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Characterization of Urinary Phthalate Metabolites Among Custodians

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ABSTRACT

Phthalates, a ubiquitous class of chemicals found in consumer, personal care, and cleaning products, have been linked to adverse health effects. Our goal was to characterize urinary phthalate metabolite concentrations and to identify work and nonwork sources among custodians using traditional cleaning chemicals and 'green' or environmentally preferable products (EPP). Sixty-eight custodians provided four urine samples on a workday (first void, before shift, end of shift, and before bedtime) and trained observers recorded cleaning tasks and types of products used (traditional, EPP, or disinfectant) hourly over the work shifts. Questionnaires were used to assess personal care product use. Four different phthalate metabolites [monoethyl phthalate (MEP), monomethyl phthalate (MMP), mono (2-ethylhexyl) phthalate (MEHP), and monobenzyl phthalate (MBzP)] were quantified using liquid chromatography mass spectrometry. Geometric means (GM) and 95% confidence intervals (95% CI) were calculated for creatinine-adjusted urinary phthalate concentrations. Mixed effects univariate and multivariate modeling, using a random intercept for each individual, was performed to identify predictors of phthalate metabolites including demographics, workplace factors, and personal care product use. Creatinine-adjusted urinary concentrations [GM (95% CI)] of MEP, MMP, MEHP, and MBzP were 107 (91.0–126), 2.69 (2.18–3.30), 6.93 (6.00–7.99), 8.79 (7.84–9.86) μg g^{-1}, respectively. An increasing trend in phthalate concentrations from before to after shift was not observed. Creatinine-adjusted urinary MEP was significantly associated with frequency of traditional cleaning chemical intensity in the multivariate model after adjusting for potential confounding by demographics, workplace factors, and personal care product use. While numerous demographics, workplace factors, and personal care products were statistically significant univariate predictors of MMP, MEHP, and MBzP, few associations persisted in multivariate models. In summary, among this population of custodians, we identified both occupational and nonoccupational predictors of phthalate exposures. Identification of phthalates as ingredients in cleaning chemicals and consumer products would allow workers and consumers to avoid phthalate exposure.

KEYWORDS: biomonitoring; custodians; cleaners; environmentally preferable products; phthalates

INTRODUCTION

Exposure to phthalates is widespread and concern about phthalate exposure has increased with reported associations between urinary concentrations of phthalate metabolites and adverse reproductive health effects (Hoppin 2003; Duty *et al.*, 2005; Hauser *et al.*, 2006; Hauser, 2008; Meeker *et al.*, 2009; Knez, 2013; Kay *et al.*, 2013) and decreased pulmonary function in males (Hoppin *et al.*, 2004; Park *et al.*, 2013). Phthalates represent a class of ubiquitous chemicals commonly found in consumer and personal care products. Low molecular weight phthalates including diethyl phthalate (DEP) and dimethyl phthalate (DMP) are used as solvents and are commonly found in consumer products with fragrances including cosmetics, personal care products, and cleaning products (Dodson *et al.*, 2012). High molecular weight phthalates including di-(2-ethylhexyl) phthalate (DEHP) and butylbenzyl phthalate (BBzP) are used as plasticizers and stabilizers and are commonly found in vinyl products (Dodson *et al.*, 2012) and building materials (Hauser and Calafat, 2005).

Urinary monitoring for phthalates is an effective way to integrate multiple sources of exposures across absorption routes. Phthalates are metabolized rapidly to their monoesters in urine, and further to oxidative products of their lipophilic aliphatic side chain. For example, DEP is metabolized to monoethyl phthalate (MEP), DMP to monomethyl phthalate (MMP), DEHP to mono(2-ethylhexyl) phthalate (MEHP) and BBzP to monobenzyl phthalate (MBzP). Excretion rates differ depending on the species of monoester with shorter alkyl chain length metabolites excreting faster than longer alkyl chain metabolites (Dirven *et al.*, 1993; Koch *et al.*, 2003). Phthalates tend to have short biological half-lives ranging from 2 to 12 h, with DEHP metabolites having a half-life of 10–15 h (Lorber *et al.*, 2010). In heavily exposed workers, increased urinary phthalate levels have been observed postexposure in end-shift urine samples. Hines *et al.* (2009) found end-shift geometric mean (GM) concentrations of several metabolites greater than the United States National Health and Nutrition Examination Survey (NHANES) 2001–2002 population levels including DEP (4 to >1000-fold), DEHP (3–8-fold), and DBzP (10–26-fold). Yet, little is known about the occupational phthalate exposures among custodians.

Custodians may be at increased risk for phthalate exposures from multiple occupational sources through inhalation, dermal, as well as ingestion exposure routes. Common bathroom cleaning tasks lasting as short as 10 min have been shown to produce airborne exposures that remain aerosolized for as long as 20 min after task cessation (Bello *et al.*, 2010). The aerosolization of phthalate-containing cleaning products presents an inhalation risk for phthalate exposures, especially for the more volatile low molecular weight phthalates. Buildings also contain flooring and wall materials that may contain high-molecular weight phthalates, which despite having low volatility have been shown to off-gas (Adibi *et al.*, 2003, 2008; Rudel *et al.*, 2003), presenting an additional inhalation risk for phthalate exposures. Dermal exposure to phthalates can occur through direct skin contact with products during mixing or cleaning, which can be mitigated with glove use. Poor hand hygiene as well as consumption of food or drinks in the workplace may contribute to ingestion of phthalates from occupational sources.

The substitution of environmentally preferable products (EPP), or 'green', cleaning chemicals for traditional cleaning chemicals may reduce harmful exposures to a variety of chemicals including phthalates. However, the elimination of phthalates among EPP cleaning chemicals has been gradual by product type and EPP cleaning chemicals are not universally free of phthalates. Furthermore, estimation of the contribution of phthalate exposures due to cleaning products among custodians is difficult as phthalates are often not disclosed as product ingredients nor listed on material safety data sheets (MSDS, currently called safety data sheets), as is also the case for consumer products phthalates (Saravanabhavan *et al.*, 2013).

