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Biomarkers of Organophosphate and Polybrominated Diphenyl Ether (PBDE) Flame Retardants of American Workers and Associations with Inhalation and Dermal Exposures

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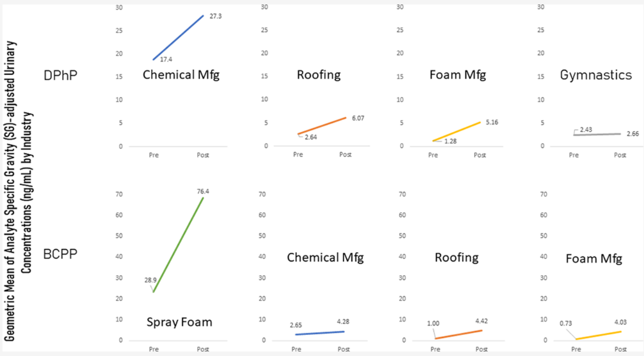

ABSTRACT: This study evaluated workers' exposures to flame retardants, including polybrominated diphenyl ethers (PBDEs), organophosphate esters (OPEs), and other brominated flame retardants (BFRs), in various industries. The study aimed to characterize OPE metabolite urinary concentrations and PBDE serum concentrations among workers from different industries, compare these concentrations between industries and the general population, and evaluate the likely route of exposure (dermal or inhalation). The results showed that workers from chemical manufacturing had significantly higher (p <0.05) urinary concentrations of OPE metabolites compared to other industries. Spray polyurethane foam workers had significantly higher (p <0.05) urinary concentrations of bis(1-chloro-2-propyl) phosphate (BCPP) compared to other industries. Electronic scrap workers had higher serum concentrations of certain PBDE congeners compared to the general population. Correlations were observed between hand wipe samples and air samples containing specific flame-retardant parent chemicals and urinary metabolite concentrations for some industries, suggesting both dermal absorption and inhalation as primary routes of exposure for OPEs. Overall, this study provides insights into occupational exposure to flame retardants in different industries and highlights the need for further research on emerging flame retardants and exposure reduction interventions.

KEYWORDS: *polybrominated diphenyl ethers (PBDEs), brominated flame retardants (BFRs), bis(1-chloro-2-propyl) phosphate (BCPP)*

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1. INTRODUCTION

Flame retardants in products have changed rapidly in the past two decades, primarily because polybrominated diphenyl ethers (PBDEs), the most common flame retardants previously, were phased out of manufactured products from 2004 to 2013 in the United States.[1,2] In addition, the Stockholm Convention restricted the use of PBDEs globally in 2017.[3] PBDEs are often replaced with organophosphate esters (OPEs) and other brominated flame retardants (BFRs). Flame retardants are added to consumer and industrial materials like flexible polyurethane foams, printed circuit boards, computer monitor casings, children's products, carpets, plastics, automotive and aviation components, and building insulation to slow and/or stop the spread of fire.[4−6] OPEs (e.g., triphenyl phosphate (TPhP)) are also added to consumer products like nail polish as plasticizers.[7,8]

PBDEs are persistent and known to accumulate in humans[9] and the environment.[10] Lower molecular weight PBDEs (e.g., -47 and -99) and some of the higher molecular weight PBDEs (i.e., -153) have relatively long half-lives (e.g., years), while BDE-209 has a shorter half-life (e.g., 15 days).[9,11] PBDEs have been associated with adverse health outcomes like thyroid disruption and reproductive changes.[12−14] Additionally, BDE-209 has been classified as possible human carcinogens by the EPA.[15] PBDE congeners are lipophilic and are not found in urine; therefore, biological monitoring is commonly performed using serum samples.[16]

OPEs and other BFRs have been associated with adverse health effects as well. Specifically, tris(2-chloroethyl) phosphate (TCEP) and tris(1,3-dichloro-2-propyl) phosphate (TDCPP) are listed under California Proposition 65 as potentially carcinogenic.[17] Animal studies showed that exposure to TCEP resulted in kidney tumors, tributyl

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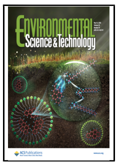

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phosphate (TBP) resulted in urinary bladder and liver tumors, and TDCPP resulted in liver, kidney, testes, and adrenal gland tumors.[18] Exposure to OPEs like TDCPP[19] and TPhP[20,21] can affect development in zebrafish. Additionally, TPhP and tris(1-chloro-2-propyl) phosphate (TCPP) could be toxic to human cells,[22] while TDCPP has been found to potentially alter human cell homeostasis.[23] 2-Ethylhexyl 2,3,4,5-tetrabromobenzoate (EH-TBB), a brominated flame retardant often found in commercial mixtures known as Firemaster 550 and 600, is an endocrine disruptor.[24] As such, understanding occupational exposure to OPEs and BFRs is of interest. OPEs readily metabolize, allowing for biological monitoring to be performed by analyzing metabolites in urine.[25] Biomonitoring results of the use of OPEs in urine are reported in the literature as concentration per volume (ng/mL) or they are sometimes adjusted using creatinine or specific gravity (SG). A recent review of the literature[26] proposed standardization of analysis and reporting to enable comparison between studies.

Workers, in addition to the U.S. general population, have been shown to be exposed to flame retardants.[9,27] Workers can be occupationally exposed to flame retardants during primary production (e.g., chemical manufacturing), secondary production (e.g., foam production), downstream use (e.g., spray polyurethane foam application, roofing, and nail salons), and decommissioning (e.g., electronic scrap industry). Air and dermal exposure to flame retardants, reported previously in workers in some of these industries (e.g., chemical manufacturing), was elevated compared to other studies.[27] There have been relatively few occupational-specific biological monitoring studies, but non-occupational studies have been conducted to determine human exposure to flame retardants in the general population and within specific groups such as gymnasts or those seeking reproductive counseling.[12,25,28,29] Gravel et al. identified a gap in occupational exposure assessment to flame retardants; most studies evaluated PBDEs with fewer studies evaluating OPEs.[26]

A review of the limited occupational studies to date reported that firefighters, waste incinerators, and cable manufacturing workers have the highest mean blood concentration of BDE-47, BDE-183, and BDE-209, respectively, compared to the other occupations studied.[26] Shaw et al. reported that firefighters had elevated PBDE serum concentrations compared to the general population.[30] Other studies have reported elevated PBDE concentrations for workers exposed to recycled foam,[31] manufacturing workers,[32] and electronic scrap workers.[33] A more recent study in China examining workers manufacturing BDE-209 and decabromodiphenyl ethane (DBDPE) found that serum levels for individuals working with each respective chemical were several orders of magnitude higher than those for electronic scrap workers.[34]

Fewer studies have characterized occupational exposure to OPE flame retardants through biomonitoring, with one review finding only five occupational studies in aircraft, aircraft maintenance, construction, hotels, and offices.[26] Additional studies were published recently characterizing OPE exposures for firefighters,[35] nail salon workers,[7] spray foam workers,[36,37] and electronic scrap workers.[38,39] Studies found that spray polyurethane foam workers had high urinary concentrations of TCPP biomarkers,[36,37] and other studies reported that firefighter OPE urinary concentrations were higher than the U.S. general population.[29,35] Three recent Chinese studies reported elevated urinary concentrations of OPE metabolites with bis(2-chloroethyl) phosphate (BCEP) (a metabolite of TCEP) being the most abundant OPE compared to the other metabolites among electronic scrap workers.[38−40] Knowledge about exposure pathways provides information so that workplace recommendations for reducing exposure can be made.

This study evaluated workers' exposures to flame retardants in select industries to (1) characterize urinary concentrations of the OPE metabolites and PBDE serum concentrations among workers from different industries, (2) compare industries to each other and to the U.S. general population, and (3) evaluate the most likely route of exposure (i.e., dermal or inhalation).

2. METHODS AND MATERIALS

2.1. Study Design. The study design was described previously along with results from personal air and hand wipe samples.[27] Briefly, a convenience sample of 18 companies was recruited across the following industries from 2015 to 2017: chemical manufacturing, gymnastics schools, roofing, foam manufacturing, nail salons, electronic scrap, rigid board installation, and spray polyurethane foam application. At each company, all workers performing job tasks with potential exposures to flame retardants were invited to participate in the study. All participants consented to participate in the study and were asked demographic and career-related questions to better understand how these factors affected their exposures. This study was reviewed and approved by the Centers for Disease Control and Prevention (CDC)/National Institute for Occupational Safety and Health (NIOSH) Institutional Review Board (IRB) (§ See 45 CFR part 46.101(c); 21 CFR part 56). All participants provided their written consent.

