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

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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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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 $> 200\ ^{\circ}C$ 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-