Within a population of custodians, we sought to characterize urinary phthalate metabolite concentrations and to identify the work and nonwork phthalate exposure sources. We chose to identify urinary phthalates most likely found in a typical custodian's work environment including low molecular weight phthalates (DEP, DMP) that may be associated with fragrances found in cleaning products and high molecular weight phthalates (DEHP, BBzP) which may be found in building materials. All four phthalates (DEP, DMP, DEHP, BBzP) have also been found in consumer and personal care products (Dodson *et al.*, 2012). We hypothesized that due to occupational

exposure to phthalates, urinary phthalate metabolite concentrations would increase over a workday. We hypothesized that both traditional and EPP cleaning chemicals would be sources of phthalate exposures with higher levels of fragrance-related low molecular weight phthalate exposures (DEP and DMP) among participants using traditional cleaning chemicals.

METHODS

The current study is part of a larger project designed to investigate the use and impact of EPP and disinfectants among custodians, to assess general health effects associated with cleaning products, and to implement effective strategies to reduce chemical exposures. We used a community-based participatory action research approach to characterize custodians' exposures to phthalates by evaluating urinary phthalate metabolite concentrations and observing cleaning use patterns. Details of the study partners can be found in more detail elsewhere (Simcox *et al.*, 2012). Briefly, in partnership with the Connecticut Employees Union Independent, an affiliate of the Service Employees International Union (CEUI-SEIU) Local 511, a total of 456 custodians and 49 cooks (with cleaning and disinfection job duties) who were working with cleaning products were identified from union membership. Focus group results conducted with custodians at these sites during the first phase of the study (Simcox *et al.*, 2012) were used to guide site selection, recruitment process, and survey tools for the current biomonitoring study.

Study design

The study was designed to capture occupational and nonoccupational exposures by evaluating the temporal variation of phthalate exposures, low molecular weight phthalates (DEP, DMP), and high-molecular weight phthalates (DEHP, BBzP), over the course of the day. We hypothesized that we would observe increased urinary phthalate metabolite concentrations following workday exposure. We employed a repeated measures sampling strategy collecting four urine samples (first void, before shift, end shift, before bed) over a 24-h work period from 68 custodians working at four survey sites.

Site surveys

The four sites included state university campuses (Sites A and B), a hospital (Site C), and a residential training facility for individuals with cognitive disabilities (Site D). Prior to participant enrollment, each institution was visited to interview the management staff who order, purchase, and manage the inventory of cleaning products and the equipment and to perform walkthrough visits. MSDS were requested for all cleaning products and disinfectants and several custodial closets at each building were inspected to characterize the cleaning chemicals (e.g. EPP or traditional) and equipment. Some sites provided a list of product names, and others provided copies of MSDS. MSDS do not contain information regarding EPP status. 'Green' cleaning alternatives to traditional cleaning agents are certified as an EPP by third-party organizations, such as Green Seal and Ecologo. For purposes of this study, an EPP is defined as an industrial or institutional cleaner certified by Green Seal (GS) under the GS-37 Standard (restroom, glass, carpet, and general purpose cleaners), GS-40 Standard (floor care products) and Ecologo Standards 110, 112, 146, and 147.

Custodian recruitment

Participants were recruited from April to June 2011 using flyers distributed by Environmental Health & Safety or Facility Departments, presentations at union meetings, and union representatives. Targeted custodians included those working during first and third shift. Workers were reimbursed $50 for participation. All workers gave signed, informed consent as approved by the UConn Health Institutional Review Board (IRB Approval No. 10-050-1).

Urine sample collection

The day before urine collection, each worker was provided four 120-ml sterile plastic specimen cups (prescreened for phthalates) with instructions. First void (typically morning, except for third shift) urine samples were collected at home to represent phthalate exposure before work and before use of any personal care products. A second preshift urine sample was collected at the work site before workers started their cleaning duties and to represent phthalate exposure from personal care products used prior to shift. A third postshift sample was collected in the workplace. The fourth sample was collected at bedtime in the worker's home. A study team member collected the first three urine samples from custodians onsite, and returned the next morning to collect the fourth

(before bedtime) urine sample. Workers were asked to place their before bedtime urine sample in a plastic bag in their home refrigerator overnight. Specimens were transported to the UConn Health laboratory on wet ice in a cooler.

Potential predictors of phthalate levels

Interview, formal questionnaires, and observations were used to collect information on potential predictors of urinary phthalate concentrations including demographics, workplace factors, and consumer products used. During sample collection, participants were asked information about their sex, age, race, Hispanic origin, and primary language. At the end of the sampling period, participants were asked to complete a product use questionnaire to indicate types of personal care and household products used within the last 24 h, over the duration of urine collection. Participants were also asked if they had smoked in the past 24 h.

Workplace factors were collected by one of five observers trained by a UConn Health industrial hygienist to conduct work observations on the day of urine monitoring. Each observer followed one to four workers during each hour of the shift. A data collection form developed by the National Institute of Occupational Safety and Health (NIOSH) (LeBouf *et al.*, 2014) was modified and used by the observers. During each hour of the work shift, observers recorded custodian cleaning tasks and cleaning product use. The number and type of rooms (e.g. bathroom, office, etc.) as well as the surfaces/objects cleaned (e.g. floors, toilets, desks), the use of personal protective equipment (e.g. gloves), cleaning equipment and tools (e.g. microfiber cloths, mops, brooms) were also documented.

All chemical products used by each custodian over the observation period were recorded. The products were grouped according to type: traditional, EPP, and disinfectant. Custodians' exposures were characterized by these types. For each product type, the frequency of use of within the chemical group over the 8-h shift was also captured. A product was recorded on the observation sheet if used at least once during the 1-h observation period of the shift. Exposure intensity was coded as none, low, or high. A worker was assigned none when he or she reported no chemical use. A categorization of low exposure intensity was given when a worker was observed using the product less than four times over the 8-h observation periods. Likewise, a category of high exposure intensity was assigned when the worker was observed using the product four or more times over the 8-h observation periods. The total time of chemical use and the quantity of chemical use was not recorded. The categories of reported use are consistent with a prior evaluation of exposures among custodians using the interval of more or less than 4 h to describe exposure intensity (Obadia *et al.*, 2009).

Laboratory methods

Each urine sample was transferred to a 15-ml Corning centrifuge tube (# 430052) and placed in a freezer at −20°C. Samples were transferred to Harvard T. H. Chan School of Public Health Department of Environmental Health in June 2011 and stored at −80°C until analysis by December 2011.

The four different phthalate monoester metabolites (MEP, MMP, MEHP, and MBzP) were quantified in the urine using liquid chromatography-tandem mass spectrometry (LC-MS/MS) according to the analytical and quality control methods previously described (Chen *et al.*, 2012). The limit of quantitation (LOQ) for each phthalate metabolite was: MEP (0.5 ng ml^{-1}), MMP (0.25 ng ml^{-1}), MEHP (1.00 ng ml^{-1}), and MBzP (0.25 ng ml^{-1}).