Sampling methods were the same for all industries and included the collection of urine and serum samples, which were analyzed per Sections 2.2 and 2.3. Table 1 provides a full list of the urinary and serum chemical exposure biomarkers measured in all of the workers. Results of personal air and hand wipe samples collected concurrently were reported previously.[27] Briefly, air samples consisted of a time weighted average of two full workdays of the parent chemicals shown in Table 1. Based on a review of safety data sheets and knowledge of the manufacturing processes, air and hand wipe samples were evaluated for flame retardant classes known or suspected to be present—therefore, not all air and hand wipe samples were analyzed for all analytes. Other information collected included gender, age, race, ethnicity, body mass index (BMI), length of time working in the industry, hand washing practices (categorized as yes and no, based on whether the participants reported that they washed their hands at least once during their shift), glove use (categorized as yes, no, and intermittent glove use), and wearing nail polish. Data collection was not always on the first day of the work week, so we collected the day they last worked (e.g., yesterday, 2 days ago).

2.2. Urine Sampling and Analysis. The urine sampling design was described previously.[37] Briefly, each worker provided two spot urine samples over 2 days (preshift on the first day and postshift on the following day). The timing of urine collection was chosen to best determine biomarker differences over 2 days and to compare to chemical concentrations from 2 days of air sampling. All participants provided a minimum of 60 mL (mL) of urine for each collection.

Following collection, samples were kept in coolers with ice for up to 4 h, aliquoted into 10 mL polypropylene vials, and

Table 1. Flame Retardant Parent Chemicals and Biomarkers Quantified in Urine and Serum

parent chemical	biomarker in urine
organophosphate esters (OPEs)	
triphenyl phosphate (TPP or TPhP)	diphenyl phosphate (DPhP)[a]
tris(1,3-dichloro-2-propyl) phosphate (TDCPP)	bis(1,3-dichloro-2-propyl) phosphate (BDCPP)
tri-p-cresyl phosphate (TpCP)	di-p-cresyl phosphate (DpCP)
tris(1-chloro-2-propyl) phosphate (TCPP or TCIPP)	bis(1-chloro-2-propyl) phosphate (BCPP)
tributyl phosphate or tri-*n*-butyl phosphate (TBP or TnBP)	dibutyl phosphate (DBP or DBuP)
tribenzyl phosphate (TBzP)	dibenzyl phosphate (DBzP)
tris(2-chloroethyl) phosphate (TCEP)	bis(2-chloroethyl) phosphate (BCEtP)
tri-o-cresyl phosphate (ToCP)	di-o-cresyl phosphate (DoCP)
other brominated flame retardants (BFRs)	
2-ethylhexyl 2,3,4,5-tetrabromobenzoate (EH-TBB)	2,3,4,5-tetrabromobenzoic acid (TBBA)

parent chemical	biomarker in serum
polybrominated diphenyl ethers (PBDEs)	
2,2′,4-tribromodiphenyl ether (BDE-17)	BDE-17
2,4,4′-tribromodiphenyl ether (BDE-28)	BDE-28
2,2′,4,4′-tetrabromodiphenyl ether (BDE-47)	BDE-47
2,3′,4,4′-tetrabromodiphenyl ether (BDE-66)	BDE-66
2,2′,3,4,4′-pentabromodiphenyl ether (BDE-85)	BDE-85
2,2′,4,4′,5-pentabromodiphenyl ether (BDE-99)	BDE-99
2,2′,4,4′,6-pentabromodiphenyl ether (BDE-100)	BDE-100
2,2′,4,4′,5,5′-hexabromodiphenyl ether (BDE-153)	BDE-153
2,2′,4,4′,5,6′-hexabromodiphenyl ether (BDE-154)	BDE-154
2,2′,3,4,4′,5′,6-heptabromodiphenyl ether (BDE-183)	BDE-183
2,2′,3,3′,4,4′,5,5′,6-nonabromodiphenyl ether (BDE-206)	BDE-206
decabromodiphenyl ether (BDE-209)	BDE-209

[a] Other examples of parent compounds for this biomarker: isopropylphenyl diphenyl phosphate, *t*-butylphenyl diphenyl phosphate, and EH-DPhP.

stored at or below −20 °C. Specific gravity (SG) was measured in the field with a Master Refractometer (Master-SUR/Nα, Atago, Tokyo, Japan). Urine samples were shipped overnight on dry ice to the CDC Environmental Health Laboratory and stored at or below −40 °C until analysis. After enzymatic hydrolysis of 400 μL urine samples and off-line solid phase extraction, the nine target metabolites were separated via reversed phase high-performance liquid chromatography and detected by isotope dilution-electrospray ionization tandem mass spectrometry.[29] Quality control was conducted by repeat analysis of two in-house pools, whose target concentrations and confidence limits were previously determined for each metabolite of interest. Creatinine was measured at the CDC in spot urine samples using an enzymatic method with a Roche/Hitachi Cobas c501 chemical analyzer (Roche Diagnostics, Inc., Indianapolis, IN). This study reports specific gravity (SG)-adjusted concentrations in the main text, with unadjusted and creatinine-adjusted concentrations in the Supporting Information to enable comparisons between industries and the U.S. general population.

2.3. Blood Sampling and Analysis. Two blood samples were collected at the same time as the urine samples in two red top collection tubes, and samples were placed in a rack to clot for 2 h at room temperature. They were then centrifuged for 15 min at 2400 rpm. Using a transfer pipet in the field, serum was aliquoted from the red-top tube into a separate 1/2 oz glass jar for serum lipid analysis. Lipids were determined using commercially available test kits from Roche Diagnostics Corp. (Indianapolis, IN) for the quantitative determination of total triglycerides (product no. 011002803-0600) and total cholesterol (product no. 011573303-0600). Blood collection tubes were stored in the freezer (−20 °C) until shipment for analysis.

Serum samples were analyzed at CDC for a panel of 12 PBDEs by gas chromatography isotope dilution high resolution mass spectrometry as previously detailed.[9,41] Quality control included analysis of three blank samples and three quality control samples in every set of 30 samples and subtracting any results found in the blanks. PBDE concentrations were adjusted for lipids before the statistical analyses.

2.4. Statistical Analysis. Summary statistics were displayed as the frequency (%), mean ± standard deviation (SD), median, and range for worker characteristics. The total number of samples (N), percentage of concentrations above the limit of detection (LOD), geometric mean (GM), and geometric standard deviation (GSD) were provided for urinary and serum concentrations by industry. In calculating the descriptive statistics, values assigned to nondetectable concentrations were imputed using LOD divided by the square root of 2.[42,43] Likewise, the National Health and Nutrition Examination Survey (NHANES) data, which were compared to the industrial data, were imputed the same way. Because of long half-lives in the body for the PBDEs (e.g., 15 days to 4 years) detected in serum,[9,11] concentrations in the two serum sample results were averaged. Urinary pre- and postshift concentrations and averaged serum concentrations were log-transformed because corresponding distributions were right-skewed and log-normal.

A paired *t*-test was carried out to examine differences between specific gravity (SG)-adjusted urinary concentrations for preshift day one and postshift day two. Multiple comparisons were conducted to determine significant differences ($p < 0.05$) among industries of urinary preshift and postshift biomarker concentrations and averaged serum biomarker concentrations. Spearman correlation coefficients for time-weighted average (TWA) air (ng/m^3) and hand wipe postshift (μg/sample) samples and for SG-adjusted urinary postshift concentration (ng/mL) by industry were also calculated. Note that the TWA method was only applied to the air samples. Welch's *t* test was used to determine differences in unadjusted and creatinine-adjusted urinary concentrations of target biomarkers (shown in the Supporting Information) between individual industries and the U.S. general population from NHANES 2015−2016 for unweighted urine biomarkers.[44] For serum data, median values from the general population from NHANES are provided.[45] NHANES data were limited to participants aged 18 and older for urine concentrations and 20 and older for serum concentrations.

A mixed model with industry as a random effect was utilized to account for the statistical correlation among participants from the same industry. The model incorporated the use of maximum likelihood estimation method to reduce bias resulting from the data in the presence of nondetectable biomarker concentrations.[46] Univariable and multivariable analyses were carried out using the log-transformed, SG-adjusted urinary postshift biomarker concentrations (ng/mL) and averaged serum biomarker concentrations (ng/g lipid) as the dependent variables while adjusting for industry. The logarithmic urinary creatinine level (mg/dL) was also adjusted for in the urinary models in the Supporting Information.[47] Note that we analyzed only the biomarkers or analytes detected in greater than 50% of samples. Covariates treated as fixed effects were evaluated: air and hand wipe concentrations, age, BMI, length of working time, and hand washing practices. A multivariate regression model was conducted using covariates that had $p \leq 0.2$. A stepwise selection approach was implemented in which the covariates were entered one at a time into the model until all remaining variables had the greatest impact. All analyses were performed in SAS ver. 9.4 (SAS Institute, Cary, NC).

