Environment International 113 (2018) 55–65

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Exposure to organophosphate flame retardants in spray polyurethane foam applicators: Role of dermal exposure

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ARTICLE INFO

Handling Editor: Kalantzi Olga Ioanna

Keywords:
TCIPP
Tris 1-chloro 2-propyl phosphate
Tris (2-chloroethyl) phosphate
Spray polyurethane foam
Urinary biomarkers
Organophosphate flame retardants

ABSTRACT

Background: Spray polyurethane foam (SPF) is a highly effective thermal insulation material that has seen considerable market growth in the past decade. Organophosphate flame retardants (PFRs) are added to SPF formulations to meet fire code requirements. A common flame retardant used in SPF formulations is tris 1-chloro 2-propyl phosphate (TCIPP), a suspected endocrine disruptor. Exposure monitoring efforts during SPF applications have focused primarily on the isocyanate component, a potent respiratory and dermal sensitizer. However, to our knowledge, there is no monitoring data for TCIPP.

Objective: To characterize occupational exposures to TCIPP and other flame retardants during SPF insulation.

Methods: Workers at four SPF insulation sites and one foam removal site (total $n = 14$) were recruited as part of this pilot study. Personal inhalation exposure to TCIPP was monitored with a CIP-10MI inhalable sampler and potential dermal exposure was assessed through the use of a glove dosimeter. Biomarkers of TCIPP and three other PFRs were measured in urine collected from workers pre-and post-shift. Linear mixed effect models were used to analyze associations of urinary biomarkers with inhalation and dermal exposures and paired *t*-tests were used to examine the difference on the means of urinary biomarkers pre-and post-shift. Chemical analysis of all species was performed with liquid chromatography-electrospray ionization tandem mass spectrometry.

Results: Geometric mean (GM) concentrations of TCIPP in personal air monitors and glove dosimeters collected from SPF applicators, 294.7 μg/m^3 and 18.8 mg/pair respectively. Overall, GM concentrations of the two TCIPP urinary biomarkers BCIPP and BCIPHIPP and (6.2 and 88.8 μg/mL) were 26–35 times higher than reported in the general population. Post-shift levels of TCIPP biomarkers were higher than pre-shift even though workers at insulation sites wore supplied air respirators, gloves and coveralls. The urinary biomarkers for the other PFRs were not elevated post shift. Concentrations of TCIPP on glove dosimeters were positively associated with post-shift urinary TCIPP biomarkers ($p < 0.05$) whereas concentrations in personal air samples were not.

Conclusions: High levels of urinary biomarkers for TCIPP among SPF applicators, including post-shift, points to absorption of TCIPP during the work shift, in spite of the use of best industry exposure control practices. Dermal exposure appears to be an important, if not the primary exposure pathway for TCIPP, although inhalation or incidental ingestion of foam particles post-SPF application cannot be ruled out in this pilot study.

1. Introduction

Spray polyurethane foam (SPF) is a highly effective thermal insulation material used in numerous applications in the construction of residential and commercial buildings, including internal and external wall insulation, basement and celling insulation, as well as floor and flat roof insulation. The number of insulation jobs in construction has increased recently, reaching 55,600 in 2014, and it is expected to grow by 13% in the next decade (BLS, 2016–2017). SPF is a two-component foam system. Part A comprises of the isocyanate component, which is based on polymeric methylene diphenyl diisocyanate (pMDI). Part B is a mixture of various ingredients such as polyols, cross-linkers, amine catalysts, solvents, and other proprietary additives. Flame retardants (FR) are added in part B of SPF formulations to meet fire code

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https://doi.org/10.1016/j.envint.2018.01.020
Received 15 November 2017; Received in revised form 20 January 2018; Accepted 20 January 2018
Available online 06 February 2018

requirements. There are no comprehensive market surveys of commercial SPF formulation with regards to the types and frequency of FR in use. The most common FR in SPF products is tris 1-chloro 2-propyl phosphate (TCIPP; CAS #1367-84-5), a chlorinated organophosphate flame retardant (EPA, 2015a; NIOSH, 2014). Use of organophosphate flame retardants (PFRs) increased with the phase out of the polybrominated diphenyl ether (PBDE) flame retardants starting in 2005 (Stapleton et al., 2012; Van der Veen and de Boer, 2012) and coupled with the increased demand for energy savings through building insulation has contributed to a steady increase in production of TCIPP. Most of the TCIPP produced in the EU (over 98%) is used as flame retardant in construction and furniture applications (EU, 2008). An estimated 38,000 tons of TCIPP were used in the USA in 2012 and its production is predicted to grow steadily through 2020 (Schreder et al., 2016).

PFRs have become ubiquitous contaminants in the indoor environment, and the widespread use of TCIPP in SPF formulations raises questions about potential for occupational and consumer exposures. They have been detected in indoor air and dust collected from homes, offices and other environments in several studies (Carlsson et al., 1997; La Guardia and Hale, 2015; Schreder et al., 2016; Stapleton et al., 2009; Yang et al., 2014). TCIPP has been the most predominant PFR measured in the indoor air. Recent research has raised concerns about the toxicity of TCIPP due to its structural similarity with two other flame retardants, namely tris (2 chloroethyl) phosphate (TCEP) and tris (1,3 dichloro-2-propyl) phosphate (TDCIPP). Both TCEP and TDCIPP are listed as substances known to cause cancer in humans under California Proposition 65 (CA EPA, 2011; Schreder et al., 2016). Animal toxicity studies report that TCIPP can disrupt the endocrine system, with indications of antiandrogenic and antiestrogenic activity in vitro (Farhat et al., 2013; Liu et al., 2012). In addition, TCIPP can impact the expression of genes associated with xenobiotic metabolism, lipid regulation, and growth (Crump et al., 2012). A recent study of toxic effects in human hepatic cells indicated that TCIPP can cause disturbance in cell growth and division, gene expression, energy and metabolism (Li et al., 2017). In vivo studies report morphological changes in the thyroid (Freudenthal and Henrich, 1999) and adverse effects on reproduction including changes to the estrous cycle and increased uterine weights (TNO Quality of Life, 2007), low birth weight (EPA, 2015b) and delayed pipping (Farhat et al., 2013). Toxicology of TCIPP in humans is not well researched. The first epidemiologic study investigating the effects of PFRs on female reproduction found PFR exposures to be associated with a reduction in the likelihood of successful fertilization, implantation, clinical pregnancy, and live birth (Carignan et al., 2017).

Insulation workers may be exposed to TCIPP during and after SPF insulation jobs. Exposures can happen through inhalation of aerosol particles generated during product spraying and trimming, as well as through contact with the skin. TCIPP is a semi volatile compound under normal conditions, with a boiling point > 200 °C and vapor pressure of 1.4×10^{-3} Pa at 25 °C (EPA, 2015a; EU, 2008). Due to its low volatility, the potential for vapor exposures is generally low, except perhaps during foam application itself due to foam over/heating to temperatures over 100 °C. Although exposure data on TCIPP vapor concentrations during SPF applications are lacking, the vast majority of airborne TCIPP is expected to be in the aerosol phase, trapped inside the SPF foam particles. This has been confirmed in preliminary studies aimed at quantifying the vapor and aerosol phases of TCIPP during SPF (personal communication with Dr. RP Streicher of NIOSH). Dermal exposure to TCIPP can happen through direct contact of the skin with the SPF foam during application and afterwards during foam inspection, cleaning/removal of foam shavings, and from aerosol deposition on various body parts. Since TCIPP is relatively lipophilic (log K_{ow} of 2.59) (Van der Veen and de Boer, 2012), skin absorption is possible. Data on TCIPP skin penetration and permeation, skin exposure levels during SPF applications, and permeation of protective clothing by TCIPP (gloves, coverall, etc.) are lacking in the peer-reviewed literature. Abdallah et al. in a recent in vitro study suggest that dermal absorption of TCIPP in human is likely (Abdallah et al., 2016). Urinary biomarkers of PFRs in the general population have been measured in several studies (Butt et al., 2014; Butt et al., 2016; Carignan et al., 2016; Cooper et al., 2011; Schindler et al., 2009; Van den Eede et al., 2015). However, the extent of occupational exposure to TCIPP among insulation workers is not known. Exposure biomarkers in urine are particularly helpful in assessing exposure levels in the workplace, especially for chemicals that can enter the body via multiple pathways, and/or if workers use protective clothing, coveralls and respirators, as is the case during SPF installation.