Creatinine was measured photometrically using kinetic colorimetric assay technology with a Hitachi 911 automated chemistry analyzer (Roche Diagnostics, Indianapolis, IN, USA). Unadjusted concentrations are reported in nanograms per milliliter (ng ml^{-1}). Unless noted, all the reported urinary metabolite concentrations were adjusted for creatinine. Creatinine-adjusted concentrations are reported in micrograms per gram (μg g^{-1}). Concentrations below the LOQ were substituted with a value equal to the LOQ divided by 2 for statistical analyses. Analysts were blind to all participant information.

Statistical methods

Based on visual inspection, the distributions of urinary metabolite concentrations were skewed, so the data were $\log_{10}$ transformed to yield approximately normal distributions. Geometric mean and 95% confidence intervals (95% CI) of unadjusted and creatinine-adjusted urinary phthalate concentrations were calculated. Correlation between the log transformed metabolites was evaluated with Pearson correlation coefficients.

Mixed effects modeling, using a random intercept for each individual, was performed with $\log_{10}$ transformed creatinine-adjusted urinary phthalate concentrations as outcome variables. Potential predictors of urinary phthalate levels included urine collection time, demographic factors, workplace factors, as well as personal care products used. All predictors varied between, not within, individuals and did not vary by sampling time. Univariate analyses were performed to identify statistically significant differences by demographic, workplace, and personal care product characteristics using mixed effects models and *P* values from these comparisons were presented. However, many participants reported numerous work and consumer product phthalate sources. Therefore, univariate results were further examined in multivariate models, created separately for each metabolite by considering univariate predictors that were statistically significant at $P < 0.10$. Due to potential colinearity, correlations between significant univariate predictors were examined using kappa coefficients. Simple kappa coefficients were calculated to determine the correlation between categorical variables and weighted kappa coefficients were calculated to determine the correlation between ordinal variables. The kappa coefficients were generally in the 'slight' (0–0.20) to 'fair' (0.21–0.40) agreement categories for most pairs of predictors. One pair (shampoo and conditioner use) had 'moderate' agreement (kappa coefficient = 0.48) and one pair (laundry detergent and fabric softener use) had 'substantial' agreement (kappa coefficient = 0.77) (Landis and Koch, 1977). One predictor was chosen from each pair (shampoo, laundry detergent) for the multivariate models. Full multivariate models including all potential predictors, regardless of significance were evaluated. Due to the large number of predictors and small number of participants, all predictors were retained in the final model, regardless of significance. In the final models for MEP, a sensitivity analysis was performed by forcing EPP use intensity into the analysis.

Because 13% of urine creatinine levels were less than 0.3 g l^{-1}, which is considered outside the normal range, mixed model results were confirmed by removing these values. Study results were not affected by urine creatinine levels less than 0.3 g l^{-1}, therefore, all sample results were used in analyses. Likewise, similar results were observed when creatinine was modeled as a predictor or unadjusted phthalate concentrations. Statistical significance was set as $P < 0.05$, unless otherwise noted. All statistical analyses were performed in SAS 9.3 (SAS Institute, Cary, NC, USA).

RESULTS

Site characteristics

Walk-throughs of each site were performed to identify characteristics related to custodians' exposures. The majority of custodians worked alone in a designated area of a building, with the exception of Site B that used teams. Multiple cleaning tasks were observed in bathrooms, classrooms, offices, dormitory areas, gymnasiums, locker rooms, hallways, and stairs. Bathroom cleaning was the most labor intensive and required the use of several different cleaning products to clean toilets, counters, floors, and mirrors. Floors were primarily washed with a single type of floor cleaner. Most sites hired contract workers to perform floor stripping, with the exception of Site D, where five workers worked as a single crew and focused primarily on floor care tasks. During monitoring, this group used traditional chemical floor strippers and polishes in several classrooms.

The type of the equipment used for cleaning varied across the sites. At the beginning of our study, only Site C used microfiber technology (hospital), and the other three used cotton mops, cotton cloths and paper towels for routine cleaning. However, most sites were in the process of piloting new cleaning technology and equipment. For example, Site A used a no-touch cleaning system (e.g. kaivac) in locker rooms.

Custodians had access to both traditional and EPP cleaning chemicals. Three sites used the same vendor and dilution stations that automatically mix and dilute concentrated cleaning products through a dispenser with cold water and one site used a different vendor without mixing stations. In addition, each site used bottled cleaning chemicals outside of mixing stations. Only a few sites reported using aerosols (e.g. gum remover and stainless steel polish), and some sites used air fresheners in bathrooms as a common practice. Glove use was common but not universal. Eighty-five percent (85%) of workers wore latex or nitrile gloves during chemical use.

The MSDS of the most common types of traditional and EPP cleaning chemicals were evaluated for more

detailed chemical information to identify the types of ingredients found in these products. A total of 73 MSDS were collected across four sites, and ingredients were reviewed to determine if chemical ingredients were comparable to other occupational studies involving housekeepers, janitors, and custodians. Ingredients in traditional products were typical of those reported in other occupational cleaner studies found in the literature (Bello *et al.*, 2009). No studies were found in the literature that described the ingredients commonly found in EPPs. As expected, phthalates were not listed as an ingredient on MSDS for traditional or EPP cleaning chemicals. Supplementary Table 1, available at *Annals of Occupational Hygiene* online, provides detailed information (e.g. chemical name, Chemical Abstract Services (CAS) number, ingredient product concentration, and chemical function) of the ingredients frequently reported in EPP cleaning chemicals. Within our study, EPP ingredients included chemicals such as alcohol ethoxylates, hydrogen peroxide, fruit derived acids (e.g. citric acid), as well as other ingredients found in traditional cleaning chemicals such as glycols and ethanolamine. In addition, 'fragrance' was listed; however, few manufacturers provide complete disclosure of fragrance ingredients on MSDS for any type of cleaning product including EPPs.