3. RESULTS

3.1. Demographics. One hundred eleven workers from 18 companies consisting of eight industries consented to participate in the study. Eight of these participants were excluded because of missing urine or blood samples, resulting in 103 participants. Characteristics of the 103 participants are listed in Table 2. Air and hand wipe samples were only analyzed for select analytes expected in the worker's industry, as reported previously.[27]

3.2. Urine Results. Summary and statistical testing results of specific gravity (SG)-adjusted urine metabolite concentrations (ng/mL) are provided in Table 3 and Figure 1 (see Table S1 and Figure S1 for unadjusted urine metabolite concentrations (ng/mL) and Table S2 and Figure S2 for creatinine-adjusted concentrations (μg/g creatinine)). Because some of the participants worked outside on hot days (90 °F+), which impacted their urinary creatinine levels, results that have been adjusted for SG could be less affected by hot environments or other factors. However, NHANES does not provide SG-adjusted results, so comparisons to the U.S. general population were made using unadjusted and creatinine-adjusted concentrations as shown in the Supporting Information.

Sixty-three (61%) of the participants worked the previous day, while 34 participants' (32%) last shift worked was 3 or more days before. Preshift SG-adjusted and creatinine-adjusted urinary concentrations were statistically higher for workers who worked "yesterday" compared to those who last worked "3 or 4 days ago" for BCPP (see Tables S3 and S4).

In general, concentrations of OPE metabolites, with the exception of bis(1,3-dichloro-2-propyl) phosphate (BDCPP) increased from preshift to postshift across many industries. BDCPP worker SG-adjusted urinary concentrations from only spray polyurethane foam application increased statistically from pre- to postshift. For many of the OPEs, both pre- and postshift unadjusted and creatinine-adjusted levels were orders of magnitude higher than the general populations, likely due to the long half-life (54 days) of BDCPP.

Diphenyl phosphate (DPhP) urinary pre- and postshift SG-adjusted concentrations in chemical manufacturing workers were significantly higher ($p < 0.001$) than those from other industries. Urinary postshift SG-adjusted GM concentrations of DPhP were significantly higher than preshift GM concentrations among roofing, foam manufacturing, spray polyurethane foam, electronic scrap, and nail salon workers. DPhP urinary pre- and postshift unadjusted and creatinine-adjusted GM concentrations in chemical manufacturing ($p < 0.001$) were significantly higher than the concentrations reported in the U.S. general population.[44] In addition, compared to the concentrations reported in the U.S. general population, roofing and foam manufacturing workers had significantly higher DPhP postshift unadjusted and creatinine-adjusted GM concentrations (all $p \leq 0.012$).

Chemical manufacturing workers' BDCPP pre- and postshift SG-adjusted urinary concentrations were 2.3−49 times higher than those of the other industries. Compared to the U.S.

Table 2. Characteristics of Study Participants, $N = 103$ (2015−2017)

characteristic	frequency (%)
gender	
male	79 (76.7)
female	24 (23.3)
age, years	mean ± SD = 35.1 ± 11.2; median = 34.0; range = 18.0−64.0
race	
White	79 (76.7)
Black	6 (5.8)
Asian	12 (11.7)
other	6 (5.8)
ethnicity	
Hispanic or Latino	6 (5.8)
not Hispanic or Latino	97 (94.2)
creatinine[a], mg/dL	mean ± SD = 186.7 ± 102.9; median = 169.8; range = 7.2−653.5
specific gravity (SG), μg/L	mean ± SD = 1.023 ± 0.007; median = 1.024; range = 1.004−1.038
BMI, kg/m^2	mean ± SD = 26.8 ± 5.3; median = 25.1; range = 18.9−43.0
length of working time, years	mean ± SD = 4.4 ± 4.9; median = 2.5; range = 0.005−23.0
hand-washed[b]	
no	29 (28.2)
yes	73 (70.9)
missing	1 (1.0)
glove worn	
no	30 (29.1)
intermittent	40 (38.8)
yes	33 (32.0)
nails polished last week	
no	98 (95.2)
yes	5 (4.9)
industry (no. of companies)	
chemical manufacturing (1)	10 (9.7)
electronic scrap (2)	19 (18.5)
foam manufacturing (2)	11 (10.7)
gymnastics schools (1)	9 (8.7)
install rigid board (1)	3 (2.9)
nail salons (4)	12 (11.7)
roofing (1)	10 (9.7)
spray polyurethane (6)	29 (28.2)

[a] Analyzed from spot urine samples. [b] Workers were asked if they washed their hands since the beginning of their shift.

Table 3. OPE Urine Metabolite Concentrations Adjusted for Specific Gravity (SG) (ng/mL) by Industry (2015−2017)[a,e]

		preshift concentration (ng/mL)				postshift concentration (ng/mL)				
analyte	industry	N	% >LOD[b]	GM (GSD)	multiple comparisons[c]	N	% >LOD[b]	GM (GSD)	multiple comparisons[c]	p-value[d] (pre vs post)
DPhP	overall	102	93	1.84 (3.14)		102	99	3.07 (3.19)		
	chemical mfg. (C)	10	100	17.4 (2.20)		10	100	27.3 (2.06)		0.183
	roofing (R)	9	100	2.64 (1.86)	C-R	10	100	6.07 (1.97)	C-R	0.020
	gymnastics (G)	9	100	2.43 (1.25)	C-G	9	100	2.66 (1.87)	C-G	0.614
	electronic scrap (E)	19	95	1.40 (2.72)	C-E	19	100	1.96 (1.85)	C-E, R-E, F-E	0.046
	spray poly. (S)	29	97	1.32 (2.38)	C-S	29	97	2.04 (2.07)	C-S, R-S, F-S	0.010
	foam mfg. (F)	11	91	1.28 (3.35)	C-F	10	100	5.16 (4.22)	C-F	0.023
	nail salon (N)	12	75	1.03 (1.90)	C-N	12	100	1.70 (2.15)	C-N, R-N, F-N	0.010
	rigid board (B)	3	67	0.86 (2.16)	C-B	3	100	0.57 (1.47)	C-B, R-B, F-B	0.372
BDCPP	overall	103	96	3.45 (3.51)		103	97	3.83 (4.19)		
	chemical mfg.	10	100	19.9 (2.63)		10	100	25.5 (3.03)		0.471
	roofing	10	100	7.61 (1.85)		10	100	10.9 (2.03)		0.076
	spray poly.	29	100	4.63 (2.56)	C-S	29	100	6.08 (2.52)	C-S	0.043
	gymnastics	9	100	4.61 (1.78)	C-G	9	100	5.28 (2.27)	C-G	0.580
	electronic scrap	19	95	2.06 (3.21)	C-E, R-E	19	100	2.22 (3.11)	C-E, R-E, S-E	0.591
	foam mfg.	11	100	2.00 (2.14)	C-F, R-F	11	100	2.29 (1.91)	C-F, R-F	0.417
	rigid board	3	67	1.25 (3.82)	C-B	3	67	0.55 (4.64)	C-B, R-B, S-B, G-B	0.020
	nail salon	12	83	0.78 (2.58)	C-N, R-N, S-N, G-N	12	83	0.52 (2.71)	C-N, R-N, S-N, G-N, F-N, E-N	0.007
BCPP	overall	103	89	1.69 (8.51)		103	91	3.04 (12.7)		
	spray poly.	29	100	28.9 (4.49)		29	100	76.4 (4.05)		<0.001
	chemical mfg.	10	100	2.65 (1.94)	S-C	10	100	4.28 (3.34)	S-C	0.190
	roofing	10	100	1.00 (1.72)	S-R	10	100	4.42 (1.75)	S-R	<0.001
	foam mfg.	11	100	0.73 (2.02)	S-F	11	100	4.03 (2.32)	S-F	<0.001
	electronic scrap	19	74	0.34 (2.55)	S-E, C-E	19	89	0.33 (2.54)	S-E, R-E, C-E, F-E	0.784
	gymnastics	9	100	0.32 (2.05)	S-G, C-G	9	78	0.28 (1.74)	S-G, R-G, C-G, F-G	0.626
	nail salon	12	58	0.28 (1.71)	S-N, C-N	12	67	0.23 (1.78)	S-N, R-N, C-N, F-N	0.246
	rigid board	3	67	0.26 (1.39)	S-B, C-B	3	67	0.14 (1.60)	S-B, R-B, C-B, F-B	0.242
		preshift concentration (ng/mL)				postshift concentration (ng/mL)				
analyte	industry	*N*	% >LOD[b]	GM (GSD)	multiple comparisons[c]	*N*	% >LOD[b]	GM (GSD)	multiple comparisons[c]	*p*-value[d] (pre vs post)
DBuP	overall	103	88	0.31 (3.72)		103	93	0.45 (4.57)		
	chemical mfg.	10	100	2.31 (2.65)		10	100	5.91 (2.40)		0.013
	rigid board	3	100	0.44 (1.60)		3	100	0.29 (1.27)	C-B	0.369
	gymnastics	9	100	0.40 (2.35)	C-G	9	100	0.38 (1.55)	C-G	0.762
	foam mfg.	11	91	0.35 (3.17)	C-F	11	100	0.47 (1.84)	C-F	0.453
	roofing	10	100	0.31 (2.00)	C-R	10	100	0.42 (1.51)	C-R	0.086
	spray poly.	29	86	0.24 (4.51)	C-S	29	86	0.52 (6.27)	C-S	0.002
	nail salon	12	75	0.21 (2.12)	C-N	12	92	0.21 (2.28)	C-N	0.990
	electronic scrap	19	79	0.15 (2.73)	C-E	19	89	0.18 (3.55)	C-E	0.562
BCEtP	overall	103	95	0.72 (2.62)		103	96	0.75 (2.85)		
	roofing	10	100	1.16 (2.14)		10	100	1.05 (1.97)		0.649
	gymnastics	9	100	0.97 (1.82)		9	100	0.68 (2.09)		0.016
	electronic scrap	19	95	0.80 (2.58)		19	100	1.02 (2.07)		0.170
	spray poly.	29	90	0.79 (3.08)		29	93	1.01 (3.26)		0.272
	rigid board	3	100	0.77 (3.15)		3	100	0.36 (3.01)		0.390
	foam mfg.	11	100	0.56 (2.77)		11	91	0.53 (5.39)		0.891
	nail salon	12	92	0.51 (2.13)		12	92	0.46 (2.10)		0.442
	chemical mfg.	10	100	0.44 (2.47)		10	100	0.48 (2.13)		0.766
DpCP	overall	103	31	0.08 (3.84)		103	27	0.08 (4.59)		
	chemical mfg.	10	100	2.89 (3.11)		10	100	4.74 (3.32)		0.185
	roofing	10	60	0.07 (2.27)	C-R	10	60	0.08 (2.57)	C-R	0.225
	electronic scrap	19	16	0.05 (2.00)	C-E	19	11	0.04 (1.61)	C-E	0.047