In this paper, we characterize, for the first time, exposures to TCIPP among SPF construction workers utilizing personal inhalation and dermal exposure assessment in combination with urinary biomonitoring pre- and post-shift. Findings of this work are helpful in assessing effectiveness of current exposure controls and work practices and can guide further interventions to reduce exposures to TCIPP.

2. Methods

2.1. Chemicals and supplies

TCIPP and TDCPP were purchased from Sigma-Aldrich (St. Louis, MO). Acetonitrile and methanol, HPLC grade, from VWR (NJ, USA), Trifluoroacetic Acid and Formic Acid, LCMS grade from (Fisher Scientific (Waltham, MA, USA). Acrodiscs were purchased from Pall Life Sciences (New Jersey).

Metabolites bis(1-chloro-2-propyl) phosphate (BCIPP) and d10- diphenyl phosphate (d10-DPHP) were synthesized by the Max Planck Institute for Biophysical Chemistry Goettingen, Germany). 1-hydroxy-2-propyl bis(1-chloro-2-propyl) phosphate (BCIPHIPP) was a gift from Professor Adrian Covaci, University of Antwerp (Antwerp, Belgium) to Prof. Stapleton. Bis(1,3-dichloro-2-propyl) phosphate (BDCIPP) and d10-BDCIPP, were purchased from Wellington Laboratories (Guelph, ON). The ip-PPP, tert-butyl-phenyl phenyl phosphate (tb-PPP), and ^{13}C2-DPHP were synthesized by the Small Molecule Synthesis Facility at Duke University (Durham, NC). Ammonium acetate, trimethylamine, pyrrolidine and 2,3,5- triiodobenzoic acid (TIBA), β-glucuronidase from limpets (N1 M units/g) and sulfatase from *Helix pomatia* (N10,000 units/g) were purchased from Sigma-Aldrich (St. Louis, MO). Strata X-AW (60 mg, 3 mL) solid phase extraction columns (SPE) and the Luna C18 (2) (2.5 µm, 50 Å ~2 mm) analytical column were purchased from Phenomenex (Torrance, CA, USA). Methanol and acetonitrile were HPLC grade (EMD Millipore Corporation, Bellerica, MA).

2.2. SPF jobs and sampling sites

This work was performed as part of a larger study that focused on assessing and controlling occupational exposures to isocyanates during SPF jobs in construction. Study participants were construction workers performing SPF installation in the New England region. Sampling was performed at five SPF sites, summarized in Table 1. Four sites involved SPF installation in 3 new residential constructions as well as a garage being insulated as part of a SPF training. The fifth site was a residential home in which a crew of two workers was conducting remediation work to remove the SPF from the basement in response to smell complaints by the residents.

SPF insulation jobs were performed by different crews of 2–3 workers/site. Their main tasks consisted of site preparation, SPF product spaying, foam cutting, and site cleanup. Worker 'sprayers' performed SPF application using spray guns, while 'helpers' were mainly responsible for cutting the excess foam flat against the studs using saw blades (Fig. 1a), collecting and removing excess foam, as well as assisting the sprayer in a variety of ways (checking drums of raw materials, relocating supply foam lines and supplied air, repositioning the ladder, etc.). At the training site, SPF applicators participated in hands-

Table 1
Summary description of spray polyurethane foam job sites and flame retardants in products used at each site.

Site		Activity	Tasks performed	Type of foam	# of workers	PPEs used	Flame retardants as reported in the products' SDS	
							Chemical	Weight (%)
A	Residential homes New construction	Insulation	SPF spraying with a spray gun	Open cell	2	- Supplied Air Respirators (SAR) - Disposable coverall	TCIPP (Tris phosphate (2-chloro isopropyl) CAS: 13674-84-5	30–60
B			Foam shaving against studs with a powered blade saw	Open & closed cell	3	- -Nitrile gloves, thin (3 mil)	TCIPP (2-Propanol, 1-chloro-2,2′,2″-phosphate) CAS: 13674-84-5	7–13
C			Gun cleaning Site cleaning (removal of foam waste)	Open cell	2		2,2,4-Trimethyl-1,3-pentanediolmono (2-methylpropanoate) CAS: 1244733-77-4	40–50
D	Training site, new garage	Roofing insulation	SPF spraying with a spray gun	Roofing product	5	Sprayers: PPEs as in sites A–C Trainees/Bystanders: 1/2 - face piece with OVC cartridge instead of SAR	Chlorinated phosphate ester CAS: Trade secret	3–7
E	Residential home	Foam removal/ remediation	Foam removal using a powered brush tool	Closed cell	2	Dust mask & regular clothing (jeans and cotton sweater)	Halogenated phosphate CAS: Trade secret	5–10

SAR, supplied air respirator; OVC, Organic vapor cartridge respirator (half face and full face).

on SPF spraying of the side walls, ceiling, as well as building floor using a roofing insulation product. The closed cell foam remediation job (aka trimming and removal) was performed by the same crew who had sprayed the foam six months earlier. The foam was removed with a hand held powered circular brush tool, generating clouds of visible dust in the process (Fig. 1b). Among the 14 workers who participated in this study, 10 were sprayers and helpers, 2 were involved with foam remediation work and 2 were site managers.

For each site, we collected systematic contextual information on products used, tasks/activities performed and their duration, environmental conditions, use of personal protective equipment and other engineering controls. Table 1 lists flame retardants reported in products' safety data sheets (SDS) of part B at these sites. Products used in all sites consisted of open and closed cell foams, which provide different thermal insulation values and differ from each other by part B composition, including the content and proportion of each ingredient.

2.3. Exposure assessment

The overall sampling strategy was based on combining airborne and dermal exposure sampling with pre-post shift urine collection. All samples were collected as part of the larger study designed to assess exposures to isocyanates during SPF applications. Each participant signed a consent form approved by the institutional review board at UMASS Lowell.

2.3.1. Airborne exposure sampling

Personal sampling of airborne exposures generated during SPF applications was achieved by using a newly developed sampler CIP-10MI (Arelco, Fontenay-Sous-Bios Cedex, France), which has been adopted successfully for measuring isocyanate aerosols during SPF (Puscasu et al., 2015). The SPF aerosol was collected inside a rotating cup (7600 rpm) that contains 2 mL of a liquid solution that comprised of butyl benzoate containing 5 mM 1-(9-anthracenylmethyl) piperazine (MAP), a derivatizing reaction for isocyanates. The MAP reagent reacts with isocyanates to form stable MAP-ureas, which were then analyzed by liquid chromatography-tandem mass spectrometry in the positive electrospray ionization mode (LC-ESI-MS/MS). The CIP-10MI unit collects the inhalable fraction of aerosol at a flow rate of 10 L/min (Gorner et al., 2006). The rotation speed of the CIP-10MI was measured in the

(a) Spraying and shaving of foam (b) Foam removal using a powered brush tool

Fig. 1. Representative images of spray foam insulation (SPF) activities.

field using a 6236 SI tachometer. Air sampling times ranged from 15 to 176 min (GM 71 min) depending on duration of tasks and workers' participation. The CIP-10 MI samples were collected in the breathing zone of 10 insulation workers, while 2 managers at these sites provided only urine samples. At the end of the sampling period, the sampling medium was transferred into clean amber glass vials and transported to the lab in coolers with ice packs. Samples were stored at −20 °C until analyzed for TCIPP content using LC-ESI-MS/MS as described in a later section.

