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Skin Exposure to Aliphatic Polyisocyanates in the Auto Body Repair and Refinishing Industry: II. A Quantitative Assessment

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Background: Skin exposure to isocyanates, in addition to respiratory exposures, may contribute to sensitization and asthma. Quantitative skin exposure data are scarce and quantitative methods limited. Methods: As part of the Survey of Painters and Repairers of Autobodies by Yale study, a method to sample and quantify human isocyanate skin exposure was developed (based on NIOSH 5525 method) and used to evaluate aliphatic isocyanate skin exposure in 81 auto body shop painters and body technicians. Wipe samples were collected from unprotected skin and from under PPE (gloves, clothing and respirator) using a polypropylene glycol-impregnated wipe. Hexamethylene diisocyanate (HDI), its polyisocyanates [HDI-derived polyisocyanates (pHDI)], isophorone diisocyanate (IPDI) and its polyisocyanates and IPDI-derived polyisocyanates (pIPDI) were quantified separately and also expressed as the total free isocyanate groups (total NCO). Results: For unprotected skin areas, 49 samples were collected for spray painting, 13 for mixing, 27 for paint-related tasks (e.g. sanding and compounding) and 53 for non-paint-related tasks. Forty-three samples were also collected under PPE. The geometric mean (GM) [geometric standard deviation (GSD)] total NCO concentrations (ng NCO cm^{-2}) for unprotected skin (hands, face and forearms) was 1.9 (10.9) and range 0.0–64.4. pHDI species were the major contributor to the total NCO content. Levels were very variable, with the highest concentrations measured for clear coating and paint mixing tasks. Isocyanate skin exposure was also commonly detected under PPE, with 92% of samples above the limit of detection. Levels were very variable with the overall GM (GSD) total NCO (ng NCO cm^{-2}) under PPE 1.0 (5.2) and range (0.0–47.0) and similar under the different PPE (glove, respirator and clothing). The highest concentrations were detected for mixing and spraying tasks, 6.9 (5.3) and 1.0 (5.2), respectively. Levels under PPE were generally lower than unpaired samples obtained with no PPE, but not statistically significant. Total isocyanate GM load on exposed skin and under PPE was commonly 100–300 ng NCO per sample, except for higher levels on exposed forearms during spraying (GM 5.9 μg NCO). Conclusions: A quantitative method was developed for skin sampling of isocyanates. Using this method, the study demonstrates that skin exposure to aliphatic polyisocyanates during painting, mixing and paint-related tasks in auto body shop workers is common and also commonly detected under routine PPE.

Keywords: auto body refinishing; dermal exposure assessment; gloves; isocyanates; PPE; skin exposure; SPRAY

INTRODUCTION

Isocyanates are important reactive chemicals in the polyurethane industry and a leading cause of

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occupational asthma in industrialized countries (Di Stefano *et al.*, 2004; Wisnewski *et al.*, 2006; Redlich *et al.*, 2007). Although inhalation exposure has been considered the primary route of isocyanate sensitization in exposed workers, concerns recently have been raised about the role of skin exposure in isocyanate sensitization and subsequently asthma (Bello *et al.*, 2007a). Isocyanate skin exposure can also cause allergic contact dermatitis and skin irritation (Goossens *et al.*, 2002; Redlich *et al.*, 2007).

The SPRAY (Survey of Painters and Repairers of Autobody by Yale) study, a cross-sectional epidemiologic study of isocyanate asthma in auto body shops, in collaboration with researchers at University of Massachusetts Lowell, MA, USA, initially focused on respiratory isocyanate exposures (Redlich *et al.*, 2001; Sparer *et al.*, 2004; Woskie *et al.*, 2004). Noting clear opportunities for isocyanate skin exposure in the auto body shops, yet a lack of information on such exposures, including a lack of standardized methods to assess such exposures, SPRAY was expanded to explore qualitative and quantitative skin exposure assessment methodologies (Liu *et al.*, 2007; Bello *et al.*, 2007b).

This paper describes the method developed to measure human isocyanate skin exposure and reports quantitative data using the method on exposed skin and under Personal Protective Equipment (PPE) in auto body workers. An earlier paper (Liu *et al.*, 2007) reports on evaluation of a qualitative tool, SWYPE™, and its use for skin and surface contamination assessment.

METHODS

Subject and task selection

The skin exposure assessment supplemented the ongoing SPRAY study. Work processes, study design, study population and sampled tasks are described in previous publications (Redlich *et al.*, 2001; Sparer *et al.*, 2004; Woskie *et al.*, 2004; Liu *et al.*, 2007). A subset of 22 consecutive shops from the 35 SPRAY shops were targeted for isocyanate skin exposure sampling and quantitative analysis. Sampling was focused on tasks and workers with potential for skin exposure, resulting from direct deposition of overspray aerosol and/or direct contact with paints and contaminated surfaces. Tasks included paint mixing and the spray application of primer, sealer and clear coat layers.