Table 3. continued

		preshift concentration (ng/mL)				postshift concentration (ng/mL)				
analyte	industry	*N*	% >LOD[b]	GM (GSD)	multiple comparisons[c]	*N*	% >LOD[b]	GM (GSD)	multiple comparisons[c]	*p*-value[d] (pre vs post)
	spray poly.	29	31	0.05 (1.52)	C-S	29	21	0.05 (1.75)	C-S	0.481
	gymnastics	9	33	0.05 (1.44)	C-G	9	33	0.07 (1.93)	C-G	0.278
	foam mfg.	11	9	0.04		11	9	0.04		
	rigid board	3	0			3	0			
	nail salon	12	0			12	0			

		preshift concentration (ng/mL)				postshift concentration (ng/mL)				
analyte	industry	N	% >LOD[b]	GM (GSD)	multiple comparisons[c]	N	% >LOD[b]	GM (GSD)	multiple comparisons[c]	p-value[d] (pre vs post)
TBBA	overall	103	10	0.05 (2.08)		103	17	0.05 (2.39)		
	spray poly.	29	24	0.07 (2.66)		29	38	0.09 (3.49)		0.078
	electronic scrap	19	5	0.05		19	5	0.04		
	gymnastics	9	11	0.04		9	44	0.07 (1.92)		
	roofing	10	10	0.03		10	10	0.03		
	chemical mfg.	10	0			10	0			
	foam mfg.	11	0			11	9	0.04		
	rigid board	3	0			3	0			
	nail salon	12	0			12	0			

[a] Analytes DBzP and DoCP not listed due to all samples being below the limit of detection. [b] Limit of detection (LOD) for each analyte in ng/mL: DPhP = 0.16, BDCPP = 0.11, BCPP = 0.10, DBuP = 0.05, BCEtP = 0.08, DpCP = 0.05, TBBA = 0.05, DBzP = 0.05, and DoCP = 0.05. [c] Only significant differences in means of log-concentrations are listed. [d] A one-sample Student's *t* test was utilized to examine differences of logarithm urine pre- and postshift concentrations. [e] The abbreviations in the multiple comparisons are chemical manufacturing (C), electronic scrap (E), foam manufacturing (F), gymnastics (G), nail salon (N), rigid board installation (B), roofing (R), and spray polyurethane (S). If the means of log-concentrations for two industries were significantly different, the comparison of the two industries would be presented in the table. For example, "C-E" means that the mean of log-concentrations for chemical manufacturing was significantly different from electronic scrap.

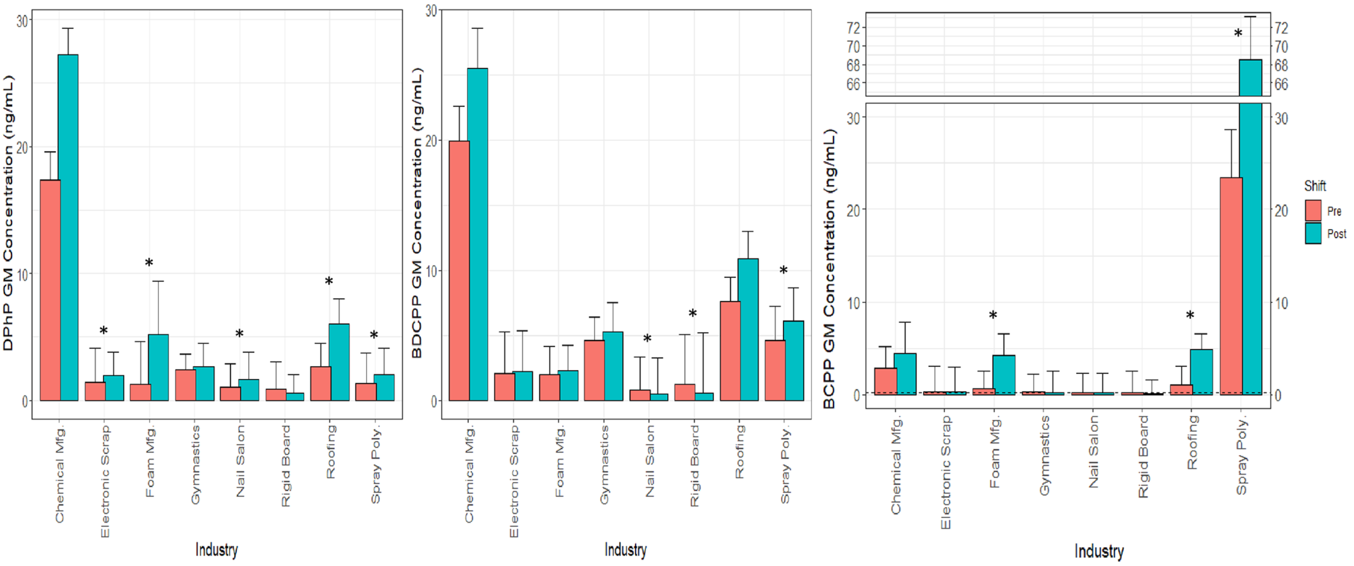

Figure 1. Specific gravity (SG)-adjusted urinary geometric mean (GM) concentrations and corresponding geometric standard deviations of DPhP, BDCPP, and BCPP (ng/mL) by industry. Asterisks (*) represent the significant mean differences between pre- and postshift concentrations by industry and analyte.

general population, chemical manufacturing, roofing, gymnastics instructors, and spray polyurethane foam workers had significantly higher BDCPP pre- and postshift unadjusted and creatinine-adjusted GM concentrations (all $p \leq 0.014$).

Bis(1-chloro-2-propyl) phosphate (BCPP) urinary pre- and postshift SG-adjusted concentrations for spray polyurethane foam workers were notably higher than those for all other industries. Postshift GM concentrations of BCPP collected from spray polyurethane foam, roofing, and foam manufacturing workers were significantly higher than the preshift concentrations. Spray polyurethane foam, chemical manufacturing, roofing, and foam manufacturing workers had significantly greater BCPP pre- and postshift unadjusted and creatinine-adjusted GM concentrations relative to the U.S. general population (all $p < 0.001$).

Dibutyl phosphate (DBuP) pre- and postshift SG-adjusted concentrations for chemical manufacturing workers were higher than those for all other industries. Postshift SG-adjusted

Table 4. Multivariable Analysis Results Using Log-Transformed, Specific Gravity-Adjusted OPE Urinary Postshift Concentration (ng/mL) as the Outcome or Dependent Variable[c]

urinary outcome (N)	covariate or independent variable	N of air or hand wipe samples	estimate (SE)	p-value	factor[b]
DPhP(N = 102)	time-weighted average (TWA) air concentration, ng/m^3[a]	66	0.12 (0.10)	0.289	1.12
	hand wipe post concentration, μg/sample[a]	51	1.2×10^{-4} (4×10^{-5})	0.036	1.00012
BDCPP (N = 103)	time-weighted average (TWA) air concentration, ng/m^3[a]	91	0.38 (0.18)	0.096	1.46
	hand wipe post concentration, μg/sample[a]	76	6×10^{-6} (3×10^{-6})	0.151	1.00001
BCPP(N = 103)	time-weighted average (TWA) air concentration, ng/m^3[a]	91	0.005 (0.001)	0.016	1.005
	hand wipe post concentration, μg/sample[a]	90	7×10^{-6} (2×10^{-6})	0.013	1.00001

[a]Air and hand wipe environmental measures are for the relevant parent chemical as shown in Table 1. TPhP was compared to DPhP, TDCPP was compared to BDCPP, and TCPP was compared to BCPP. [b]Exponent of the estimate, e.g., interpretation of the factor = 1.12 is that for every increment, after adjusting for industry, if the TWA air concentration increases by 1 ng/m^3, then DPhP increases by 1.12 ng/mL. [c]Industry was adjusted for in the analyses.