2.3.1.1. Aerosol sampling during SPF remediation (or trimming). Removal of the cured foam with powered brush tools generated clouds of visible dust. We performed sampling on the breathing zone of the workers that performed foam removal. Since each SPF foam particle contains considerable amounts of TCIPP (max 30–60% based on data from safety data sheets), it is expected that even a few inhaled SPF particles can deliver a measurable TCIPP amount in urine. Aerosol dust generated during trimming was collected on a 25-mm quartz filter housed inside an Institute of Occupational Medicine (IOM) inhalable sampler connected to a sampling pump (GilAir 3, Sensidyne, Clearwater, Fl) at 2 L/min. The filter was then transferred in butyl benzoate and kept in the refrigerator at −20 °C until preparation for chemical analysis. Dust samples were analyzed for TCIPP content using LC-ESI-MS/MS method as described below.

2.3.2. Dermal exposure sampling

Potential dermal exposure to hands was assessed using a glove dosimeter method consisting of medical grade cotton gloves worn by the worker over thin (3 mil) nitrile gloves. Our workplace observations had shown that hands are one of the most contaminated anatomical parts of the body. The cotton gloves were impregnated with the MAP reagent for the purpose of simultaneously stabilizing and quantifying isocyanates. Participants wore the gloves for a period of 15 to 123 min (GM 44 min) depending on the length of tasks and workers' preference for using them. Immediately after sampling, each pair of gloves (n = 11 pairs) was transferred into 120 mL capacity jars containing 50 mL solution of 50 mM MAP in ethyl acetate. The jars were capped with a PTFE lid, stored and transported to the lab in a cooler with ice packs and stored at −20 °C until ready for chemical analysis. TCIPP content was analyzed with the same LC-ESI-MS/MS method as described below.

2.3.3. Urine specimen collection

Spot urine samples were collected in sterile urine specimen collection cups at the beginning of the work shift (typically by 9 AM), and at the end of the spray task, or as close to the end of the shift as possible, depending on the size and duration of the spray job, worker preferences and schedules. The time interval between pre- and post-shift urine collection ranged from 115 to 300 min with a GM of 195 min. A total of 24 urine samples were collected from 10 workers who provided pre- and post –shift urine samples and 4 workers who provided only post shift urine. At the end of sampling urine samples were transported to the lab inside coolers with ice packs and either processed immediately or stored at −80 °C until further processing. The urine was centrifuged (after thawing when in −80 °C) at 1000 rpm for 10 min to remove any cellular debris. An aliquot of 5 mL urine sample was shipped to Prof. Stapleton's Lab at Duke University overnight in dry ice for biomarker analysis as described below. Urine specific gravity was measured with a hand held digital pocket refractometer (PAL -10S Atago, Japan) and creatinine concentration was measured with LC-ESI-MS/MS (see Supplemental material).

2.4. Air and dermal sample analysis

2.4.1. Sample processing

2.4.1.1. Air samples. Samples were allowed to warm to room temperature, vortexed for 1 min, then diluted 100–1000 times in acetonitrile, spiked with 10 µL of TDCIPP (internal standard IS, 100 ng/mL final), filtered through a 0.45 µm Acrodisc® filter, and analyzed by liquid chromatography tandem mass spectrometry in the positive electrospray ionization mode (LC-ESI-MS/MS) as described under the Analysis section (2.4.2).

2.4.1.2. Glove samples. Jars containing gloves were shaken for 5 min at moderate speed to homogenize the sample and then placed in a sonication bath for 30 min. After sonication, an aliquot of 10 mL was taken out, spiked with 10 µL of the TDCIPP (IS) and filtered first through a 0.45 µm filter and then a second 0.25 µm filter to remove cotton fibers and particles. Solutions were concentrated in a Visiprep (Sigma-Aldrich, USA) under vacuum with a stream of N_2 (Airgas, Billerica, MA, USA) to a final volume of 1 mL (final IS concentration of 100 ng/mL) and transferred into a 2 mL amber LC vial followed by LC-ESI-MS/MS analysis (2.4.2).

2.4.1.3. SPF dust from remediation. Samples were thawed then vortexed for 2 min. One millilter of the solution was double filtered, first through an Acrodisc® 0.45 µm pore filter then through a 0.25 µm filter, spiked with 10 µL of the IS, diluted 100 times with acetonitrile and analyzed for TCIPP as described in the Analysis section (2.4.2).

2.4.2. LC-ESI-MS/MS analysis of TCIPP

Chromatographic separation of flame retardants was performed on an ultra-high performance liquid chromatography (UHPLC) system (Shimadzu, Japan), consisting of a solvent delivery unit (LC-20AB), degasser (DGU-20A3), along with an auto-sampler (SIL-20 AC) and column oven (CTO-20AC). Separation was carried out on a Kinetex C18 column, 100 × 4.6 mm I.D., 2.6 µm particle size column (Phenomenex, CA, USA), preceded by a matching phase guard column (Phenomenex, CA, USA). Gradient elution was performed using mobile phase A: 100% water; 0.1% formic acid; and mobile phase B: 100% acetonitrile; 0.1% formic Acid; 0.01% trifluoroacetic acid. Column oven temperature was set to 40 °C and injection volume 10 µL. Compounds were eluted with a flow rate of 0.6 mL min^{-1} using a chromatographic gradient from 50% (at 0.01 min) to 90% B (at 7 min), followed by 3 min post analysis re-equilibration at 50% B. The retention time of TCIPP and internal standard (TDCIPP) were 4.21 and 4.82 min, respectively, and the peaks were fully resolved from each-other and other sample components.

The UHPLC system was attached to an Applied Biosystems–MDS SCIEX API 3200 triple quadrupole spectrometer equipped with a Turbo V IonSpray source. The MS source parameters for the source were as follows: Curtain gas (CUR) 30, collision gas (CAD) 5, Ion spray voltage 5500, source temperature 600 °C, ion source gas 1 and 2 (GS 1, GS2) 60 and 50, respectively, and interface heater was ON.

Quantitation of TCIPP species was based on their respective standards calibrations, using TDCIPP as the internal standard, spiked at 100 ng/mL, and multiple reaction monitoring (MRM), using the following respective MRM transitions. For TCIPP, we monitored transition 327.1 → 99.0, whereas for TDCPP, 431.1 → 99.0. Optimized MRM compound-specific parameters for these compounds are summarized in the Supplemental material, Table S1. Ten standards in the range of 650 pg/mL to 1.3 µg/mL were routinely used for the calibration curve. The calibration curve for TCIPP was linear up to ~1.3 µg/mL (R = 0.999). The limit of detection of TCIPP (as 3 times the S/N ratio) was 250 pg/mL. All air and dermal samples analyzed were above the method limit of quantitation (3× LOD).

2.4.3. Stability and recovery of TCIPP

In this study TCIPP was co-collected with other SPF ingredients in the presence of MAP, a secondary amine used as the derivatizing reagent for isocyanates, either in butyl benzoate (air samples) or ethyl acetate (glove dosimeter). Concerned over possible reactivity of MAP with TCIPP, we conducted separate experiments in which TCIPP was spiked in the respective sample matrix (MAP in butyl benzoate, MAP in

ethyl acetate or MAP in methanol) at 100 ng/mL. Concentration of TCIPP was monitored kinetically in MRM from 1 min to 140 h. Concentration of MAP was monitored with ultraviolet detection at 254 nm (UV254 nm) and UV370 nm using the online diode array detection. A second Q1 scan experiment was performed simultaneously to track MAP, TCIPP, and any additional reaction byproducts.

