologically relevant dust sample provided the area sampled corresponds to that where exposure occurs.

Whether vacuum cleaner bags or researcher-collected samples are more suitable is unclear. In the only study of this issue, comparison of PBDEs in vacuum cleaner dust with researcher-collected samples for 20 homes found poor to moderate correlation between concentrations in the two sample types, with concentrations significantly lower in vacuum cleaner dust (*46*). The authors attributed this to the fact that researcher-collected dust was taken from rooms sampled specifically because of the likelihood of having sources of PBDEs. While confirming the influence of sampling method; without matching measurements of body burden, it does not indicate which is more biologically relevant (*46*). Similarly, no data exist comparing contamination in "whole-room" rather than "specific-area" dust samples. Combined with the absence of matched body burden measurements, assessment of the relative biological relevance of the two methods is not possible.

All the above studies sampled *floor* dust. The biological relevance of this is debatable. Instead, dust from elevated surfaces (e.g., bookshelves and tables) may reflect adult exposure better. While data on BFR concentrations in such samples exists (*55*), there is no systematic study of how concentrations in such samples compare with floor dust from identical microenvironments and their comparative biological-relevance.

Also pertinent is the upper and lower size fraction of dust collected. This is influenced by the pore size of the sampling receptacle (e.g., Soxhlet thimble) and the mesh size of any sieve employed postsampling. Assessment of the comparative biological relevance of different dust size fractions is required.

No universally agreed standard method exists for sampling indoor dust. Given the respective pitfalls/advantages of each method deployed, and uncertainty regarding their biological-relevance; there is insufficient information to allow development of a standardized method. Further research is required to identify the most biologically relevant approaches. Moreover, care should be taken when generalizing to larger populations from a relatively small number of samples, typically not randomly selected. It is recommended to provide as much detail as possible about sampling methods when reporting results.

Contamination of Indoor Environments. The database on indoor contamination with BFRs and PFCs was considered. We covered all indoor environments except occupational environments relating to BFR and PFC production or processes involving their incorporation into products and their dismantling. While the initial focus was on air, many recent papers report concentrations in dust. A comprehensive listing is not our aim, but Tables 1 and S1 and references therein illustrate the following key observations:

• While a substantial quantity of data for PBDEs exists, most relates to trihexabrominated congeners originating predominantly from the Penta-BDE product. The database for higher brominated congeners like BDE-209 in indoor dust is also substantial, but far less information is available for such congeners in air, as most studies have employed passive air samplers that sample mainly the vapor phase. More information is needed on HBCDs and PFCs in indoor air and dust. Additionally, while a past impediment to monitoring more volatile PFCs like FTOHs was the inability of conventional passive and active air sampling sorbents to retain such chemicals; recent development and application of XAD impregnated PUFs and alternative sorbent media should generate more data on such compounds (*41, 56*−*58*).

• Atmospheric concentrations of BFRs and PFCs indoors exceed substantially those outdoors.

• Distributions of BFR concentrations in indoor dust are highly skewed. Most studies report concentrations in a few samples that far exceed the median or geometric mean. This resembles the skewed pattern of human body burdens (*10, 59, 60*) and may indicate a causal link that would substantiate dust as the main source of exposure.

• The major PBDE in dust is usually BDE-209.

• Concentrations of Σtrihexa-BDEs in North American air and dust exceed those in Europe. This may explain higher body burdens in North Americans than in Europeans (*10, 59, 60*). However, those of BDE-209 in dust are highest in the U.K. and North America. The limited data suggest while international differences in indoor contamination with HBCDs exist, they are not substantial. There are too few data to evaluate whether such trends exist for PFCs.