Table 5. Spearman Correlation Coefficients (r) for Time-Weighted Average (TWA) Air (ng/m^3) and Hand Wipe Post (μg/sample) Samples and Specific Gravity-Adjusted OPE Urinary Postshift Concentration (ng/mL)

	SG-adjusted														
	DPhP					BDCPP					BCPP				
		air TPhP		hand TPhP			air TDCPP		hand TDCPP			air TCPP		hand TCPP	
industry	N	coeff.	p-value[d]	coeff.	p-value[d]	N	coeff.	p-value[d]	coeff.	p-value[d]	N	coeff.	p-value[d]	coeff.	p-value[d]
chemical mfg.	5	0.700	0.188	0.200	0.747	10	0.479	0.162	0.794	0.006	10	0.576	0.082	0.697	0.025
electronic scrap	19	0.063	0.797	0.279	0.248	19	−0.079	0.748	0.300	0.211	19	0.032	0.898	0.393	0.096
foam mfg.	0					11	−0.418	0.201	0.219	0.517	11	0.164	0.631	−0.100	0.770
gymnastics	9	0.400	0.286	0.917	<0.001	9	−0.033	0.932	0.717	0.030	9	0.117	0.765	−0.542	0.131
nail salon	12[a]	−0.308	0.331	0.245	0.467	0					0				
roofing	0					10	0.176	0.627	0.248	0.489	10	0.127	0.726	0.879	<.001
spray poly.	21[b]	−0.362	0.107	0.464	0.294	29[c]	0.220	0.251	0.250	0.369	29	0.227	0.237	0.170	0.378
overall	66	0.179	0.151	0.410	0.003	88	0.360	<.001	0.661	<.001	88	0.892	<.001	0.828	<.001

[a]N = 12, except for hand wipe post TPhP, where N = 11. [b]N = 21, except for hand wipe post TPhP, where N = 7. [c]N = 29, except for hand wipe post TDCPP, where N = 15. [d]Red p-values are significantly different from the correlation coefficient equal to zero.

GM concentrations of DBuP collected from chemical manufacturing and spray polyurethane foam workers were significantly greater than preshift GM concentrations (both $p \leq 0.013$). Chemical manufacturing, gymnastics instructors, and foam manufacturing workers had higher pre- and postshift GM unadjusted and creatinine-adjusted concentrations than the U.S. general population ($p \leq 0.042$), while roofing and spray polyurethane foam workers had higher postshift unadjusted and creatinine-adjusted GM concentrations ($p \leq 0.03$).

Di-p-cresyl phosphate (DpCP) urinary concentrations were detected in fewer than 50% of samples, but DpCP was detected in 100% of urine samples collected from chemical manufacturing workers and 60% of urine samples collected from roofers (LOD of 0.05 ng/mL). 2,3,4,5-Tetrabromobenzoic acid (TBBA) urinary concentrations were detected in fewer than 50% of the samples. Concentrations of other urinary biomarkers, dibenzyl phosphate (DBzP) and di-o-cresyl phosphate (DoCP), were all below the LOD of 0.05 ng/mL and will not be discussed further.

The results of the multivariable analysis using urinary SG-adjusted concentrations are shown in Table 4 (see Table S5 for results of univariable analyses). SG-adjusted results were used in these analyses because they may be less impacted by heat, as previously stated. We also included univariable and multivariable analysis results using urinary creatinine-adjusted concentrations in Tables S6 and S7 accordingly. Both TCPP TWA air and hand wipe postshift concentrations were positively associated with BCPP urine postshift SG-adjusted concentration (p = 0.016 and 0.013, respectively). In addition, TPhP hand wipe postshift concentrations were positively and significantly associated with DPhP urine postshift SG-adjusted concentration when adjusting for TPhP TWA air concentrations in the model (p = 0.036). Note that we excluded DBuP from univariable analyses because air or hand wipe samples were not analyzed for TBuP.

Correlation coefficients (r) were calculated overall and by industry group to determine the correlations of TWA air and hand wipe postshift parent compound concentrations to SG-adjusted concentrations of DPhP, BDCPP, and BCPP. Significant correlations were found between hand wipe TPhP and DPhP in gymnastic instructors, hand wipe TDCPP and BDCPP in chemical manufacturing workers and gymnastic instructors, and hand wipe TCPP and BCPP in chemical manufacturing and roofing workers (Table 5; see Table S8 for unadjusted and creatinine-adjusted urinary concentrations).

3.3. Blood Results.

All workers were asked to provide blood samples but could participate in the study without providing them. As a result, serum sampling results were evaluated for 91 participants (Table 6 and Figure 2). Figure 2 shows PBDE results by industry; data for BDE-17 and BDE-66 with relatively low detection frequency (both 12%) are provided in Table S9. Electronic scrap workers had greater median serum concentrations than those in the U.S. general population for BDE-183 (0.55 vs 0.21 ng/g lipid) and BDE-

Table 6. PBDE Average of Geometric Mean (GM) Serum Concentrations (ng/g lipid) by Industry (2015−2017)

analyte	industry	*N*	% >LOD[a]	GM (ng/g lipid) (GSD)	median(ng/g lipid)	multiple comparisons of industries[b]
BDE-28	overall	91	90.1	0.46 (2.20)	0.43	
	electronic scrap	18	94.4	0.81 (2.23)	0.85	
	roofing	10	100.0	0.53 (2.39)	0.57	
	gymnastics	9	88.9	0.47 (2.00)	0.49	
	nail salon	8	100.0	0.43 (1.63)	0.44	
	spray poly.	24	87.5	0.41 (2.11)	0.35	
	chemical mfg.	10	90.0	0.39 (1.55)	0.41	
	foam mfg.	9	77.8	0.28 (2.45)	0.24	E-F
	rigid board	3	66.7	0.17 (1.28)	0.17	E-B
	NHANES[c]	1637	89.1		0.74	
BDE-47	overall	91	100.0	7.71 (2.66)	7.20	
	electronic scrap	18	100.0	12.25 (2.72)	13.05	
	gymnastics	9	100.0	11.24 (2.18)	13.31	
	roofing	10	100.0	10.20 (2.50)	10.05	
	spray poly.	24	100.0	7.26 (2.80)	6.36	
	chemical mfg.	10	100.0	6.64 (1.88)	8.25	
	nail salon	8	100.0	5.84 (1.73)	6.25	
	foam mfg.	9	100.0	4.20 (3.25)	2.40	
	rigid board	3	100.0	2.11 (1.40)	2.51	
	NHANES[c]	1637	100.0		12.99	
BDE-85	overall	91	47.3	0.22 (1.91)	0.19	
	gymnastics	9	77.8	0.36 (1.88)	0.43	
	electronic scrap	18	61.1	0.25 (2.38)	0.21	
	roofing	10	40.0	0.24 (1.54)	0.24	
	spray poly.	24	37.5	0.23 (1.90)	0.19	
	chemical mfg.	10	90.0	0.22 (1.41)	0.23	
	nail salon	8	12.5	0.15 (1.24)	0.15	
	foam mfg.	9	22.2	0.14 (1.69)	0.12	
	rigid board	3	0.0			
	NHANES[c]	1637	32.8		0.17	
BDE-99	overall	91	100.0	1.53 (2.66)	1.43	
	gymnastics	9	100.0	2.97 (2.32)	4.17	
	electronic scrap	18	100.0	2.15 (3.07)	1.80	
	roofing	10	100.0	1.81 (2.41)	2.00	
	chemical mfg.	10	100.0	1.64 (2.09)	1.80	
	spray poly.	24	100.0	1.37 (2.48)	1.23	
	nail salon	8	100.0	1.23 (1.60)	1.13	
	foam mfg.	9	100.0	0.82 (2.68)	0.48	
	rigid board	3	100.0	0.32 (1.93)	0.34	G-B, E-B
	NHANES[c]	1637	100.0		2.45	
analyte	industry	*N*	% >LOD[a]	GM (ng/g lipid) (GSD)	median(ng/g lipid)	multiple comparisons of industries[b]
BDE-100	overall	91	100.0	1.70 (2.55)	1.74	
	gymnastics	9	100.0	2.60 (2.08)	3.30	
	electronic scrap	18	100.0	2.13 (2.27)	2.08	
	roofing	10	100.0	1.87 (2.48)	2.06	
	chemical mfg.	10	100.0	1.77 (1.98)	2.00	
	spray poly.	24	100.0	1.74 (2.96)	1.57	
	nail salon	8	100.0	1.29 (1.83)	1.48	
	foam mfg.	9	100.0	1.04 (3.56)	0.90	
	rigid board	3	100.0	0.54 (1.20)	0.58	
	NHANES[c]	1637	100.0		2.61	
BDE-153	overall	91	100.0	7.22 (2.76)	6.14	
	spray poly.	24	100.0	10.47 (2.51)	8.17	
	roofing	10	100.0	10.34 (2.80)	6.72	
	gymnastics	9	100.0	10.33 (2.58)	9.25	
	rigid board	3	100.0	7.99 (2.07)	6.14	
	chemical mfg.	10	100.0	7.06 (3.20)	5.36	
	electronic scrap	18	100.0	5.65 (2.59)	4.94	
	foam mfg.	9	100.0	5.35 (2.67)	4.15	
	nail salon	8	100.0	2.43 (1.91)	2.11	S-N, R-N, G-N