Urinary phthalate metabolite concentrations

A total of 68 workers provided a total of 269 urine samples (Table 1). Sixty-five workers provided all four urine samples, three workers lacked one sample, and five samples were not collected according to protocol. We primarily report urinary creatinine-adjusted levels (Table 1). Unadjusted metabolite concentrations are available as Supplementary Table 2, available at *Annals of Occupational Hygiene* online. Twenty-four workers had one or more urine samples with low creatinine levels <0.3 g l^{-1}, and these workers varied in age, came from all four sites and worked during different shifts. Correlation between log transformed urinary metabolites was weak with Pearson correlation coefficients ranging from 0.003 to 0.28 (data not shown). For MEP and MBzP, all samples were above the LOQ. For MMP, 64 (24%) were below LOQ while 26 (10%) were below LOQ for MEHP.

Using mixed effects models, GM creatinine-adjusted urinary metabolite concentrations were significantly different across collection times for MEP and MMP (Table 1). The highest GM [geometric standard deviation (GSD)] concentration of MEP were observed before shift (138 (4.1) μg g^{-1}) while the highest GM (GSD) concentration of MMP was observed before bedtime (3.2 (5.3) μg g^{-1}). GM urinary metabolite concentrations were not statistically different across the four time periods for MEHP or MBzP (Table 1). Notably, the highest urinary concentrations of MEP (11 377 μg g^{-1}) and MBzP (12 409 μg g^{-1}) were found among workers just beginning their shift (preshift). The GMs of each phthalate metabolite concentration observed among adults in the 2009–2010 NHANES study (CDC, 2009) were lower than the GM concentrations and outside the 95% CIs of the concentrations from all time points combined within the current population of custodians (Table 1).

Urinary phthalate concentrations by demographics

The population demographics and variations in creatinine-adjusted urinary phthalates concentrations by demographic characteristics are presented in Table 2. A slight majority of the population (54%) were female. MEP concentrations were significantly higher in males, as compared to females (141 versus 78 μg g^{-1}, $P = 0.04$). Small gender differences in the remaining metabolites were not statistically significant. The majority (53%) of participants were aged 50 years or more. Statistically significant differences in urinary MEHP and MMP by age were observed, but there were no trends with increasing or decreasing age. The majority of participants (75%) identified as white. Non-white participants had nearly the three times the creatinine-adjusted urinary MEP levels as compared to white participants (225 versus 84 μg g^{-1}, $P = 0.002$). The Hispanic participants ($n = 18$) had significantly lower MEP (67 versus 126 μg g^{-1}, $P = 0.048$) and MBzP (6.5 versus 9.8 μg g^{-1}, $P = 0.049$). Differences in MEP and MBzP were also observed by primary language, with significantly lower levels of MEP, MEHP, and MBzP observed among Spanish and other language speakers as compared to English speakers. Significantly lower concentration of MMP (1.7 versus 3.4 μg g^{-1}, $P = 0.045$) were observed among the 21 participants who had smoked in the last 24 h.

Urinary phthalate concentrations by workplace factors

Creatinine-adjusted urinary phthalate concentrations by workplace characteristics and exposure factors are

Table 1. Geometric mean (95% CI) creatinine-adjusted urinary phthalate metabolite concentrations (μg g^{-1}) among 68 custodians across the four sampling time periods or the US population 20 years or older from the National Health and Nutrition Examination Survey (NHANES) from 2009 to 2010 (CDC, 2009)

n	First void 67	Before shift 67	End shift 68	Before bed 67	All 269	NHANES 09-10
MEP	110	138	111	78.6	107	73.0
	(80.4–150)	(97.5–195)	(79.4–154)	(56.6–109)	(91.0–126)	(65.1–81.9)
MMP	2.95	1.78	3.06	3.23	2.69	1.09[a]
	(1.99–4.39)	(1.12–2.84)	(2.03–4.59)	(2.16–4.83)	(2.18–3.30)	(<LOD–1.23)
MEHP	7.16	6.30	6.46	7.90	6.93	1.65
	(5.60–9.17)	(4.43–8.97)	(4.81–8.67)	(6.11–10.2)	(6.00–7.99)	(1.43–1.90)
MBzP	8.87	8.57	9.09	8.65	8.79	5.94
	(7.32–10.8)	(6.43–11.4)	(7.33–11.3)	(6.88–10.9)	(7.84–9.86)	(5.31–6.66)

CI, confidence interval; LOD, limit of detection.
[a]Median presented as proportion of results below the limit of detection were too high to provide a valid geometric mean.

presented in Table 3. Statistically significant differences in urinary MEP, MMP, MEHP, and MBzP concentrations were observed between sites with trends by phthalate metabolite varying by site. The majority (76%) of participants worked first shift and no significant differences in urinary phthalate concentrations were observed between shifts.

Custodians used traditional and EPP cleaning chemicals as well as disinfectants throughout a shift. Twelve custodians exclusively used EPP cleaning chemicals, 11 custodians exclusively used traditional products and 1 custodian exclusively used disinfectant over the work shift. The remaining 44 (65%) participants used a mixture of two or more types of product types. A statistically significant ($P = 0.01$) higher concentration of MEHP was observed with increasing EPP intensity: 4.8, 7.0, and 11.3 μg g^{-1} among none, medium, and high intensity EPP users, respectively. Differences in the remaining urinary phthalate levels by increasing EPP intensity were not significant. Trends in urinary phthalate concentrations were also observed with increasing traditional cleaning chemical intensity. While urinary MEP GM concentrations were similar in the none and medium intensity traditional cleaning chemical categories (87 and 95 μg g^{-1}, respectively), the highest GM MEP was observed in the high intensity traditional cleaning chemical category, 231 μg g^{-1} ($P = 0.06$). For MEHP, decreases were observed from none, to medium, to high intensity traditional cleaning chemical categories (9.7, 7.0, 3.9 μg g^{-1}, respectively; $P = 0.01$). The opposite trend was observed for MBzP with increases in concentrations from none, to medium, to high intensity traditional cleaning chemical categories (9.7, 6.9, 17.1 μg g^{-1}, respectively; $P = 0.002$). Significant differences in urinary phthalate concentrations were also observed with differences in disinfectant intensity for MEP, MEHP, and MBzP, but no trends were observed.

Urinary phthalate concentrations varied by cleaning location. As compared to cleaning patient rooms, custodians cleaning classrooms, offices and/or laboratories had significantly increased MEP (137 versus 42 μg g^{-1}, $P = 0.0004$), increased MEHP (8.2 versus 3.6 μg g^{-1}, $P = 0.002$), and decreased MMP (6.0 versus 2.2 μg g^{-1}, $P = 0.01$). No significant trends in urinary phthalate concentrations were observed by number of toilets cleaned. A small percentage (12%) of participants reported stripping floors and had significantly lower MEHP concentrations (3.6 versus 7.6 μg g^{-1}, $P = 0.03$).