• Most studies focus on homes, then offices; data exist that permit preliminary assessment of differences in contamination between microenvironment categories. However, we recognize the database is scant by comparison with that for outdoors and a more extensive database may reveal different trends. Current data suggest Σtrihexa-BDEs in offices exceed those in homes but there appears little difference between these microenvironment categories for other BFRs and PFCs. Far fewer data exist for cars, but vehicles in both the U.S.A. and Europe display measurable concentrations of PBDEs and HBCDs in air and dust with some samples displaying extremely high concentrations. Table 1 shows airplane dust can also display very high PBDE concentrations. In general, for HBCDs, cars, and for PBDEs, planes and cars appear to be heavily contaminated microenvironments. HBCDs and some PFCs are present in dust from primary school classrooms and child daycare centers in both Europe and the U.S.A. Too few data exist to permit meta-analysis of differences between microenvironment categories for PFCs, but differences between concentrations of PFOS and PFOA in different microenvironment categories do not appear significant.

Sources and Pathways of Contamination of Indoor Environments. The processes and rates via which BFRs and PFCs escape from treated products into the indoor environment remains poorly understood. Experimental evidence suggests some BFRs volatilize (*61*−*63*) before partitioning to dust, but this mechanism is not a convincing explanation of the elevated concentrations of BDE-209 in dust. While volatilization may explain low levels in air and dust of this

TABLE 1. Summary of Median Concentrations (Range in Parentheses) of BFRs, PFOS, and PFOA in Indoor Dust (ng g^{-1}) and Indoor and Outdoor Air (pg m^{-3})

		microenvironment category						
number of samples and location	target POPs	homes	offices	daycare centres/ primary school classrooms	cars	outdoor	planes	ref
				Air				
n = 31, 33, 25, and 110 for U.K. homes, offices, cars, and outdoors, respectively	Σtrihexa-BDEs	24 (4−245)	71 (10−1416)	-	41 (11−8184)	8.7 (0.49−30)	-	(*38, 103*)
n = 74 and 7 for Ottawa homes and outdoors, respectively	Σtrihexa-BDEs	100 (2.0−3600)	-	-	-	2.6 (<dl-4.4)	-	(*40*)
n = 46, 24, and 14 for Kuwait homes, offices, and outdoors, respectively	Σtrihexa-BDEs	8.2 (2.5−136)	8.6 (2−385)	-	-	9.3[a] (2.5−32)	-	(*37, 104*)
n = 20, 41, and 35 for Boston homes, Greek cars, and Ontario, Canada for outdoors, respectively	BDE-209	94[b] (<48−651)	-	-	104 (nd-1,053)	19[a] (<dl-105)	-	(*36, 45, 105*)
n = 24 for U.S.A. (vapor phase)	Σtrihexa-BDEs	3200 (nr-15,000)	-	-	-	-	-	(*69*)
n = 33, 25, and 5 for U.K. homes, offices, and outdoors, respectively	ΣHBCDs	180 (67−1300)	170 (70−460)	-	-	37 (34−40)	-	(*48*)
				Dust				
n = 30, 18, and 20 for U.K. homes, offices, and cars, respectively	Σtrihexa-BDEs	46 (7.1−250)	100 (16−1100)	-	190 (54−22,000)	-	-	(*51*)
n = 46 and 60 for U.S. homes and cars, respectively	Σtrihexa-BDEs	1910 (590−34,400)	-	-	2,600 (436−59,800)	-	-	(*46, 106*)
n = 18, 15, and 9 for U.K. homes, offices, and cars, respectively	BDE-209	8100 (<dl-2,200,000)	6200 (620−280,000)	-	100,000 (12,000−2,600,000)	-	-	(*51*)
n = 46 and 60 for U.S. homes and cars, respectively	BDE-209	<dl (<dl-9600)	-	-	48,100 (4380−3,570,000)	-	-	(*46, 106*)
n = 24 for both U.S. homes and cars	ΣBDEs (inc. BDE-209)	21,000 (nr-290,000)	-	-	28,000 (nr-210,000,000)	-	-	(*69*)
n = 24 for both U.S. homes and cars	BDE-209	190 (<DL-66,000)	-	-	3,100 (<DL-210,000,000)	-	-	(*69*)
n = 20 in planes	Σtrihexa-BDEs	-	-	-	-	-	9,300 (270−760,000)	(*107*)
n = 20 in planes	BDE-209	-	-	-	-	-	17,700 (<DL-192,000)	(*107*)