In all cases, especially in ethyl acetate, MAP would react almost immediately with TCIPP, confirmed by the disappearance of TCIPP and consumption of MAP, then TCIPP will reappear in the media and its concentration will increase linearly with time. After 6 h, the TCIPP will reach original concentration and remain stable afterwards. Recoveries in all cases were 98–99% of the original amount. The evidence taken together suggests that MAP forms an intermediate complex with TCIPP, which slowly reverts back to the original concentrations of reactants. No further inquiries were made as to the exact mechanism of this transient interaction. A time delay of > 6 h is important for quantitative analysis of TCIPP in the presence of MAP. Samples were analyzed several months after their original collection.

To further confirm the stability of TCIPP in the sample matrix, we reanalyzed seven samples covering the whole range of TCIPP concentration 16 months after the original analysis of TCIPP. The original results and the new ones agreed within 2% (new values = 0.985 × old values, $R^2 = 0.998$) confirming stability of TCIPP. Based on these experiments, we conclude that TCIPP can be successfully quantified in the sample matrixes containing MAP, after 10 h of IS spike and sample storage at room temperature.

2.5. Urinary biomarkers of phosphate flame retardants

Urine samples were analyzed for a panel of biomarkers for several phosphate flame retardants, as reported in Butt et al. (2016) (Butt et al., 2016). This list included two biomarkers for TCIPP, namely bis(1-chloro-2-propyl) phosphate (BCIPP) and 1-hyrdoxyl-2-propyl bis(1-chloro-2-propyl) phosphate (BCIPHIPP). In addition, urine samples were analyzed for diphenyl phosphate (DPHP), isopropyl diphenyl phosphate (ip-DPHP), and bis(1,3-dichloro-2-propyl) phosphate (BDCIPP), which are urinary biomarkers of three other flame retardants namely triphenyl phosphate (TPHP), isopropyl triphenyl phosphate (ip-TPHP), and isopropyl diphenyl phosphate (TDCIPP), respectively (Fig. 2). Although the focus of this study was TCIPP and its metabolites, the other flame retardants were monitored in this preliminary work for exploratory purposes, taking advantage of the already developed analytical methods for the PFR urinary biomarkers.

2.5.1. Urine analysis

The methodology for urine analysis was based on a previously published method by Butt et al., 2016 and is summarized here for clarity (Butt et al., 2016). Briefly, 5 mL urine was thawed, transferred to a clean glass tube and spiked with the internal standard mixture (10 ng of d10-BDCIPP, 8.8 ng of d10-DPHP). After the addition of 1.75 mL of sodium acetate (pH 5, 1 M) and 250 μL of enzyme solution (1000 units/mL of β-glucuronidase, 33 units/mL of sulfatase in 0.2 M sodium acetate buffer), the samples were vortexed and incubated overnight at 37 °C in a water bath. Samples were cleaned and concentrated using SPE techniques as described by Van den Eede et al. (Van den Eede et al., 2015) with the exception that the extracts were reconstituted in 500 μL of methanol: water. Internal standard recovery was quantified by spiking with 13C2-DPHP. Samples were transferred to Mini-UniPrep vials (GE Healthcare Life Sciences) immediately prior to instrumental analysis.

Extracts were analyzed by LC-ESI-MS/MS in the positive ion mode as previously described (Butt et al., 2016), but with the addition of BCIPHIPP and d12-TCEP. Data were acquired under multiple reaction monitoring conditions using optimized parameters (Butt et al., 2014). BCIPHIPP was quantified by monitoring the *m/z* 309.0 → 99.1 and 309.0 → 81.1 transitions, whereas d12-TCEP transition *m/z* 297.1 → 67.2. Analyte responses were normalized to internal standard responses. BCIPP and BDCIPP were normalized using d10-BDCIPP, DPHP, ip-PPP and tb-PPP were normalized using d10-DPHP, and BCIPHIPP was normalized using d12-TCEP.

2.6. Statistical data analysis

Statistical analyses were performed with SAS 9.4 (SAS Institute Inc. Cary, NC). The data were examined for the underlying distribution using the Shapiro-Wilk statistic and by graphing probability plots and histograms. Because the data fit the lognormal distribution better than the normal distribution they were log transformed. Descriptive statistics were generated for air, glove and urinary biomarkers for pre- and post-shift, including geometric mean (GM) and geometric standard deviations (GSD). Urinary biomarkers were normalized to both specific gravity and creatinine to account for urine dilution; results of statistical analyses were similar in either case. Paired *t*-tests on log-transformed data were used to examine the difference on the means of urinary biomarkers pre-and post-shift.

Linear mixed effect models were used to investigate association between post-shift TCIPP urinary biomarkers (BCIPP and BCIPHIPP) with air and glove exposures as independent variables. We further investigated the influence of task performed (sprayer, helper), activity (insulation, roofing), and foam type (open cell, closed cell and roofing formulation) on the TCIPP air and glove levels. In the paper variables “task” and “job title” are used inter interchangeably. For the purposes of exposure data analysis, the worker responsible for helping was classified as a ‘sprayer’ and not as helper if he performed spraying even for a small portion of the day.

3. Results

3.1. Airborne exposures to TCIPP

Concentrations of TCIPP in personal air samples ranged from 9.6–1852.5 μg/m^3 with a GM of 294.7 (GSD 4.07) μg/m^3 (Table 2). The highest concentrations were measured in the aerosol dust sample collected during foam removal (1852.5 μg/m^3) as well as in the breathing zone of the worker performing SPF spraying at site C (917.3 μg/m^3). The lowest levels measured (9.6 μg/m^3) relate to exposures of the trainer at the training site (site D). Data in Table 2 indicate that sprayers *within* the same site had higher exposures compared to the helpers. However, the overall GM for helpers was higher than the sprayers (271.4 vs. 234.8 μg/m^3) due to one low concentration sample (9.6 μg/m^3) corresponding to the SPF trainer at the training site with 25 years' experience. Overall, the difference on helpers and sprayers exposures was not statistically significant (*p* value, 0.89). When analysis was restricted only to new residential homes (excluding traning center), with both sprayers and helpers onsite, sprayers had higher exposures compared to helpers, although still non-significant due to the small sample size (*p* value, 0.31) (see Fig. S1 in the Supplemental material).

Exposures generated during vertical spraying of walls with GM 397.6 (GSD 2.2) μg/m^3 were higher compared to downward floor spraying with GM 79.4 (GSD 6.2) μg/m^3 (*p* value, 0.07). Furthermore, the TCIPP GM concentrations during closed cell foam use of 1051 (GSD 2.2) μg/m^3, were higher than during open cell foam use of 371 (GSD 2.3) μg/m^3 and roofing application of 79.4 (GSD 6.2) μg/m^3 (p value, 0.10) (see Figs. S2 and S3 in the Supplemental material). These results could be related to a number of factors including the more intermittent nature (shorter duration) of spraying during simulated roofing application, directionality of spray (spraying downwards on the floor as supposed to upwards, producing less overspray aerosol), product composition and/or small number of samples.