Most custodians worked Monday through Friday, except for workers on third shift who started on Sunday

Table 2. Geometric mean of creatinine-adjusted urinary phthalate concentrations (μg g^{-1}) by demographic characteristics

	N	(%)	*n*	MEP	MMP	MEHP	MBzP
Male	31	(46)	145	141	2.4	7.7	10.1
Female	37	(54)	124	78	3.1	6.1	7.5
			P value	0.04	0.44	0.29	0.14
Age							
<40	8	(12)	32	43	5.3	6.5	10.2
≥40 < 50	13	(19)	51	131	2.2	4.6	7.9
≥50 < 60	27	(40)	108	120	2.1	6.9	8.2
≥60	9	(13)	35	86	8.4	5.7	9.5
Missing	11	(16)	43	150	1.5	13.9	10.0
			P value	0.16	0.01	0.04	0.93
Race							
White	51	(75)	203	84	2.9	6.3	8.1
Non-white	17	(25)	66	225	2.1	9.4	11.4
			P value	0.002	0.39	0.11	0.13
Hispanic							
Yes	18	(27)	71	67	3.8	9.7	6.5
No	50	(74)	198	126	2.4	6.1	9.8
			P value	0.048	0.20	0.07	0.049
Primary language							
English	33	(50)	131	162	1.9	8.0	11.7
Spanish	16	(24)	63	78	3.8	9.3	6.4
Other	17	(26)	68	71	3.9	3.8	7.1
			P value	0.02	0.09	0.005	0.01
Smoked in past 24 h							
Yes	21	(32)	84	116	1.7	6.7	8.2
No	45	(68)	177	105	3.4	7.3	9.0
			P value	0.75	0.045	0.72	0.70

P value from a mixed effects model with a random intercept for each individual.

evening. Statistically significant ($P = 0.04$) differences in urinary MBzP concentrations were observed with increased concentration on Wednesday (12.4 μg g^{-1}) and Thursday (11.7 μg g^{-1}) as compared to Tuesday (7.2 μg g^{-1}). Similar, although not statistically significant, trends were also observed for MEHP and MMP.

Table 3. Geometric mean of creatinine-adjusted urinary phthalate concentrations (μg g^{-1}) by workplace characteristics and exposures

	N	(%)	*n*	MEP	MMP	MEHP	MBzP
Site							
A	21	(31)	82	114	1.8	10.8	8.4
B	5	(7)	20	179	4.4	3.4	21.0
C	24	(35)	95	147	2.1	10.0	9.9
D	18	(26)	72	57	5.2	3.1	6.3
			P value	0.04	0.04	<0.0001	0.01
Shift							
First shift	52	(76)	205	109	2.4	7.3	8.9
Third shift	16	(24)	64	101	4.1	5.8	8.5
			P value	0.82	0.15	0.36	0.88
EPP intensity							
None	20	(30)	79	94	2.5	4.8	8.4
Medium	34	(50)	134	112	2.3	7.0	8.4
High	14	(21)	56	116	4.2	11.3	10.6
			P value	0.88	0.34	0.02	0.60
Traditional intensity							
None	18	(27)	72	87	3.5	9.7	9.7
Medium	39	(57)	153	95	2.2	7.0	6.9
High	11	(16)	44	231	3.4	3.9	17.1
			P value	0.06	0.33	0.03	0.002
Disinfectant intensity							
None	36	(53)	72	130	2.8	7.3	9.3
Medium	16	(24)	153	157	2.5	9.3	13.1
High	16	(24)	44	47	2.6	4.6	5.2
			P value	0.004	0.84	0.08	0.002
Cleaning location							
Patient rooms	14	(21)	56	42	6.0	3.6	6.4
Classroom, office, laboratory	54	(79)	213	137	2.2	8.2	9.5
			P value	0.0004	0.01	0.002	0.11

Table 3. ***Continued***

	N	(%)	*n*	MEP	MMP	MEHP	MBzP
Toilets cleaned							
None	19	(28)	76	142	3.8	7.2	12.0
1–10	28	(41)	110	79	2.1	7.0	7.4
11–19	17	(25)	68	113	2.6	6.9	7.8
20 or more	4	(6)	15	196	2.7	5.5	11.1
			P value	0.23	0.54	0.96	0.16
Floor stripping							
Yes	8	(12)	32	146	5.5	3.6	14.1
No	60	(88)	237	103	2.4	7.6	8.2
			P value	0.44	0.10	0.03	0.07
Workday							
Tuesday	41	(60)	162	90	2.4	5.7	7.2
Wednesday	9	(13)	36	113	6.4	12.0	12.4
Thursday	18	(26)	71	157	2.2	8.1	11.7
			P value	0.28	0.09	0.06	0.04

P value from a mixed effects model with a random intercept for each individual.

Urinary phthalate concentrations by personal care product use

Using mixed effects models, there were no statistically significant differences in urinary MEP, MMP, MEHP, or MBzP by participants' personal care product use including: perfume/cologne, colored cosmetics, face cream, hand/body lotion, shaving cream, or mouthwash within the last 24 h (Table 4). Participants who reported using bar soap had significantly higher concentrations of MEHP (8.2 versus 4.5 μg g^{-1}, $P = 0.02$) while those reporting liquid soap/body wash had significantly higher levels of MBzP (10.3 versus 6.9 μg g^{-1}, $P = 0.04$). For both shampoo ($P = 0.002$) and conditioner ($P = 0.01$) users, MEP concentrations were significantly lower than for nonusers. No significant differences in phthalate concentrations were observed for other hair products, including hair spray and other hair styling products. For both laundry detergent and fabric softener, concentrations of MBzP were approximately double among users as compared to non-users (16.2 versus 7.2 μg g^{-1}, $P = 0.0001$ for laundry detergent). We observed no trend in urinary phthalate concentrations with increasing number of personal care products used.