TABLE 1. Continued

number of samples and location	target POPs	microenvironment category: homes	offices	daycare centres/ primary school classrooms	cars	outdoor	planes	ref
n = 45, 28, 20, and 20 for U.K. homes, offices, primary school classrooms, and cars, respectively	ΣHBCDs	1,300 (140−140,000)	760 (90−6600)	5,200 (72−89,000)	13,000 (190−69,000)	-	-	(*48, 108*)
n = 13 for U.S. homes	ΣHBCDs	390 (110−4000)	-	-	-	-	-	(*49*)
n = 8 for Canadian homes	ΣHBCDs	640 (64−1300)	-	-	-	-	-	(*49*)
n = 20 for U.S. homes (main living area)	ΣHBCDs	354[b] (<4.5−130,200)	-	-	-	-		(*100*)
n = 10, 38, 10, 10, and 5 for Swedish houses, apartments, offices, daycare centers, and cars, respectively	PFOS	39 (15−120; houses); 19 (8−1100; apartments)	110 (29−490)	31 (23−65)	12 (8−33)	-		(*93*)
n = 20 for U.K. classrooms and child daycare centers	PFOS	-	-	1200 (85−3700)	-	-		(*108*)
n = 112 for U.S. homes and child daycare centers[c]	PFOS	142 (<dl-1960)	-	-	-	-		(*109*)
n = 67 for Ottawa homes	PFOS	38 (2.3−5065)	-	-	-	-		(*75*)
n = 10, 38, 10, 10, and 5 for Swedish houses, apartments, offices, daycare centers, and cars, respectively	PFOA	54 (15−98; houses); 93 (17−850; apartments)	70 (13−510)	41 (31−110)	33 (12−96)	-		(*93*)
n = 20 for U.K. classrooms	PFOA	-	-	220 (42−640)	-	-		(*108*)
n = 112 for U.S. homes and child daycare centers[c]	PFOA	201 (<dl-12,100)	-	-	-	-		(*109*)
n = 67 for Ottawa homes	PFOA	20 (1.2−1234)	-	-	-	-		(*75*)

[a] Average. [b] Geometric mean. [c] Concentrations for daycare centers not reported separately from those in homes; <dl = below detection limit; nr = not reported.

highly involatile congener, recent studies exploiting the utility of forensic microscopy suggest strongly physical weathering occurs of particles or fibers from flame-retarded items (*64, 65*). These studies showed heterogeneous bromine distribution within dust containing very high BDE-209 concentrations, with samples dominated by a small number of particles/fibers highly enriched in bromine. While such techniques may offer insights into mechanisms via which BFRs and other trace contaminants transfer from treated items into dust, wider application of such techniques (e.g., elucidating sources of other BFRs in less contaminated dust samples) is needed to realize their potential.

Very few emission factors for BFRs from treated goods exist (*61, 62*), and controlled chamber studies to generate such data are required. A modeling study generated Σtrihexa-BDE emission factors from a personal computer (*66*). A tandem approach using both chamber and modeling studies is thought the most effective strategy to understanding indoor "effective" emissions and fate of BFRs and PFCs where "effective" refers to the emission rate that is a function of the receiving environment as well as the source.

Despite widespread BFR use in furniture, electronic goods, and construction materials, studies correlating BFR contamination in a microenvironment with numbers of potentially BFR-containing items have had mixed success owing to exposure misclassification. Use of hand-held X-ray fluorescence (XRF) instruments to determine the bromine content of household items appears promising (*67*). XRF is nondestructive, fast, and cost-effective. Correlations using XRF-determined bromine content as opposed to item counts were much stronger (*67*), and this approach offers potential for at least semiquantitative prediction of BFR contamination and human exposure. Indeed, XRF has been used to identify significant positive correlations between PBDE concentrations in human blood of 44 Americans and bromine content of their sleeping pillows and primary car seat cushions, suggesting proximity to such flame-retarded items may constitute a major source of exposure (*68*). A caveat is that use of XRF in this fashion does not eliminate exposure misclassification completely. It does not distinguish between bromine in PBDEs from that in other BFRs nor identify which PBDE formulation is present and can only detect bromine close to the surface of tested items, thereby misclassifying bromine-containing items where BFRs lie within a product (e.g., in printed circuit boards). Another complication is that XRF cannot predict the release rate of the contaminant from the treated item as this depends on e.g. the volatility of the BFR, the mode of incorporation (reactive or additive), the nature of the product itself (i.e., release of additive BFRs from a fabric is likely easier than from HIPS), and the driving force for emission (e.g., fugacity gradient driving volatilization). Such factors suggest relationships between contaminants in products and dust are stronger than suggested by current studies (*67*).