Table 6. continued

analyte	industry	*N*	% >LOD[a]	GM (ng/g lipid) (GSD)	median(ng/g lipid)	multiple comparisons of industries[b]
	NHANES[c]	1637	100.0		9.73	
BDE-154	overall	91	49.5	0.21 (1.85)	0.17	
	gymnastics	9	77.8	0.32 (1.84)	0.39	
	electronic scrap	18	61.1	0.24 (2.09)	0.23	
	chemical mfg.	10	90.0	0.22 (1.48)	0.22	
	spray poly.	24	33.3	0.22 (1.96)	0.17	
	roofing	10	30.0	0.21 (1.47)	0.19	
	foam mfg.	9	44.4	0.16 (1.87)	0.12	
	nail salon	8	37.5	0.15 (1.34)	0.14	
	rigid board	3	0.0			
	NHANES[c]	1637	51.9		0.14	
BDE-183	overall	91	51.6	0.22 (2.20)	0.17	
	electronic scrap	18	94.4	0.50 (2.44)	0.55	
	foam mfg.	9	55.6	0.24 (2.41)	0.19	
	spray poly.	24	50.0	0.22 (2.05)	0.18	E-S
	roofing	10	40.0	0.20 (1.51)	0.19	E-R
	gymnastics	9	33.3	0.15 (1.45)	0.13	E-G
	chemical mfg.	10	40.0	0.14 (1.86)	0.10	E-C
	rigid board	3	33.3	0.13 (1.35)	0.13	E-B
	nail salon	8	12.5	0.13 (1.12)	0.14	E-N
	NHANES[c]	1637	15.9		0.21	
analyte	industry	*N*	% >LOD[a]	GM (ng/g lipid) (GSD)	median(ng/g lipid)	multiple comparisons of industries[b]
BDE-209	overall	91	95.6	1.79 (1.86)	1.73	
	electronic scrap	18	100.0	3.35 (1.89)	2.97	
	gymnastics	9	100.0	1.87 (1.39)	2.00	
	spray poly.	24	87.5	1.72 (1.90)	1.61	E-S
	nail salon	8	100.0	1.64 (1.54)	1.55	E-N
	rigid board	3	100.0	1.57 (1.38)	1.81	
	foam mfg.	9	100.0	1.46 (1.71)	1.43	E-F
	chemical mfg.	10	100.0	1.27 (1.47)	1.17	E-C
	roofing	10	90.0	1.14 (1.46)	1.05	E-R
	NHANES[c]	1637	98.4		1.79	
sum[d]	overall	91		25.65 (2.14)	21.88	
	gymnastics	9		35.40 (1.76)	38.38	
	electronic scrap	18		31.54 (2.19)	32.96	
	roofing	10		30.17 (2.17)	32.90	
	spray poly.	24		29.12 (2.19)	23.63	
	chemical mfg.	10		23.53 (1.91)	21.38	
	foam mfg.	9		16.65 (2.45)	14.09	
	nail salon	8		14.19 (1.54)	14.11	
	rigid board	3		14.06 (1.57)	10.90	
	NHANES[c]	1637			33.59	

[a] Maximum limit of detection (LOD) divided by the square root of 2 in ng/g lipid for each analyte in the general population (GP): BDE-28 = 0.37, BDE-47 = 0.31, BDE-85 = 0.35, BDE-99 = 0.30, BDE-100 = 0.25, BDE-153 = 0.25, BDE-154 = 0.24, BDE-183 = 0.29, and BDE-209 = 0.92. The maximum LOD divided by the square root of 2 for the serum samples collected: BDE-28 = 0.21, BDE-85 = 0.38, BDE-154 = 0.35, BDE-183 = 0.23, and BDE-209 = 0.85. All concentration levels were detected for BDE-47, BDE-99, BDE-100, and BDE-153. [b] Only significant differences in means of log-concentrations are listed. The abbreviations in the multiple comparisons are chemical manufacturing (C), electronic scrap (E), foam manufacturing (F), gymnastics (G), nail salon (N), rigid board installation (B), roofing (R), and spray polyurethane (S). If the means of log-concentrations for two industries were significantly different, the comparison of the two industries would be presented in the table. For example, "C-E" means that the mean of log-concentrations for chemical manufacturing (C) was significantly different from electronic scrap (E). Red *p*-values are significantly higher. [c] The data that restricted participants aged 20 years and older are from the National Health and Nutrition Examination Survey (NHANES) during 2015/16: https://wwwn.cdc.gov/Nchs/NHANES/2015-2016/BFRPOL_I.htm. [d] Summation of BDE-17, BDE-28, BDE-47, BDE-66, BDE-85, BDE-99, BDE-100, BDE-153, BDE-154, BDE-183, and BDE-209.

209 (2.97 vs 1.79 ng/g lipid); their levels were also significantly greater compared to most of the other industries evaluated in this study.

Univariable results for associations between industry and determinants of exposure are provided for BDE-183 and BDE-209 for electronic scrap workers, because they had statistically higher concentrations than most of the other industries (Table 7). BDE-209 hand wipe postshift concentrations were positively and significantly associated with BDE-209 serum concentrations in electronic scrap workers and in all workers (both $p < 0.001$). Age was significantly related to BDE-183 serum concentrations for all industries' workers. Results of the multivariable analysis show that for the electronic scrap industry workers, BDE-183 serum concentrations increased

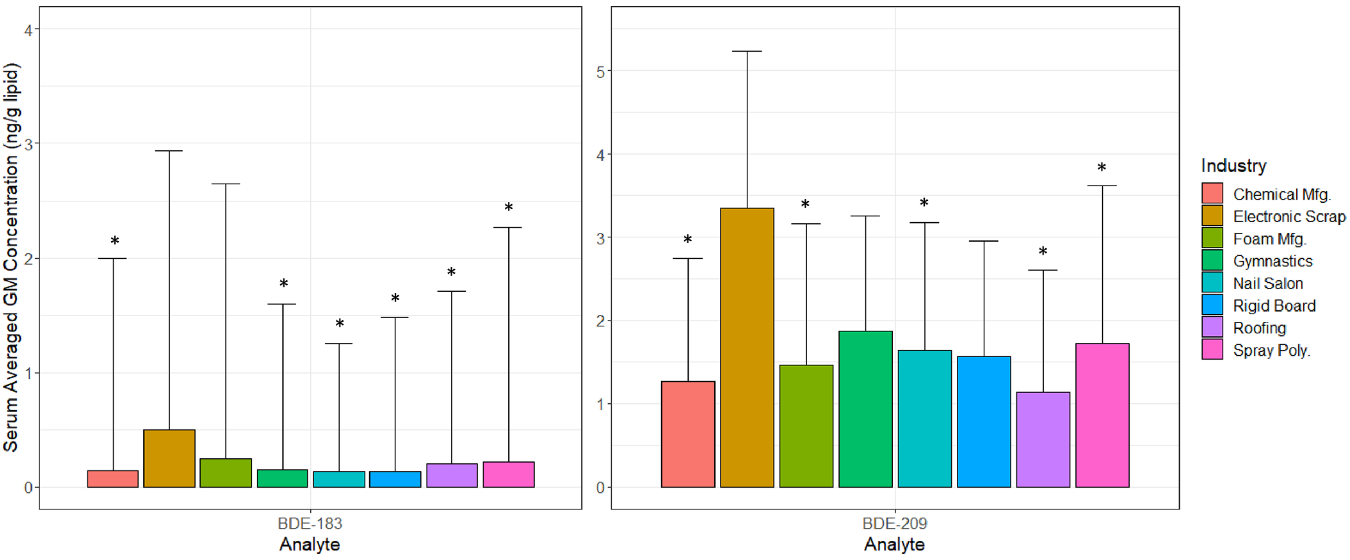

Figure 2. Serum geometric mean (GM) concentrations and corresponding geometric standard deviations of BDE-183 and BDE-209 (ng/g lipid) by industry. Asterisks (*) represent the significant mean differences between electronic scrap and specific industry by the analyte.