Multivariate models

Confirmation of univariate predictors in a multivariate model evaluating predictors of MEP is presented in Table 5. For creatinine-adjusted MEP concentrations, urine order remained a statistically significant predictor; as compared to first void, the lowest levels were observed before bedtime ($\beta = -0.30$, $P = 0.03$) and the highest before shift ($\beta = 0.20$, $P = 0.14$) after adjusting for other covariates. Additional predictors that remained significant include lower MEP concentrations among Hispanics ($\beta = -1.81$, $P = 0.02$) and shampoo users ($\beta = -0.88$, $P = 0.003$) after adjusting for other covariates. Conditioner use was not included in the model because it had moderate correlation with shampoo (kappa = 0.48). A positive trend in urinary MEP concentrations with increasing traditional cleaning chemical intensity remained: as compared to none, medium intensity ($\beta = 0.36$, $P = 0.23$) and high intensity ($\beta = 1.28$, $P = 0.01$) users urinary

Table 4. Geometric mean of creatinine-adjusted urinary phthalate metabolite concentration (μg g^{-1}) by personal care products used

	N	(%)	*n*	MEP	MMP	MEHP	MBzP
Perfume/cologne							
Yes	31	(47)	124	118	2.9	7.1	7.5
No	35	(53)	137	101	2.6	7.1	10.1
			P value	0.61	0.68	0.95	0.16
Colored cosmetics							
Yes	14	(21)	56	142	2.4	6.8	7.2
No	52	(79)	205	101	2.8	7.2	9.2
			P value	0.35	0.65	0.86	0.33
Face cream							
Yes	31	(47)	122	115	2.2	6.3	7.2
No	35	(53)	139	104	3.3	7.8	10.4
			P value	0.79	0.23	0.37	0.06
Hand/body lotion							
Yes	35	(53)	138	94	2.6	6.3	9.0
No	31	(47)	123	128	2.9	8.1	8.5
			P value	0.26	0.70	0.31	0.83
Shaving cream							
Yes	14	(22)	55	124	2.3	8.0	9.4
No	51	(78)	202	102	2.8	6.8	8.5
			P value	0.64	0.67	0.56	0.76
Mouthwash							
Yes	37	(56)	147	108	2.6	7.3	9.4
No	29	(44)	114	110	3.0	6.9	8.1
			P value	0.94	0.69	0.77	0.43
Bar soap							
Yes	50	(76)	197	111	2.5	8.2	8.7
No	16	(24)	64	101	3.6	4.5	9.1
			P value	0.78	0.35	0.02	0.81
Liquid soap/body wash							
Yes	39	(59)	155	121	2.8	6.5	10.3
No	27	(41)	106	93	2.7	8.1	6.9
			P value	0.42	0.91	0.36	0.04

Table 4. ***Continued***

	N	(%)	*n*	MEP	MMP	MEHP	MBzP
Shampoo							
Yes	41	(62)	163	78	2.9	7.3	9.0
No	25	(38)	98	191	2.4	6.7	8.4
			P value	0.002	0.57	0.71	0.68
Conditioner							
Yes	25	(38)	99	66	3.6	7.4	9.1
No	41	(62)	162	148	2.3	6.9	8.6
			P value	0.01	0.18	0.74	0.78
Hairspray							
Yes	18	(27)	72	102	4.0	5.1	7.2
No	48	(73)	189	112	2.4	8.0	9.5
			P value	0.78	0.15	0.07	0.23
Other hair styling products							
Yes	7	(11)	26	162	1.5	6.8	11.2
No	59	(89)	235	104	2.9	7.1	8.5
			P value	0.36	0.24	0.89	0.54
Laundry detergent							
Yes	16	(24)	64	77	3.4	7.7	16.2
No	50	(76)	197	122	2.5	6.9	7.2
			P value	0.18	0.45	0.71	0.0001
Fabric softener							
Yes	11	(17)	44	81	2.6	7.1	15.2
No	55	(83)	217	115	2.8	7.1	7.9
			P value	0.37	0.92	0.99	0.01
Number of personal care products							
≤3	15	(23)	58	128	2.3	6.7	10.0
4	17	(26)	68	93	4.4	9.5	7.1
5	15	(23)	59	158	2.1	8.7	12.5
≥6	19	(29)	76	83	2.5	4.9	7.3
			P value	0.40	0.39	0.11	0.15

P value from a mixed effects model with a random intercept for each individual.

Table 5. Predictors of log-transformed creatinine-adjusted urinary MEP concentration in multivariate mixed effects model with random intercept for each individual

	β (SE)	*P* value
Fixed effects		
Intercept	4.24 (0.66)	<0.0001
Site		0.60
A	0.24 (0.58)	0.68
B	−0.54 (0.81)	0.50
C	0.33 (0.59)	0.58
D	Reference	
Urine order		0.003
First void	Reference	
Before shift	0.20 (0.13)	0.14
End shift	0.001 (0.13)	0.99
Before bedtime	−0.30 (0.13)	0.03
Traditional intensity		0.050
None	Reference	
Medium	0.36 (0.30)	0.23
High	1.28 (0.52)	0.01
Disinfectant intensity		0.32
None	Reference	
Medium	0.19 (0.34)	0.57
High	−0.47 (0.41)	0.25
Type of area cleaned		0.27
Patient rooms	Reference	
Classroom, office, lab	0.68 (0.61)	0.27
Gender (female)	−0.17 (0.29)	0.57
Race (non-white)	0.41 (0.45)	0.36
Hispanic	−1.81 (0.77)	0.02
Language		0.11
English	Reference	
Spanish	1.53 (0.77)	0.05
Other	0.43 (0.49)	0.39
Shampoo	−0.88 (0.29)	0.003
Random effects		
s^2_{BW} (full)	0.73	
s^2_{BW} (intercept)	1.29	
Between-worker variability explained	44%	
s^2_{WW} (full)	0.57	
s^2_{WW} (intercept)	0.60	
Within-worker variability explained	6%	

Between-worker (s^2_{BW}) variance estimates from fully adjusted or intercept-only models. Within-worker (s^2_{WW}) variance estimates from fully adjusted or intercept-only model.

phthalate levels were increased after adjusting for additional covariates. This positive trend remained after adjusting for EPP Intensity; as compared to none, medium intensity (β = 0.29, $P = 0.37$) and high intensity (β = 1.37, $P = 0.01$) users urinary MEP concentrations were increased (data not shown). With the exception of site and language, while not statistically significant, the trends for disinfectant intensity, cleaning location, gender and race remained consistent with the univariate analysis results. As compared to a null model, the multivariate model explained 44% of the between-worker and 6% of the within-worker variance.