Sources of Variability in Concentrations. Understanding of how BFR and PFC concentrations vary over space (different rooms in a home, different parts of the same room) and time is limited. Such variations are important given their implications for source attribution and exposure. How representative is a single sample of air or dust from one room? Are there significant spatial variations in contamination within a room that impact on the accuracy of exposure assessment? Do concentrations in the most-frequented area of the room differ substantially from elsewhere?

A U.S. study reported no significant change in Penta- and Deca-BDE congeners but a statistically significant difference in Octa-BDE congeners in dust samples taken from the same rooms ($n = 40$) eight months apart (*46*). However, the latter were minor constituents in dust. More substantial temporal variability for PBDEs and HBCDs was observed in dust sampled monthly in U.K. homes over 9−10 months (*51, 52*). The maximum Σtrihexa-BDE concentration exceeded the minimum by a factor of ∼50, 3.5, and 5.5 in the three homes, respectively; for BDE-209, these figures were 7.5, ∼400, and ∼35, and for ΣHBCDs 2.6, 224, and 40. In another study, PBDE concentrations in dust collected from 12 U.S. homes in two different seasons showed little consistency (*69*). While inconclusive owing to the very small number of environments studied, the data suggest substantial variation in estimates of exposure is possible, depending when a given room is sampled. Although temporal variation may not be hugely influential when considered alongside other potential influences on exposure; it provides one possible explanation for the order of magnitude differences in BDE-209 contamination of blood serum from members of one family sampled 90 days apart (*70*), particularly since the human half-life of BDE-209 is 15 days (*71*). In contrast, BDE-153 is estimated to require much longer (several years) to reach equilibrium in serum (*72*). Hence no significant change in body burden would be anticipated to arise from the reported temporal variations in dust contamination. It appears the influence of temporal variations should be considered when designing sampling strategies for monitoring both external exposure and body burdens for BFRs and PFCs with short human half-lives. In the U.K. studies, most of the temporal variability was attributable to changes in room contents, with removal and reintroduction to one room of a TV, coinciding with significant changes in HBCD concentrations (*52*).

With respect to within-building variations, while Penta- and Deca-BDE concentrations in 20 U.S. homes were significantly higher in the main living area than the bedroom, but there was no significant difference in Octa-BDE concentrations (*46*). Within-room spatial variability of HBCDs in dust appears related to proximity to sources. Declining ΣHBCDs concentrations were reported with distance from a TV in one U.K. home, with similar declines in a U.K. lecture hall with increasing distance from a PC and video projection console (*52*). In contrast, while within-room variability for PBDEs exceeds that attributable to sampling and analytical variation; its origins were not explicable (*51*).

While no data exist about within-room spatial variability in BFR and PFC concentrations in indoor air, variability between rooms in the same building and temporal/seasonal variability within the same room have been examined for trihexa-BDEs (*63*). This U.K. study reported appreciable (sometimes statistically significant) seasonal variation in trihexa-BDEs in 4 homes and 4 offices. Seasonal variability was less than that for PCBs in outdoor air (*73*). This was attributed to the narrower temperature range indoors and mitigation of summer peaks in concentration due to enhanced ventilation. In contrast, no seasonal variation in trihexa-BDE concentrations was found in 12 U.S. homes over two seasons (*69*). These data are consistent with those for PCBs (*74*). Concentrations of Penta-BDE and Deca-BDE in 20 Boston homes measured during winter (to control for ventilation) were correlated only moderately between the two rooms sampled in each home (*36*).