Table 7. Univariable Analysis Results Using Log-Transformed, Averaged PBDE Serum Concentration (ng/g lipid) as the Outcome or Dependent Variable

BDE-183								
	electronic scrap (N = 18)				all industries (N = 91)[a]			
covariate or independent variable	N	estimate (SE)	p-value	factor[b]	N	estimate (SE)	p-value	factor[b]
time-weighted average (TWA) air, ng/m^3	18	81.4 (44.1)	0.084	2.2 × 10^{35}	37	76.2 (38.1)	0.054	1.2 × 10^{33}
hand wipe post, ng/sample	18	0.03 (0.02)	0.149	1.03	27	0.03 (0.02)	0.089	1.03
age, years	18	0.03 (0.02)	0.141	1.03	91	0.02 (0.01)	0.049	1.02
BMI, kg/m^2	18	0.01 (0.04)	0.838	1.01	91	0.01 (0.01)	0.380	1.01
length of working time, years	18	0.18 (0.11)	0.131	1.20	91	0.03 (0.02)	0.116	1.03
hand wash					91			
no					26	ref		
yes					65	0.23 (0.22)	0.307	1.26

BDE-209								
	electronic scrap (N = 18)				all industries (N = 91)[a]			
covariate or independent variable	N	estimate (SE)	p-value	factor[b]	N	estimate (SE)	p-value	factor[b]
time-weighted average (TWA) air, ng/m^3	18	2.93 (3.25)	0.380	18.7	37	1.47 (1.88)	0.440	4.35
hand wipe post, ng/sample	18	0.0003 (0.0001)	<0.001	1.0003	27	0.0003 (0.0001)	<0.001	1.0003
age, years	18	−0.003 (0.01)	0.789	0.997	91	0.001 (0.01)	0.841	1.001
BMI, kg/m^2	18	−0.01 (0.03)	0.761	0.99	91	0.001 (0.03)	0.979	1.001
length of working time, years	18	0.12 (0.08)	0.154	1.13	91	0.001 (0.01)	0.965	1.001
hand wash					91			
no					26	ref		
yes					65	0.15 (0.19)	0.420	1.16

[a] Industry was adjusted for in the models. Red p-values are significantly higher. [b] Exponent of the estimate, e.g., interpretation of the factor = 1.03 is that for every increment, after adjusting for industry, if the hand wipe post concentration increases by 1 ng/sample, then BDE-183 increases by 1.03 ng/g lipid.

for every ng/m^3 increase in BDE-183 TWA air concentration (p = 0.022) and as working time increased by 1 year (p = 0.032) (Table S10).

4. DISCUSSION

This study was designed to characterize exposure to flame retardants through urinary and serum concentrations of FR biomarkers among workers across several industries. These industries were chosen, because their workers likely had occupational exposure to one or more flame retardants. Our data suggest that workers from almost all of these industries were occupationally exposed to OPEs, and electronic scrap workers were occupationally exposed to PBDEs.

4.1. Comparing Urinary OPE Results by Industry and to the General Population. We found that chemical manufacturing workers' pre- and postshift unadjusted and creatinine-adjusted GM urinary concentrations of DPhP, BDCPP, BCPP, and DBuP were an order of magnitude higher than those in the U.S. general population. Notably, the chemicals known to be produced by the participating company at the time of sample collection in our study were TDCPP and

TCPP, although it was a large plant and had processes elsewhere in the plant. Therefore, the elevated urinary concentrations of the biomarkers of other OPEs (e.g., TPhP) were unexpected, but these other OPEs were also detected in air and hand wipe samples collected from the same workers.[27] Preshift SG-adjusted GM concentrations for DPhP, BDCPP, and DpCP were also elevated among chemical manufacturing workers compared to other industries evaluated in this study. Because the chemical manufacturing workers completed a 12 h shift (a long shift compared to other workers in this study) the previous day, they were likely still metabolizing and excreting OPEs from their previous shift. This theory is supported by a recent publication[48] that reported that urine half-lives for TPhP, TDCPP, TCPP, and TBP are 9.6, 53.8, 15.2, and 4.8 days, respectively, which were longer than previous estimates that were on the order of hours.[28] Likewise, the chemical manufacturing workers had statistically higher pre- and postshift SG-adjusted GM OPE biomarker urinary concentrations than the other industries, with the noted exception of spray polyurethane foam workers' urinary BCPP concentrations. We were not able to compare DpCP to the general population from 2015 to 16, but for 2013−2014,[25] only 11% of adults had detectable concentrations.

Spray polyurethane foam workers had pre- and postshift unadjusted and creatinine-adjusted GM concentrations of urinary BCPP that were an order of magnitude higher than all other industries in this study and 2 orders of magnitude higher than those in the U.S. general population. Other investigators reported BCPP urinary metabolite concentrations of polyurethane spray foam workers that were much lower than in this current study.[36] The higher concentrations of BCPP, a biomarker of exposure to TCPP, for spray polyurethane foam workers found in this study likely relate, at least in part, to lack of ventilation during use, as spray polyurethane foam workers were observed often applying foam in tight, poorly ventilated spaces like attics or basements. Spray polyurethane foam workers' PPE use was also sporadic, as several workers wore either no or substandard (i.e., half-face air-purifying respirator) respiratory protection.[27] Additionally, the foam-making process of mixing two liquid parts to form a reaction was similar in spray polyurethane foam installation and foam manufacturing, whereas rigid board installation and roofing workers were cutting cured, solid foam. These work practices could have contributed to the higher exposures for spray polyurethane foam workers compared to other workers.

Nail salon workers' DPhP postshift urinary SG-adjusted GM concentrations were significantly higher than preshift concentrations. Nail polish often contains TPhP, and indeed, our previous paper reported that TPhP was detected in 8 of the 11 nail polish products that were used for application during sampling.[27] Nail salon workers in the current study had GM concentrations below those of nail polish-wearing (nonoccupational) participants in another study.[8] Mendelsohn et al.'s study also reported significantly lower GM urinary DPhP concentrations of participants who had nail polish applied to a gloved hand.[8] Craig et al. reported similar pre- and postshift DPhP urinary concentrations as reported here but did not find a correlation between the urinary concentrations and silicon wristband sampling.[49] Additionally, we did not find a correlation between hand wipe TPhP concentrations and urinary DPhP concentrations.

There is limited evidence of occupational exposure of OPE for electronic scrap workers, as their DPhP SG-adjusted concentrations increased from pre- to postshift ($p = 0.046$). However, when we compared electronic scrap worker DPHP creatinine-adjusted urinary concentrations to the general population, we did not find significant differences. A 2015 evaluation of U.S. electronic scrap workers reported similar GM postshift urinary concentrations for DPhP and BDCPP; however, they reported lower or nondetectable concentrations for BCPP and BCEtP.[50] Gravel et al. evaluated occupational exposures to flame retardants among electronic scrap workers in 2017 and 2018 and reported lower urinary concentrations for DPhP and BDCPP compared to the current study.[51] The electronic scrap workers' GM levels for three OPEs (DPhP, BDCPP, and BCPP) from this study were higher than the electronic scrap workers' levels from three previous studies in China.[38−40] These differences are likely reflective of the FR content in consumer electronic scrap in the two countries.

Carignan et al. evaluated flame retardant exposure in gymnasts and reported higher GM unadjusted urinary postworkout concentrations of DPhP (8.40 ng/mL) and lower concentrations of BDCPP (0.62 ng/mL) than reported in this study (1.92 and 3.81 ng/mL, respectively).[28] The type of OPE used in the gym foam pit cubes could be the reason for these differences. This study also measured TBBA and reported detection frequencies at 90 to 100%, and our study had detection frequencies of 11 and 44% for pre- and postshift, respectively. However, our LOD for TBBA was higher (0.05 ng/mL) than in Carignan's study (0.017 μg/L).[28]

We also compared our results to those of previous studies that examined FR exposure for other industries. Firefighter OPE urinary concentrations were lower than those of workers from several industries (chemical and foam manufacturing, roofers, electronic scrap, gymnastics schools, and spray polyurethane foam) evaluated in this study.[35,52] Hotel workers in China had urinary concentrations of DPhP, BDCPP, and DBuP that were lower than the concentrations measured in this study.[53] However, the Chinese hotel workers had unexpectedly higher unadjusted urinary concentrations of DoCP and DpCP (GM = 0.13 ng/mL), which was greater than those of all industries considered in this study, except chemical manufacturers. Median postshift DBuP urinary concentrations for aircraft maintenance workers were much higher when compared to the industry with the highest concentration (i.e., chemical manufacturing measured in our study).[54] Additionally, aircrew median OPE concentrations were lower than the current study concentrations.[55]

4.2. Evaluating the Relationship between Air and Hand Wipe Samples and Urinary OPE Results, Stratified by Industry. We evaluated correlations between DPhP, BDCPP, and BCPP urinary concentrations and the parent chemicals (TPhP, TDCPP, and TCPP, respectively) in hand wipes and air samples because they were consistently above U.S. general population GM levels and most likely to increase from pre- to postshift. TPhP and TCPP hand wipe concentrations were significantly associated with DPhP and BCPP postshift urinary SG-adjusted concentrations (adjusted for industry) when conducting univariable analyses (Table S5). Univariable analyses also showed that TCPP air concentrations were significantly associated with BCPP postshift urinary SG-adjusted concentrations (Table S5). When conducting multivariable analyses (Table 4), hand wipe and air concentrations were significantly related to postshift urinary BCPP concentration. Additionally, TCPP air concentrations were significantly associated with BCPP urinary concentrations when including hand wipe concentrations.