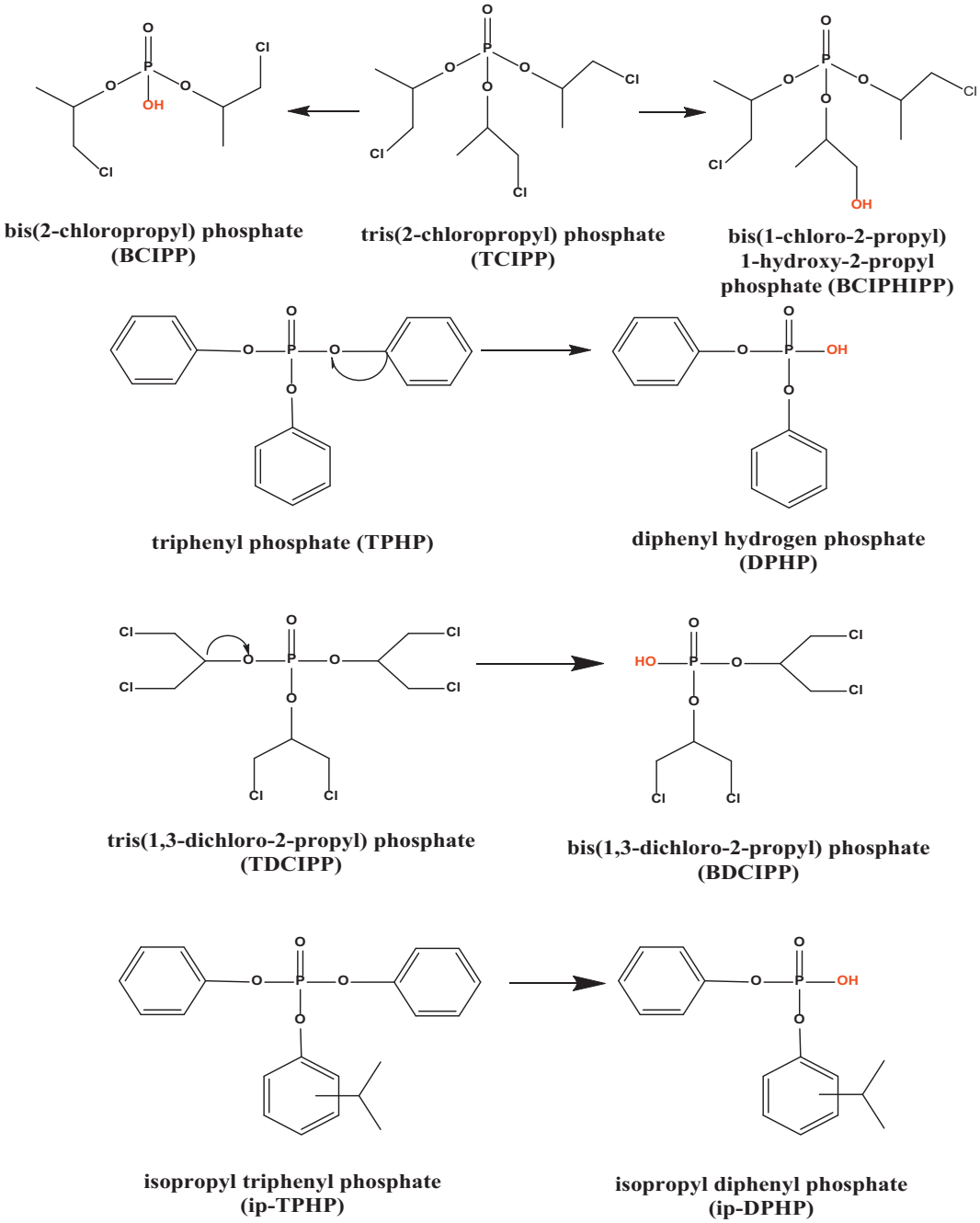

Fig. 2. Chemical structures of the organophosphate flame retardants used in SPF and their main urinary biomarkers.

3.2. Potential dermal exposure to hands

Concentrations of TCIPP accumulated on the gloves ranged from 0.71–182.2 mg/pair (Table 2). Since the TCIPP loading on the gloves is influenced by the sampling time, we normalized the glove loading data to sampling time (Table 2). The total TCIPP load measured on glove samples, normalized per 1 min of sampling, varied from 0.01 to 2.29 mg/pair/min, with a GM of 0.23 (GSD 3.8) mg/pair/min. The highest amount of TCIPP was measured in the gloves of the sprayers at the site A & B. Loading of the gloves was the lowest for the sprayer at the training site (0.01 mg/pair/min), who as previously described, had the lowest measured personal airborne exposures. Since this worker was an experienced trainer it is likely that his perfected spraying technique resulted in considerably lower overspray aerosol, and consequently lower air and dermal exposures. In should be noted that data within each site clearly indicate higher amount of TCIPP on the gloves of sprayers vs. helpers (Table 2). Statistical analysis restricted only to residential home sites, indicated higher potential for dermal exposures for sprayers compared to helpers, but this difference was not significant ($p = 0.14$). Glove loading changed significantly when different foam products were used, with the highest levels when open cell foam was used (see Figs. S4 and S5 in the Supplemental material).

3.3. Urinary biomarkers

Descriptive statistics of the distribution of urinary concentration for the five biomarkers, normalized to specific gravity are presented in Table 3. All urinary biomarkers were above the limit of detection in 100% of samples. The first noteworthy observation is that all five biomarkers, including the three biomarkers of PFRs other than TCIPP,

Table 2
Summary of air and dermal sampling results. GM, geometric mean; GSD, geometric standard deviation.

Site	Worker ID	Task/job	Duration of air samples (min)	Personal air TCIPP (μg/m^3)	Duration of glove samples (min)	Glove TCIPP (mg/pair of glove)	Glove TCIPP/min (mg/pair gloves/min)
A	1	Sprayer	80	204.6	80	182.2	2.28
	2	Helper	80	165.2	80	14.09	0.18
B	3	Sprayer	176	701.6	36	82.27	2.29
	4	Helper	175	153.1	36	50.86	1.41
	5	Sprayer	96	596.9	40	35.22	0.88
C	6	Sprayer	135	917.3	45	73.80	1.64
	7	Helper	123	790.5	123	50.75	0.41
D	8	Sprayer	17	199.6	17	1.62	0.10
	9	Sprayer	60	9.6	60	0.71	0.01
	10	Sprayer	45	262.4	45	3.28	0.07
E	11	Trimming or foam removal	15	1852.5	15	4.83	0.32
Summary statistics	N = 11[a]	S, *n* = 7[b]	Range				
		H, *n* = 3	15–176	9.6–917.3	15–123	0.71–182.2	0.01–2.29
		T, n = 1	GM (GSD)				
			70.5 (2.3)	294.7 (4.1)	44.2 (1.9)	18.8 (5.9)	0.23 (3.8)

[a] N = number of workers participating in air and glove sampling.
[b] n = number of air samples collected for each task: S-Sprayer; H-Helper; T-Trimming/foam removal.

Table 3
Summary statistics for urinary biomarkers in all samples collected normalized to specific gravity (SG).

Biomarker	N	Urinary concentrations, normalized to SG (ng/mL)		Comparison of the distributions of urinary biomarkers pre- and post-shift	
		GM (GSD)	Range	Ratio of GMs post/pre shift	*p*-Values[a]
BCIPP	24	6.2 (3.2)	1.2–51.4	1.7	0.01
BCIPHIPP	24	88.8 (4.0)	5.2–703	13.4	0.05
DPHP	24	6.5 (2.4)	0.9–36.1	0.8	0.23
BDCIPP	24	5.3 (2.4)	0.5–33.4	1.1	0.54
Ip-DPHP	24	27.9 (2.5)	3.6–134	1.0	0.92

[a] *p*-Values correspond to the paired t-test on the means of the Ln-transformed biomarker data.

were at detectable levels in the urine of SPF workers. Secondly, the highest concentrations corresponded to the BCIPHIPP, one of the TCIPP biomarkers. When normalized to specific gravity, the GM concentration of BCIPHIPP was ~14 times higher than the GM of BCIPP and 3.2–13.6 fold higher than the other urinary metabolites. Several individuals had particularly elevated urinary BCIPHIPP as well as ip-DPHP. The overall trend of the biomarker values did not change when normalized to creatinine and while the values were lower than when normalized to specific gravity differences were similar. For example, the GM of the most abundant urinary biomarker, BCIPHIPP, at 41.6 μg/g creatinine and maximum of 236.6 μg/g creatinine, was 14.3 times higher than that of BCIPP (see Supplemental material, Table S2). The values of other PFR biomarkers were in a similar range to BCIPP.