While a significant positive correlation between PFCs including PFOA and PFOS in indoor air and house dust and percentage of home carpeting was reported for 59 Ottawa homes (*75*), no correlation was found for perfluorooctanesulfonamides and sulfonamidoethanols (*76*). Using window films as a passive sampler of indoor concentrations, considerable differences were observed in PFC profiles in several buildings. The extent of carpeting and use of floor wax contributed to this variability (*77*). Within room and within building differences depended on the presence of a central building ventilation system and indoor-outdoor air exchange rates.

Changes in room contents can influence airborne contamination. Within-room temporal variation offers insights into the validity of basing exposure assessments on a single spot measurement of contamination as well as source attribution. For example, monthly monitoring of office air over 10 months revealed an approximately 75% decrease in Σtrihexa-BDEs concentrations following replacement of a computer (*63*).

Indoor Exposure to and Its Influence on Human Body Burdens. A pivotal issue is the influence of indoor contamination on human body burdens. Understanding of this remains incomplete. Current thinking is that for BFRs indoor exposures may be for many individuals comparable to or greater than dietary intake. Ingestion of dust is considered the principal indoor exposure pathway, especially for young children (*78*). This is consistent with Penta-BDE congener concentrations in pooled Norwegian blood serum from 0−4 year-olds exceeding substantially those in adults (*79*). Likewise, in Australia, PBDE concentrations in pooled blood serum peaked at 2.6−3 years when breastfeeding has typically stopped (*80*). Similarly, a U.S. study showed higher PFOS and PFOA concentrations in pooled blood serum from 3−5 year olds compared to adults (*81*). Moreover, PFOA, perfluorohexanesulfonate (PFHxS), and perfluorononanoate concentrations in blood were highest in Australians <15 years, while PFOS levels peaked in adults >60 years (*32*). In contrast, another study found that while a subgroup of children displayed considerably higher PFHxS concentrations than adults, concentrations of other PFCs were similar in adults and children (*82*).

A recent study used a steady-state first order relationship (eq 1) to predict observed body burdens of PBDEs for Americans from observed intakes (*83*)

$$C = D/(k^* \text{ Vd}) \quad (1)$$

where C= concentration in humans (mass per mass lipid for PBDEs/HBCDs or mass per blood volume for PFCs), D = intake from one or more pathways (mass per mass body weight per day), k = first order elimination rate constant (day^{-1}), and Vd = volume into which chemical is distributed in the body (mass of lipid for PBDEs/HBCDs or blood volume for PFCs).

Lorber (*83*) found substantial underprediction of body burdens when only dietary intake was considered but much closer agreement when exposure via ingestion of indoor dust was also considered. It was thus concluded that dust ingestion constitutes the principal exposure pathway to ΣPBDEs (BDEs 28, 47, 99, 100, 138, 153, 154, 183, and 209) for Americans (*83*). In addition, this pharmacokinetic modeling approach provides a conceptual framework for understanding relationships between exposure and body burden and for identifying knowledge gaps. While for PBDEs, parameters C, Vd, and D (for dietary intake) are well-characterized, aspects where understanding is incomplete are congener-specific human elimination rate constants (an overerestimate of the elimination rate constant for BDE-47 was identified as the likely cause of the substantial underprediction of this congener (*83*)), the scant database on human body burdens of BDE-209, and the reliance on the assumption that human body burdens are at steady state. Other uncertainties exist. While PBDE concentrations in indoor dust are well-established, intakes via ingestion of dust are influenced strongly by the dust ingestion rate. This is very uncertain, based on a very small number of primary studies designed to derive estimates of soil ingestion (*84, 85*). Better characterization of human dust ingestion rates constitutes a significant research gap. As it is thought dust ingestion occurs primarily via hand-to-mouth contact, a recently explored approach used contamination present in hand wipes to estimate exposure to PBDEs (*86*). However, uncertainties remain including the frequency and duration of hand-to-mouth events and efficiency of hand-to-mouth transfer. Furthermore, the bioavailability of BFRs and PFCs received by different pathways, i.e. inhalation, dust ingestion and diet, exerts a crucial influence on the intake (D) but remains currently little understood. The only peer-reviewed study reported the bioavailability to rats of PBDEs was similar regardless of whether the dose was administered as indoor dust or dissolved in corn oil, implying bioavailability of PBDEs from dust could be similar to that from diet (*87*). A pilot study of HBCD bioaccessibility from dust using an *in vitro* colon-enhanced physiologically based extraction test model found ΣHBCDs bioaccessibility was substantial. As with the PBDE bioavailability study in which the proportion retained varied between 69% (BDE-47) to 4% (BDE-209), substantial diastereomer-specific variation in bioaccessibility was observed (*88*). Such studies suggest human uptake of PBDEs and HBCDs from indoor dust is compound-specific and similar to that from diet.