Supplementary Table 3, available at *Annals of Occupational Hygiene* online, contains full models for creatinine-adjusted MEHP, MMP, and MBzP concentrations. For creatinine-adjusted MMP concentrations, the only univariate predictor that remained significant was weekday. However, the trends for the remaining predictors remained similar to univariate results, although not statistically significant. As compared to a null model, the multivariate model for MMP explained 38% of the between-worker and 3% of the within-worker variance. Multivariate models for MEHP produced no statistically significant predictors, although similar to the multivariate model for MMP, trends for the predictors remained similar to univariate results and, as compared to a null model, the multivariate model explained 43% of the between-worker variance. Similar to the multivariate models for MMP and MEHP, multivariate models for MBzP concentrations produced few statistically significant

predictors although trends observed for univariate results persisted.

DISCUSSION

This study is the first to characterize urinary phthalate levels among custodians. As compared to the 2009–2010 NHANES population sample (CDC, 2009), phthalate levels from 2011 urine samples among this custodian population appear to be elevated. To clarify, the elevated urinary phthalate levels among this custodian population reflect divergence from national norms, but are not necessarily indicators of toxicity. Since phthalates are ubiquitous chemicals it is difficult to identify exposure sources. Yet, our data suggest that custodians are exposed to phthalates, specifically MEP, from occupational as well as from nonoccupational sources.

Urinary biological monitoring for occupational exposures to phthalates has been performed in selected industries and occupations (Dirven *et al.*, 1993; Pan *et al.*, 2006; Gaudin *et al.*, 2008; Hines *et al.*, 2009; Gaudin *et al.*, 2011; Koch *et al.*, 2012; Fong *et al.*, 2014). In a pilot study of US workers from a variety of manufacturing industries, Hines *et al.* (2009) observed increased urinary phthalate concentrations as compared to the NHANES population, as was the case within the current populations of custodians. End-shift GM concentrations among the current population of custodians are within the lower range of concentrations observed in the pilot study (Hines *et al.*, 2009). For example, the GM of end-shift level of MEP in our study was 111 μg g^{-1} compared to GM levels ranging from 60.2 to 716 μg g^{-1} depending on the manufacturing sector (Hines *et al.*, 2009).

We chose to identify urinary phthalates most likely found in a typical custodian's work environment including low molecular weight phthalates (DEP, DMP) that may be associated with fragrances found in cleaning products and high molecular weight phthalates (DEHP, BBzP) which may be found in building materials. Given the short half-life of phthalates in urine, we expected to see an increase in urinary phthalate level across a work shift in the postshift and bedtime samples. In fact, this was the case among the pilot study of manufacturing workers where as compared to preshift, increased postshift GM phthalates concentrations were observed among the highest exposed workers (Hines *et al.*, 2009). However, this was not the case within the current population of custodians. While MEP varied significantly by sampling time, for MEP, the highest GM concentration was before shift and the lowest at bedtime. However, we did observe occupational predictors of DEP.

Since DEP is a phthalate found in cleaning products (Dodson *et al.*, 2012), potentially related to fragrance additives, we expected to observe increased urinary MEP concentrations, the urinary metabolite for DEP, with increased cleaning chemical use. When we classified urinary metabolite levels by cleaning chemical exposure intensity (Table 5), this was confirmed with an increase in MEP with increasing intensity of exposure to traditional cleaning chemicals both in univariate and multivariate models. This association also remained after adjusting for EPP product use. Our results indicate that DEP may be related to the fragrance used in traditional cleaning chemicals, however, we were unable to confirm since phthalates were not listed on the MSDS for the cleaning chemicals.

We observed no association between EPP cleaning chemical exposure intensity and MEP. Connecticut is one of several states in the US implementing green cleaning programs as a result of a state law introduced in 2007. This provided a unique opportunity to evaluate phthalate occupational exposures among custodians making the transition to green cleaners because phthalates were discontinued in some of the cleaning products at the time of this study. Although the law was in place for four years before we performed this study, less than 50% of the cleaning chemicals used by custodians at the sites were EPPs. We hypothesized that traditional, but not EPP cleaning chemicals would be a source of low molecular weight phthalate (DEP, DMP) exposures. However, EPP cleaning chemicals are not universally free of phthalates since different standards are used for different cleaning chemical product groups. At the time of this study, cleaning products certified under the Green Seal Standard for Industrial and Institutional Cleaners (GS-37), which includes general purpose, restroom, and carpet cleaners, prohibited phthalates. However, GS standards for other cleaning products such as floor care products (GS-40) and hand cleaners (GS-41) allow International Fragrance Association approved fragrances, including approximately 3000 fragrance ingredients including phthalates, such as DEP. Phthalates were not listed as ingredients on traditional or EPP cleaning chemicals,

however fragrance was listed as an ingredient on both types of cleaning chemicals.

Custodians may work with several chemicals over a shift including EPP and traditional cleaning chemicals as well as disinfectants. Interestingly, we observed a decreasing trend in MEP concentrations with increasing disinfectant intensity. We also observed decreased concentrations of MEP among participants cleaning primarily patient rooms where disinfectants are the main chemical used, although this did not remain significant in the multivariate model. The trend observed in our results may be a reflection of the multiple exposures within the population where increased disinfectant use may be a marker of decreased traditional chemical use; when a custodian spends the majority of time with one type or class of cleaning chemical, there is less time left within the day to spend with alternate cleaning chemicals.

In addition to being present in cleaning chemicals, DEP is also found in a variety of personal and home products (Dodson *et al.*, 2012). In fact, for MEP, the highest GM concentration was before shift, which given the half-life of DEP, suggests a home-based or before-work source. However, with the exception of shampoo and conditioner use, our study found no associations between MEP and personal care products. Interestingly, we observed that shampoo and conditioner use were associated with lower MEP concentrations, which persisted in the multivariate models. This is contrary what we expected and to results observed among Mexican women where higher urinary MEP concentrations were observed among shampoo users (Romero-Franco *et al.*, 2011), yet similar to the trend observed in a population of pregnant women in Puerto Rico (Cantonwine *et al.*, 2014), although differences in metabolism of phthalates during pregnancy may limit comparisons to this population. Other population studies have demonstrated links between urinary MEP and perfume/cologne use (Lewis *et al.*, 2013; Cantonwine *et al.*, 2014) and the use of colored cosmetics (Cantonwine *et al.*, 2014), yet we observed no trends within this population of custodians.