3.3.1. Pre- vs. post shift changes in urinary biomarkers

Table 3 summarizes the *p*-values for the paired *t*-test of ln-transformed urinary biomarker data normalized to SG (uncorrected and creatinine adjusted biomarkers results are presented in Table S2). The pre- to post-shift concentrations of the two TCIPP biomarkers were significantly different, regardless of the normalization procedure (e.g. *p* values were 0.01 and 0.05 respectively for BCIPP & BCIPHIPP normalized to SG). Post-shift GM concentrations of urinary BCIPP was higher (GM 6.3 ng/mL, GSD 3.7) compared to the pre-shift (GM 5.9 ng/mL, GSD 2.7), indicating TCIPP absorption resulting from work (Fig. 3). On the other hand, the GM BCIPHIPP concentration was higher pre-shift (GM 99.5 ng/mL, GSD 4.2) than post-shift (GM 81.9 ng/mL, GSD 4.2). The BCIPHIPP GM values are strongly influenced by 2 samples. Among the 10 workers who provided pre-and post-shift urine samples, 8 had higher post-shift BCIPHIPP levels compared to pre-shift. When these 2 samples were excluded from the analysis, post-shift BCIPHIPP values were significantly higher than pre-shift (paired *t*-test *p*-value = 0.02) (Fig. S6). In addition, Fig. 4 plots the distribution of the ln [(post-pre shift) BCIPHIPP concentration (normalized to specific gravity). The mean difference greater than zero indicates an overall higher post-shift BCIPHIPP concentrations compared to pre-shift. These apparently contradicting findings are influenced by the results from two participants who had lower post-shift biomarker levels. One of these participants was the trainer at the training site who had the lowest measured air and dermal TCIPP values and the other was the helper at site A, who had a pre-shift urinary BCIPHIPP at the highest levels we measured (703.2 ng/mL).

Concentrations of the three other urinary biomarkers did not change significantly pre-and post-shift as presented in Fig. 3 (for DPHP, $p = 0.23$; BCIDPP, $p = 0.54$ and for ip-DPHP, $p = 0.92$). The only exception was the urinary DPHP adjusted for creatinine, for which $p = 0.04$ (Table S2). These three biomarkers correspond to other plasticizers and flame retardants that were not used on the monitored SPF sites in this study based on the SDS information; however, we can't rule out the possibility that they received exposure from close contact with other construction materials at these sites.

At the SPF removal site, we collected only post-shift urine samples from the two workers. At the day of sampling one of the workers performed foam removal while the other was helping with small tasks such as tool and area cleaning. The second worker was currently living at the residence and had been participating in the SPF foam removal for several days prior. Notably, he was on a several months break from working as a SPF sprayer due to health concerns. The worker performing the foam removal had the lowest post-shift BCIPHIPP values we measured (5.2 ng/mL, normalized to SG). The owner had a higher post-shift BCIPHIPP concentration, 22.9 ng/mL normalized to SG. The post-shift urinary BCIPP levels (normalized to SG) for this crew were also among the lowest we measured. In addition, only post-shift urine samples were collected from two administrative workers at the training site. These workers had detectable levels of TCIPP and all other FR biomarkers in their urine. The average urinary BCIPP and BCIPHIPP for the managers were 2.7 and 61.9 ng/mL, respectively.

3.4. Air and dermal exposure association with urinary biomarkers

It is important to note that all other workers at the SPF insulation sites were wearing industry standard PPEs, including purified supplied

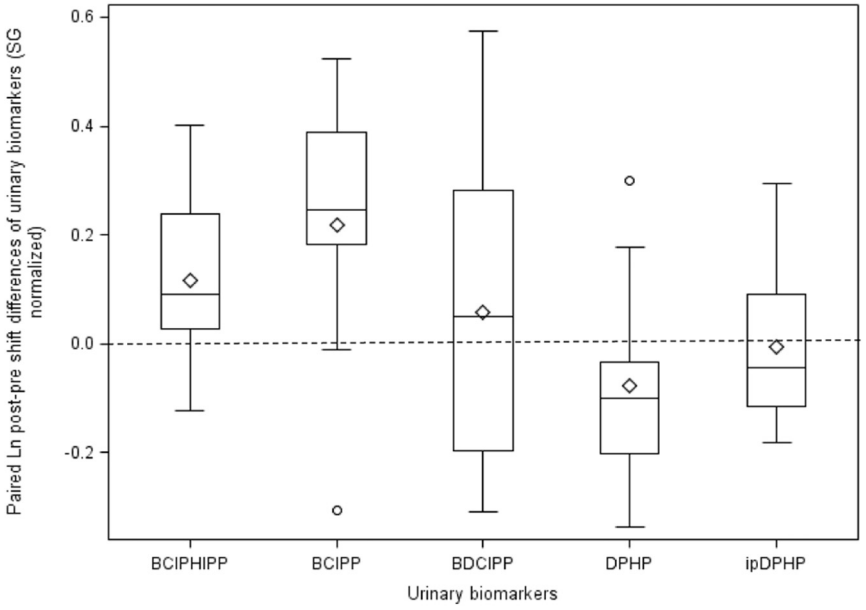

Fig. 3. Distribution of intra-individual differences (post-shift – pre-shift) for all urinary biomarkers measured in this study.

air respirators, full coverall, and nitrile gloves, which raises questions about why their urinary FR values were so high. What exposure pathways are influencing these high FR biomarker values and how? In order to investigate this question, we utilized linear mixed models with urinary data as the outcome variable and air and glove data as the independent variable. Glove contamination was a significant predictor (p value < 0.05) of both urinary TCIPP biomarkers (Table 4). Post-shift urinary BCIPHIPP levels increased with the increase of TCIPP load on gloves while air exposures did not predict post-shift BCIPHIPP (p value, 0.12) and BCIPP (p value, 0.29) levels. This finding may reflect the fact that all SPF workers wore supplied air respirators. However, it may also reflect limited study power to detect small differences.

Table 4
Association of post shift TCIPP biomarkers with air and glove TCIPP levels.

Biomarkers Normalized to SG	Variable (β)	Parameter estimate	Pr. > t	95% Confidence limits	
Post-BCIPHIPP	Intercept	10.2	< 0.01	3.69	16.75
	Air TCIPP[a]	−0.73	0.12	−1.68	0.23
	Glove TCIPP[b]	1.01	< 0.05	0.01	2.01
Post-BCIPP	Intercept	5.74	0.05	−0.11	11.60
	Air TCIPP	−0.41	0.29	−1.27	0.43
	Glove TCIPP	0.89	< 0.05	0.01	1.77

[a] Air concentrations of TCIPP (μg/m^3).
[b] Amount of TCIPP accumulated in workers' gloves (mg/pair/min).