The pharmacokinetic approach founded on eq 1 has also been applied to PFOS and PFOA. Several similar modeling approaches found dust and inhalation contribute to total intakes but that relative to diet (a major source) may not be as important as estimated for PBDEs (*89*−*92*). Specifically, indoor dust ingestion contributed ∼5−10% of total PFOA intake when background contamination of drinking water was assumed (*92*). Drinking water was found to be an important pathway when water supplies were impacted by a point source of PFOA (*92*). However, hand-to-mouth contact with carpets was considered a major pathway of PFOS and PFOA exposure for infants, toddlers, and children (*89*). Moreover, while a Swedish study considered diet the most important exposure route, dust ingestion was significant under scenarios assuming a high dust ingestion rate (*93*). In addition to the uncertainties noted for PBDEs, additional research gaps exist for PFCs. Examples are the volume of blood assumed to be available for PFC distribution (substantial disagreement exists between otherwise similar studies (*92, 94*), the lack of spatially consistent estimates of intake from different exposure pathways (the study of Vestergren and Cousins (*92*) used U.S. dust intakes and German dietary intakes), and the infrequent detection of PFCs in the human diet (the German study (*94*) used by Vestergren and Cousins (*92*) could not detect PFOA in 117 and PFHxS in 208 out of the 214 diet samples analyzed).

A complementary approach to elucidating the influence of indoor exposures on human body burdens is regression of concentrations in dust and diet to which an individual is exposed with concentrations in blood, milk, or placental tissue. Six such studies exist for PBDEs (*11, 54, 95*−*98*) with one examining HBCDs (*21*). With two possible exceptions (*96, 97*), study power is limited by small participant numbers. A U.S. study of 12 participants detected significant positive correlations between Penta-BDE congeners in human milk and indoor dust and with exposure estimated via reported dietary habits from consumption of both dairy products and meat (*54*). A study of five Swedes reported a positive linear relationship between ΣBDE concentrations (including BDE-209) in house dust and plasma (*98*). However, the relationship was dependent strongly on one observation. Most recently, a Danish study of 47 volunteers detected a significant positive correlation between BDE-47 concentrations in indoor dust and placental tissue but not for other congeners (*96*). Neither the Belgian study of 19 individuals (*11*) nor that of 50 German subjects (*97*) could detect any correlation between Penta-BDE congener concentrations in human blood serum and in indoor dust and duplicate diets (and air for the German study). With two small exceptions (most notably a correlation between BDE-99 in air (but not dust) and milk), a similar

lack of correlation between PBDEs in dust, air, and human milk was observed for the Australian study of 10 women (*95*). HBCD concentrations in dust but not diet were correlated positively with those in Belgian serum (*21*). In both the Belgian and U.S. studies (*11, 54*), difficulties in detecting BDE-209 in the milk or serum of participants meant the existence of a relationship between intake and body burden for BDE-209 could not be assessed. In contrast, BDE-209 was detected in the majority of Australian human milk samples but displayed no correlation with either air or dust (*95*). The absence of correlation between PBDEs in Belgian dust and diet and in matched serum samples was attributed to higher past and episodic current intakes being more important determinants of body burden than spot measurements of exposures made during the week-long study (*11*). Such findings underline the difficulties in obtaining biologically relevant measures of intake. Larger, more powerful, studies of the relationship between dust exposure and body burdens are required. As well as larger numbers of subjects, measurements of dietary and indoor intakes and body burdens should cover longer time periods to allow as far as possible for temporal fluctuations.