When looking more closely at each industry (Table 5), TPhP hand wipe and DPhP urinary concentrations were strongly correlated for gymnastics instructors ($r = 0.917$, $p < 0.001$). Likewise, there were a strong correlation between TCPP hand wipe and urinary BCPP concentrations for roofing workers ($r = 0.879$, $p < 0.001$) and a moderate correlation for chemical manufacturing workers ($r = 0.697$, $p = 0.025$). Hammel et al. provided correlation coefficients to compare hand wipe concentrations from the parent chemicals to urinary metabolites and reported a significant correlation for TDCPP to BDCPP (0.37, $p < 0.05$).[56] We found a strong Spearman correlation coefficient between gymnastics instructors TDCPP hand wipe and BDCPP urinary SG-adjusted concentrations ($r = 0.717$, $p = 0.030$). This is similar to previous papers, including one that reported a relationship for Chinese hotel workers (0.62, $p < 0.01$)[53] and a low correlation among a group of U.S. mothers who participated in a study to evaluate the effectiveness of house cleaning and hand washing practices to reduce flame retardant exposure (0.26, $p = 0.18$).[57]

These results suggest that both dermal absorption and inhalation are the primary routes of exposure for the resulting OPEs. Of the industries evaluated in this study, chemical manufacturing workers are exposed through both exposure routes, but dermal is likely the primary route due to the statistically significant correlations with BDCPP and BCPP SG-adjusted urinary concentrations and TDCPP and TCPP hand wipe concentrations. Gymnastics instructors are also likely exposed through their skin, as shown by correlation coefficients with SG-adjusted urinary DPhP and BCPP concentrations and TPhP and TCPP hand wipe concentrations.

4.3. PBDE Flame Retardants. PBDE serum concentrations may be declining[58,59] as a result of the phasing out of PBDE production and use in the United States and internationally. Electronic scrap workers' median serum concentrations, which reflect the decommissioning phase of the electronic scrap work products, were higher than those of the U.S. general population for BDE-183 and BDE-209 (BDE-183 is detectable in only 16% of the U.S. general population but 94% of electronic scrap workers in this study). The workers from other industries evaluated in this study do not appear to be occupationally exposed to PBDEs; however, gymnastics instructors did have higher detection frequencies for some congeners with lower detection frequencies in the U.S. general population, including BDE-85 (78%) and BDE-154 (78%). Previous studies have suggested that electronic scrap workers[26,50] are occupationally exposed to PBDEs. In the current study, electronic scrap workers' serum concentrations were statistically greater than those of most of the other industries for BDE-183 and BDE-209 (Table 6). However, the electronic scrap workers in this study had BDE-183 and BDE-209 concentrations that were an order of magnitude lower than those of female Vietnamese electronic scrap workers.[60] Also, electronic scrap workers in this study and the U.S. general population had median serum levels that were higher than those of the Vietnamese electronic scrap workers for BDE-47, BDE-99, and BDE-100.

Additionally, electronic scrap workers in our study had higher serum concentrations of BDE-17 and BDE-183 than those reported for U.S. foam recycling and carpet installation workers (BDE-209 was not measured).[31] Pakistani workers (university, clothing store, and electronic scrap) had reported BDE-47, BDE-99, and BDE-153 median concentrations at ≤1.1 ng/g lipid, which were lower than the present study.[61] Chinese chemical manufacturing workers who were producing BDE-209 had blood serum concentrations of BDE-209 that were 3 orders of magnitude higher than this study's chemical manufacturing workers and mostly nondetectable concentrations of BDE-99, BDE-100, and BDE-154, whereas our study has 100, 100, and 90% detection rates for these congeners, respectively.[62] These observed differences may be an artifact of the differences in PBDE usage between the two countries. Gravel et al. evaluated electronic scrap workers in Canada and found serum concentrations to be higher for BDE-209 compared to the current study (18 vs 3.35 ng/g lipids). However, the same study reported lower serum concentrations in electronic scrap workers for BDE-153 (4.6 vs 5.56 ng/g lipids), BDE-47 (3.8 vs 12.25 ng/g lipids), and BDE-17 (nondetectable vs 0.19 ng/g lipids) compared to the current study.[50]

Positive association between electronic scrap workers' BDE-209 hand wipe levels and serum concentrations ($p < 0.001$) potentially points to a dermal exposure pathway for BDE-209. BDE-209 has a half-life of 15 days,[9,11] so BDE-209 serum concentrations likely result from recent exposures over the past 2 weeks. BDE-183, on the other hand, has a half-life of 94 days,[11] suggesting this could represent accumulated exposure over months and therefore would be less likely to be highly correlated with air and hand wipe samples collected concurrently.

4.4. Limitations and Future Work. The number of workers in each industry was relatively low, which limited some analyses. Additionally, the participants in this study were primarily (over 75%) white non-Hispanic males, which may not accurately reflect the demographics of workers in these industries across the USA. However, FR occupational exposure data in the USA are rather limited, and this study adds relevant information to the body of literature on this topic. Although many of the urinary metabolites of the OPE are specific for the parent compounds, some OPEs have other metabolites (e.g., hydroxyl triphenyl phosphate for TPhP and 1-hydroxy-2-propyl bis(1-chloro-2- propyl) phosphate for TCPP) that were not measured in this study. Additionally, DPhP is a metabolite for several other compounds and DPhP itself is also applied to some products, meaning that DPhP concentrations in urine do not necessarily reflect an exposure to TPhP.[63,64] Additionally, the extended half-lives (i.e., 11−54 days) of some of these chemicals (e.g., DPhP, BDCPP, and BDE-209) allow for the possibility that other non-occupationally related sources of exposure, including through diet and exposure to consumer products, may contribute to the biomarker concentrations reported here. Also, many of the participants worked the previous day, so the previous day's work exposure also contributed to the preshift urinary concentrations. Nevertheless, results from this study suggest that some inhalation or dermal exposures in this study (e.g., TPhP, TCPP, and BDE-209) are associated with increased postshift concentrations of the chemical biomarkers in the body (e.g., DPhP, BCPP, and BDE-209), suggesting that workers in these industries were exposed to and absorbed these chemicals during their work shift. Although we have reported higher concentrations of the OPE and PBDE flame retardant biomarkers compared to the general population, it is unclear if these concentrations are associated with health effects. Last, as previously mentioned in the results, we primarily reported the SG-adjusted urinary OPE metabolite concentrations but needed to use unadjusted and creatinine-adjusted urinary concentrations to compare with the U.S. general population. Results that have been adjusted for SG are the preferred option for some because it minimizes errors due to urine dilution. However, NHANES does not provide SG-adjusted results. All analyses, figures, and tables are provided for SG-adjusted, creatinine-adjusted, and unadjusted results in either the main text or the Supporting Information.

Overall, workers from all industries evaluated in this study were exposed to flame retardants, but the specific exposure of concern was dependent on the industry examined. Results from this study also suggest that inhalation and dermal absorption are both likely routes of workplace exposure to flame retardants, although more research is needed to fully understand how the route of absorption affects excretion rates for the flame retardants analyzed here. Future studies could also provide a larger, more comprehensive exposure assessment on occupations found to have high exposures (e.g., chemical manufacturers and electronic scrap) to flame retardants, which may lead to recommendations for exposure reduction interventions. Moving forward, exposure assessments focusing on emerging flame retardants may be more important than PBDEs, given the global restrictions, and OPEs, given the Consumer Products Safety Commission's granted petition to declare that products are hazardous substances if they contain organohalogen flame retardants.[4]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.est.3c09342.

> Additional experimental methods for specific gravity and creatinine adjustments; additional figures (S1 and S2) and tables (S1−S10) provided for unadjusted and creatinine-adjusted results, univariable and multivariable analysis results, PBDE serum results for analytes below our reporting threshold (<60% above the limit of detection (LOD)), and PBDE multivariable results (PDF)

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Notes

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