4. Discussion

In this study, we characterized exposures to the flame retardant TCIPP among construction workers performing SPF insulation utilizing simultaneous personal inhalation and dermal exposure assessment, and urinary biomonitoring pre- and post-shift. We document high potential for inhalation and dermal exposure to TCIPP, as well as high levels of urinary BCIPHIPP and BCIPP, the two main urinary biomarkers of TCIPP. Urinary TCIPP biomarker levels increased during the work shift for 8 of the 10 insulation workers, even though they workers wore supplied air respirators, gloves and coveralls. Post-shift urinary TCIPP biomarker levels were strongly associated with glove TCIPP levels, suggesting that dermal exposure may be the primary exposure pathway

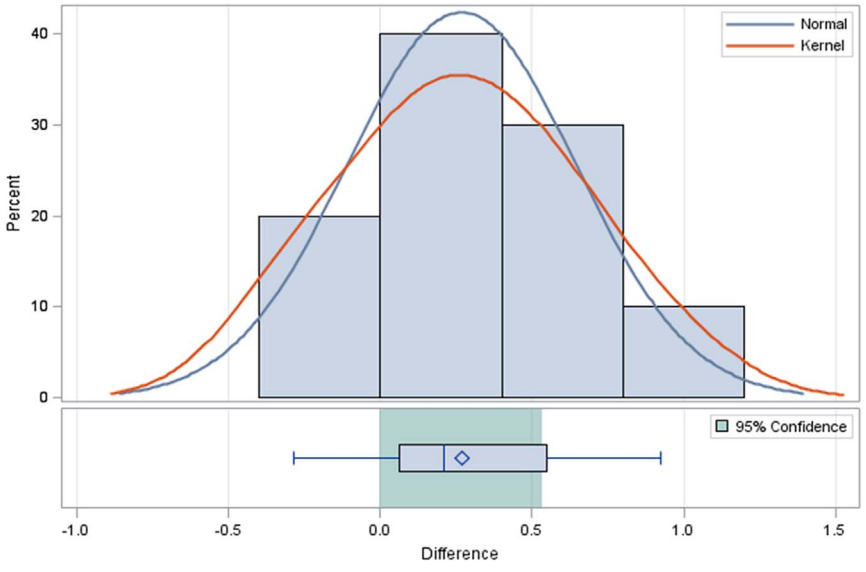

Fig. 4. Distribution of the ln [(post-pre shift) BCIPHIPP concentration (normalized to specific gravity)] has a mean greater than zero. The outcome was the same for the second urinary biomarker of TCIPP (aka BCIPP).

for TCIPP.

Air concentrations we present here are the highest reported in the literature to date. Results indicate elevated exposures to TCIPP among insulation workers during SPF installation. Occupational exposure data related to TCIPP levels among SPF applicators are limited in the literature. A recent survey conducted by National Institute of Occupational Safety and Health (NIOSH) reports TCIPP exposures from area samples collected during SPF application inside a building. Area samples were collected 10–50 ft away from the sprayers using XAD-2 OVS tubes and measured TCIPP exposures at 4.6–12.5 μg/m^3. XAD-2 tubes are designed to collect primarily TCIPP in the gas phase (e.g. not associated with particles/aerosols). Results of our study indicate about 8- fold higher TCIPP levels compared to the NIOSH survey data. These differences could be due to the different sampling approaches used (personal vs. area sampling), as well as sampling methods (CIP-10MI vs. sorbent tubes), which collect aerosols and the gas phase, respectively. There are no occupational standards related to TCIPP exposures in the workplace. Makinen et al. (2009) report TCIPP levels in a number of workplaces that included a furniture workshop, a circuit board factory, and electronic dismantling facilities. Concentrations of TCIPP in personal samples ranged from 7 to 510 ng/m^3 and the highest concentration was measured in the electronic dismantling facilities (Makinen et al., 2009). In comparison, concentrations of TCIPP we measured during SPF applications and remediation are in the mg/m^3 range, suggesting that insulation workers have substantially higher TCIPP exposures compared to workers in other occupations.

Concentrations of TCIPP in our air samples are in mg/m^3 range compared to the μg/m^3 levels measured in indoor air by numerous environmental studies. TCIPP is one of the most predominant PFRs detected in indoor air, and is likely generated from a number of sources including textiles, leather, electronics, as well as numerous polyurethane foam articles at homes (coaches, sofas, rugs, etc.)(Van der Veen and de Boer, 2012). Schreder et al. (2016) found that TCIPP levels in personal inhalable and respirable dust among white collar workers had a maximum of 1.19 μg/m^3, the highest of all chlorinated PFRs measured as part of that study (Schreder et al., 2016). La Guardia and Hale (2015) also reported elevated TCIPP concentrations of 1.36 μg/m^3 from aerosol dust samples collected in houses and gym facilities in the US (La Guardia and Hale, 2015). The highest median TCIPP concentrations in living rooms reported by a study in Norway was 42.3 ng/m^3 (Cequier et al., 2014). Indoor air TCIPP concentrations in office environments in Sweden (mean of 110 ng/m^3) were higher than in day cares and homes included in the study (Bergh et al., 2011). Similarity, TCIPP levels in indoor air in the ng/m^3 range, have been reported by Carlsson et al. (1997) from samples collected in office buildings (Carlsson et al., 1997). While gas phase TCIPP levels are present in the indoor air after spraying, SPF overspray aerosol may remain airborne in the indoor environment for long periods of time after SPF application. By monitoring the airborne particle number concentration during and after spraying, we have observed that high aerosols particle number concentration can continue for several hours post-spraying. Therefore, further research is needed to determine the potential for consumer exposures during and post spraying of SPF, as well as for sprayers and helpers who may inhale considerable amounts of this overspray aerosol when they remove the respirator immediately after the spraying is over, as is common practice.

Understanding factors that influence differences in (airborne and dermal) exposures and urinary biomarkers between sprayers and helpers, product formulation (e.g., foam types), and environmental conditions is of interest from an exposure reduction standpoint. Due to the modest sample size we had limited statistical power to detect statistically significant differences in airborne exposures for sprayers and helpers, as well as between products used and activities performed (see Supplemental material). The highest airborne levels were expected at site A given that the product used there had the highest % by weight of TCIPP according to the SDS data (30–60%). However, exposures were the highest at site C, which, according to the SDS, contained 30–50% by weight of another FR, 2,2,4-Trimethyl-1,3-pentanediolmono (2-methylpropanoate). Data in Table 1 indicate that FR are often listed as 'trade secret' and point to the need for chemical analysis of the bulk product to determine its composition. This was not done in the present study and we acknowledge this as a study limitation.

The TCIPP content in the aerosol generated during foam removal/trimming with a powered brush was the highest we measured. This process generates visible clouds of airborne dust that could potentially remain in the indoor environment for long periods. The magnitude of exposures for workers performing these foam removal tasks and of homeowners is not known. The high TCIPP levels we measured in this one case, warrants further investigations and exposure characterization.

Results from the glove dosimeters points to high potential for dermal exposure during SPF insulation tasks. Sprayers had higher levels compared to the helpers working at the same site, mostly due to their direct contact with the aerosols and spray gun cleaning procedures during spraying. Workplace observations revealed that several times during their shift the workers had to stop spraying to clean the clogged spraying gun, an activity that be a major source for dermal exposure due to the potential for direct contact with the liquid part B material. The lowest accumulation in the gloves was measured at site D during training for roofing application, where workers were not directly involved with product preparation and spray gun cleaning during the 20 min or so duration of training. Makinen et al. (2009) measured quantitatively dermal exposures by using dermal patches on worker's chest, arms and thighs and used hand washing to determine hand exposures. The highest TCIPP levels of 1.3 ng/cm^2 were measured in the chest of a worker at the electronics dismantling facility and hand exposures of < 4 ng TCIPP/hands were the highest among workers at the circuit board factory. Although not directly comparable due to different sampling times, the highest levels of TCIPP in our gloves samples (182.2 mg/pair) is several orders of magnitude higher than the nanogram levels reported for occupations studied by Makinen et al., 2009.