We observed significantly higher concentrations of MEP in men, non-whites, non-Hispanic and native English speakers, yet in the adjusted models only Hispanic ethnicity was a significant predictor. In NHANES 09-10 (CDC, 2009), non-Hispanic whites had lower creatinine-adjusted urinary metabolites (GM = 58.6 μg g^{-1}) than Mexican Americans (GM = 81.6 μg g^{-1}) or non-Hispanic Blacks (GM = 113 μg g^{-1}) (CDC, 2009). However the custodian population within this study is unlikely a reflection of the non-Hispanic population of 09-10 NHANES as the current study population consists of participants from multiple ethnicities as reflected in the distribution of languages where only 50% spoke English as their primary language.

Like DEP, DMP is also used as a scent retainer in cosmetics and personal care products and may also be used in adhesives. However, predictors of MMP differed as compared to MEP. Once again, workplace factors were significant predictors of MMP and included site and cleaning location with higher concentrations observed among workers cleaning patient rooms, yet neither association persisted in multivariate models. However, for MMP the urine order, with highest concentration observed at first void and weekday, with higher concentrations observed on Wednesday and Thursday as compared to Tuesday persisted in both univariate and multivariate models (Supplementary Table 3, available at *Annals of Occupational Hygiene* online). We observed no statistically significant differences in MMP concentrations by personal care product use.

The high molecular weight phthalates, DEHP and BBzP, are plasticizers primarily used in items including vinyl flooring, furniture and auto upholstery, carpet tiles, and artificial leather although both DEHP and BBzP have been found in consumer products (Dodson *et al.*, 2012). Since custodians work in buildings that may contain building materials made with high molecular weight phthalates, we hypothesized a link between workplace predictors and MEHP and MBzP concentrations. The workplace factors that predicted urinary MEHP concentrations in univariate models included site, EPP intensity, traditional cleaning chemical intensity, disinfectant intensity, cleaning locations, floor striping, and weekday. The results between exposure intensity and MEHP were unexpected with higher concentrations among those most highly exposed to EPP cleaning chemicals, and the highest concentrations among the unexposed for traditional cleaning chemical and disinfectant intensity. While these trends persisted in the multivariate models, no workplace predictor of MEHP reached

significance (Supplementary Table 3, available at *Annals of Occupational Hygiene* online). It is hard to disentangle sources of MEHP exposure. DEHP has been found in personal care products as well as cleaning products such as car air fresheners and dryer sheets (Dodson *et al.*, 2012). Within our study population, users of bar soap had higher levels on MEHP, which has been found to be elevated in prior studies (Dodson *et al.*, 2012). The link between MEHP and EPP cleaning chemicals may be due to either chemical additives, plastic packaging, or other sources related to when the cleaning chemical is being used.

Like MEHP, the work-related predictors of MBzP were varied, yet more expected. The cleaning chemical-related trends were as expected; as compared to unexposed, higher concentrations of MBzP were observed among the high traditional cleaning chemical intensity categories, although this relationship did not persist in multivariate suggesting the influence of another factor. The link between MBzP and traditional cleaning chemical is unclear; MBzP has been found in car interior cleaners (Dodson *et al.*, 2012) and within this population may be within the traditional cleaners themselves or be correlated with the areas which cleaning is occurring. Within our study, users of liquid/soap body wash had higher levels of MBzP, not MEP, which has been found to be elevated in both product types in prior studies (Dodson *et al.*, 2012). Both MEHP and MBzP concentrations differed in our study by primary language spoken. MEHP concentrations also differed by age. Higher concentrations of MBzP were observed among participants using laundry detergent and fabric softener which persisted when laundry detergent was retained in the multivariate model.

Phthalates are ubiquitous and while we attempted to capture numerous exposure sources, we did not collect information on all potential factors that impact phthalate urinary concentrations. Diet can provide a significant source for DEHP and BzBP due to contamination during processing, storage, and transport of food and drink (Wormuth *et al.*, 2006; Rudel *et al.*, 2011). In addition, phthalates have been linked to health status (diabetes, hypertension, hyperthyroidism, or kidney dysfunction) and medication use (Hauser *et al.*, 2004), neither of which were considered among this population.

Exposure misclassification within this study is likely. Although we classified potential work and consumer products sources of phthalates, since labels do not include phthalate levels, we assume that phthalates are present in each source in similar concentrations. Other exposure factors such as whether the cleaning chemical was sprayed and aerosolized or wiped and the ventilation within the areas being cleaned was not evaluated. Therefore, all cleaning chemical use was treated as equal regardless of potential for exposure. The potential exposure misclassification is likely to bias results towards the null, providing further support for the statistically significant associations observed. In addition, workers were monitored mid-week with no washout period from workplace or consumer product exposures. To account for this, within our models, predictors did not vary by sampling time. This assumes similar workplace and consumer product exposure occurred in the prior day which may bias results towards the null.

We assessed urinary phthalate monoesters, which represent the major human metabolite for low molecular weight phthalates with short alkyl chains. However, for higher molecular weight phthalates including DEHP, the monoester is further metabolized into oxidized products (Wittassek and Angerer, 2008). Since urinary analysis within this study was limited to monoesters, the concentrations of higher molecular weight phthalates including DEHP may be underestimated. The lack of information on oxidative metabolites and potential contamination during sample collection may contribute to exposure. This exposure misclassification may have limited our ability to identify statistically significant associations, especially for DEHP. Furthermore, a number of univariate predictors for each phthalate were considered and statistical associations may be due to chance. Despite these limitations, predictors of MEP exposure accounted for 44% of metabolite variability.

While the results of our study may be internally valid, the study findings may not be representative of the general population of workers performing cleaning duties in all workplaces due to the wide range of chemicals and procedures used during cleaning and maintenance. Custodians were from a relatively small number of institutions within a single labor union. Yet, this unique population which used both conventional and EPP cleaning chemicals, provides important information about the urinary phthalate concentrations among custodians. Furthermore, the multiple measures on

each individual and the detailed information on workplace as well as consumer products allowed us to identify signals of phthalate sources among this group.

CONCLUSION

A significant relationship was observed between occupational exposures to traditional cleaning chemicals and urinary MEP concentrations. We identified both occupational and nonoccupational sources of phthalate exposures. Identification of phthalates as ingredients in cleaning chemicals and consumer products would allow workers and consumers to avoid phthalate exposure.

SUPPLEMENTARY DATA

Supplementary data can be found at http://annhyg.oxfordjournals.org/.

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DECLARATION

The contents of this article are solely the responsibility of the authors and do not necessarily represent the official views of NIOSH.

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