Research Priorities

This review underlines the importance of indoor contamination with BFRs and PFCs. While progress has been made, there are a number of areas that should form the focus of future research. One observation is that while significant knowledge gaps remain for PBDEs, we know much less about indoor exposure to PFCs and other BFRs. Specific gaps include studies that will

1. Evaluate interventions designed to reduce indoor exposures. These should range from immediate actions to enable individuals to reduce their likely burden (e.g., manipulate room ventilation, minimize carpeted areas and other chemical sinks) to longer term strategies (e.g., minimization of chemical migration from products by modifying product formulation and design).

2. Quantify emissions and elucidate pathways via which less volatile chemicals like BDE-209 migrate from products into and between air and dust, and other compartments of the indoor environment. This may be achieved via both experimental studies and mathematical modeling. Likewise, how are we primarily exposed to chemicals in dust: via inhalation of small particles, from hand-mouth contact, or dermal contact?

3. Characterize better the emission rates of BFRs and PFCs from treated goods.

4. Provide better data on BDE-209 in indoor air, diet, and human tissues. Combined, these will establish the relative influence of different exposure pathways on human body burdens particularly for toddlers/young children. A significant barrier for both BDE-209 and other BFRs and PFCs is the lack of validated, noninvasive indicators of body burden, and evaluation of alternatives like hair, saliva, and feces is required.

5. Improve understanding of the influence of different air and dust sampling strategies on interstudy comparability and the biological relevance of samples taken.

6. Monitor a fuller range of microenvironments. Most current data are for homes. While domestic environments are likely important vectors of exposure, data on cars and planes suggests they too may be important for some (e.g., taxi-drivers and aircrew) and require more extensive monitoring. Schools and child day-care centers, offices, and other transportation microenvironments like buses and trains are other microenvironments for which more data are required.

7. Widen the international coverage of current monitoring to facilitate better understanding of connections between production/use volumes in different countries and indoor concentrations and exposures.

8. Derive accurate dust ingestion rates and simultaneously improve our ability to procure "biologically relevant" measures of exposure. This includes improved characterization of the extent and causes of within-room spatial and temporal variability and within-building spatial variability in contamination. Such knowledge can be incorporated into exposure monitoring strategies - especially for BFRs and PFCs with short human half-lives.

9. Determine better the extent of and factors influencing human bioavailability and/or bioaccessibility of BFRs and PFCs in indoor dust.

10. Consolidate and improve the database on human half-lives and relevant physicochemical properties of BFRs and PFCs.

11. Conduct larger and more powerful studies of the relationship between concentrations of BFRs and PFCs in dust and body burden.

Most importantly, we need to utilize science to develop better policies to manage the past, current, and future reservoirs of BFRs and PFCs associated with indoor environments such that exposure is minimized. Such efforts require monitoring and comprehension of environmental behavior not only for those chemicals currently on the horizon but also those now emerging into the consciousness of exposure assessors. Examples include replacements for recently restricted BFRs, such as organophosphorus flame retardants (e.g., tris(1,3-dichloro-2-propyl)phosphate) and "new" BFRs like (2-ethylhexyl)tetrabromophthalate, 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE), and decabromodiphenyl ethane (DBDPE) (*51, 99−102*). All of this must be conducted alongside programs to comprehend better the human health impacts of BFRs and PFCs. Such programs should combine both experimental and pharmacokinetic assessment of multiple exposure pathways, their influence on body burdens, and epidemiology.

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Supporting Information Available

Summary of concentrations of selected PFCs in indoor and outdoor air and indoor dust (Table S1). This material is available free of charge via the Internet at http://pubs.acs.org.

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