Concentrations of both TCIPP urinary biomarkers among insulation workers we report here are the highest reported to date. The mean urinary BCIPHIPP levels (GM 88.8 ng/mL) are close to fifty times higher than urinary levels found in the general Australian population (GM 1.86 ng/mL) (Van den Eede et al., 2015). The maximum value we measured in this study (703.2 ng/mL) is 378 times higher than the highest level reported by the same study of 9.43 ng/mL (Van den Eede et al., 2015). Similarity, Butt et al. (2016) reports much lower levels of BCIPHIPP in the urine of mothers and children (GM 3.4 ng/mL) compared to our results (Butt et al., 2016) (Fig. 5 & Table S3 in the supplemental material). Furthermore, urinary BCIPP levels among SPF workers found in our study (GM 6.2 ng/mL) are the highest reported in the literature. Much lower BCIPP levels have been reported in the urine

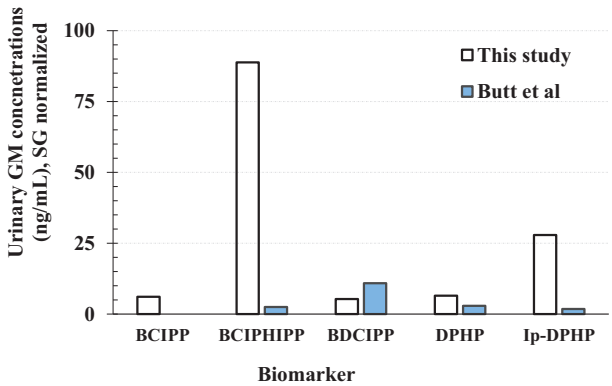

Fig. 5. Comparison of geometric mean (GM) values of several urinary flame retardant biomarkers in spray polyurethane foam applicators compared to the general population reported in Butt et al., 2016. GM data have been normalized to specific gravity (SG).

samples of infants, GM 0.02 ng/mL (max = 7.5 ng/mL). A number of studies focused on exposures in the general population indicate very low detection frequency for BCIPP when monitoring TCIPP exposures (Butt et al., 2016; Schindler et al., 2009).

Our biomonitoring results suggest that BCIPHIPP is a preferred biomarker of TCIPP exposures as it was detected at concentrations 14.3 times higher than that of BCIPP (when expressed as the GM ratio). Their concentrations were highly correlated for both pre- and post-shift samples (correlation coefficients 0.84 and 0.97, respectively). This is expected, considering that they are derived from the same parent compound. Van den Eede et al. (2015) reported greater abundance of BCIPHIPP (Van den Eede et al., 2015). While most studies detect BCIPP in very low frequencies, we detected it in all urine samples likely due to the high dermal and inhalation exposures among insulation workers in our study. As both BCIPHIPP and BCIPP were significantly associated with concentrations of TCIPP in glove dosimeters, it appears that BCIPP is as useful as BCIPHPP for monitoring exposures to TCIPP in occupational settings, however less sensitive in scenarios with lower TCIPP exposures.

Our findings indicate that TCIPP exposure is occurring during the work-shift. As previously noted, all workers in insulation sites were wearing industry standard PPEs, including purified supplied air respirators, full coverall, and gloves. Despite the use of PPE, the higher post-shift exposures compared to pre-shift for both urinary TCIPP biomarkers indicate uptake in the body during the work shift. The exact toxicokinetics of TCIPP in humans are not known, but limited data in animals suggest a short half-life ($t_{1/2}$ = 24 h) (Van den Eede et al., 2015). This implies that exposure from previous days are carried over to the next day and explains high urinary TCIPP biomarker values in pre-shift samples of chronically exposed workers. Collection of pre- and post-shift urine samples enabled us to investigate any active TCIPP uptake during the shift (post-pre). In the absence of any active TCIPP uptake during the shift, clearance kinetics would suggest lower post-TCIPP urinary biomarker values, which was the case for two subjects with low exposures. Follow-up studies to assess toxicokinetics of TCIPP (i.e. uptake and clearance) in humans are warranted.

The multilevel statistical analyses performed to test the association of urinary biomarkers with personal airborne and potential dermal exposures clearly indicate that TCIPP in gloves is a significant predictor of both TCIPP biomarkers, suggesting that dermal exposure could be an important exposure pathway. A recent study by Xu et al. (2016) investigated human exposure to TCIPP in indoor environments in a cohort of adults in Norway and found that indoors inhalation is the major exposure pathway. Exposures were estimated based on personal and stationary air sampling, hand wipes and surface dust. Our study differs from that of Xu et al. (2016) in several important ways, including presence of an active exposure source (SPF spraying), use of extensive PPEs (supplies air, gloves, coveralls, etc.) and much higher exposure levels in occupational settings. Exposure biomarker data are considered better estimates of the overall body burden to a chemical than external exposure/estimates.

The other three PFR urinary biomarkers (BDCIPP, DPHP and ip-DPHP) normalized to SG were not elevated post shift. These are biomarkers of plasticizers and flame retardants that are used less frequently, if at all, in SPF insulation products. Not having exposure monitoring data for the other PFR candidates restricts our ability to comment on the relationships between these other PFRs, their urinary biomarkers, and exposure pathways. The elevated urinary biomarker data in SPF workers indicates likely occupational exposure to other FR besides TCIPP, and future studies should aim at quantifying exposures to these other PFR in a similar fashion.

Of note, glove dosimeter data provide an index of potential for dermal exposure. There are no published data on the permeability of TCIPP and other PFR through worker gloves and garments during realistic SPF applications. Ongoing work in our lab indicates limited permeability of TCIPP through nitrile gloves and coveralls. A second consideration relates to the whole body exposures due to SPF overspray and contact with the SPF foam. Using whole body dosimetry in combination with an observational semi quantitative dermal exposures assessment techniques (DREAM), we have documented similar loads to hands for other anatomical regions of the body (data analysis in progress). High SPF loads can translate to significant whole body TCIPP exposures over the course of the work shift even with negligible TCIPP permeability through garments. This may be related to opportunities for direct skin contact when sprayers/helpers inspect foam quality and remove SPF waste (which is considered non-hazardous), during gun cleaning and other intermittent tasks. These are likely important dermal exposure and uptake pathways that are being reflected in the strong association between glove dosimeter data and urinary TCIPP levels. Additional work is needed to determine the degree of TCIPP permeation for different types of gloves and garments, as well as to assess the relative contribution of accidental exposures and the hand-to-mouth exposure pathways, especially as relates to smoking and lunch breaks.

5. Conclusions

High levels of post-shift urinary biomarkers for TCIPP among SPF applicators points to absorption of TCIPP during the work shift. Dermal exposure may be an important, if not the primary exposure pathway for TCIPP, although inhalation of re-suspended foam particles post-SPF application and possibly hand-to-mouth pathways, cannot be ruled out. It should be noted that this group of SPF workers studied here represents the ‘best industry practices’ as far as SPF application is concerned. It would be of great interest to compare these data to the SPF workers who rely on less stringent exposure control practices.

Conflict of interest statement

The authors of this work have no conflict of interest to declare

Acknowledgments

We would like to thank the SPF workers and management for their participation in and support of this study, as well as our graduate students who assisted with field data collection and sample preparation. This investigation was made possible by Grant U60-OH009762-06 and Grant No. T42 OH008416 from the National Institute for Occupational Safety and Health (NIOSH). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIOSH. The authors have no competing financial interests to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2018.01.020.

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