All workers (81 painters or body technicians) who painted or primed with an isocyanate containing paint during the survey week were selected for sampling. As previously reported, multiple different aliphatic isocyanate paints [primarily polyisocyanates of hexamethylene diisocyanate (HDI) and isophorone diisocyanate (IPDI, pHDI and pIPDI, respectively)] were used in the shops, with $<1\%$ monomeric HDI (Woskie *et al.*, 2004). Non-spray tasks, such as wet sanding of primer, untaping and compounding, which can expose hands to recently painted surfaces were also sampled, referred to as 'paint-related tasks'. Additionally, tasks that did not involve direct contact with recently painted surfaces were also evaluated, such as mechanical work, body filling and office work, referred to as 'non-paint-related tasks'. In general, if the worker was wearing PPE, samples were taken under the PPE; if the worker was not wearing PPE, exposed skin was sampled. Sample information collected included: task type (e.g. spraying and mixing), location and duration, wiped skin area and location and type of PPE.

The study protocol was approved by the Human Investigation Committee at Yale University. Informed written consent was obtained from each participant.

Skin wipe sampling

Prior to beginning the task to be sampled, the worker was asked to wash his hands and forearms with shop cleaners which effectively remove isocyanates (Bello *et al.*, 2005), but they did not routinely wash their faces. The investigator, who was wearing a clean pair of nitrile gloves during sampling, wiped the skin area (described below) immediately (within 1–2 min) after the worker completed a task. A single wipe pad was used to wipe each skin area using a standard protocol and performed by the same investigator. The wipe pad (5×5 cm) was impregnated lightly by the supplier (CLI, Des Plains, IL, USA) with polypropylene glycol (PPG) to improve recovery of unbound isocyanates from the skin surface (Wester *et al.*, 1999; Bello *et al.*, 2005).

The following exposed skin areas were sampled with the wipe pad and the skin area that was sampled measured: both sides of the dominant hand or the unprotected forearm and the exposed areas of the forehead outside head covering. For unexposed face or neck outside the respirator, a standard area (5×5 cm) was wiped as these body areas were less well defined.

To sample skin under PPE (gloves or respirator), both sides of a hand under gloves and the face area covered by the respirator were wiped and the area measured. For the three samples taken under protective clothing, the wipe pad was pinned to clothing underneath to assess breakthrough.

All sampling pads were transferred immediately post-sampling in the field into a scintillation vial containing 10 ml 2.5×10^{-4} M 1-(9-anthracenylmethyl) piperazine (MAP) derivatizing reagent in methylene chloride for extraction and derivatization. The vials were shipped in cooled containers to the laboratory for analysis.

Analytical method

Quantitative analysis of skin wipes was based on the method of Bello *et al.* (2002) for total aliphatic

polyisocyanates in air, a modification of the NIOSH 5525 method (NIOSH, 2003). Advantages of this modified NIOSH 5525 method (including an improved reagent and a greater sensitivity and specificity for various polyisocyanate species) and an evaluation of its performance for aliphatic polyisocyanates are previously described (Bello *et al.*, 2002). Additional modifications to Bello *et al.* (2002) protocol to facilitate analysis of skin wipe samples included addition of a sample cleanup step for wipes and a simpler pH gradient (described below). This method was also the basis of quantitative data reported in Bello *et al.* (2007b) and Liu *et al.* (2007).

Skin wipe samples were cleaned up through solid phase extraction (SPE) on a LC-Si Supelclean™ 6 ml (0.5 g) cartridge (Supelco, Bellefonte, PA, USA). The sample in methylene chloride was loaded into the SPE cartridge followed by a washing step with 5 ml 20/80 v/v acetonitrile/methylene chloride before elution. This step was optimized based on a separate breakthrough study (details omitted), which found that MAP derivatives of polymeric isophorone diisocyanate (IPDI) species (pIPDI) started eluting from the SPE cartridge at >30% v/v acetonitrile/methylene chloride (6 ml), whereas pHDI species did not elute even with 90% acetonitrile. The sample was eluted with 3 ml 90/10 acetonitrile/methanol followed by 3 ml methanol. After elution, evaporation under N_2 and reconstitution with acetonitrile to 1 ml, the samples were acetylated with 5 µl acetic anhydride and stored overnight in the dark prior to chromatographic analysis.

The modified gradient for the high performance liquid chromatography (HPLC) analysis, which preserved the same resolution as the longer gradient, varied as follows: from 0% B for the first 2 min, to 30% B from 2 to 6 min, to 55% B at 22 min, to 100% B at 28 min and held at 100% B until 34 min, followed by 5 min of post-column equilibration.

HDI, HDI polyisocyanate (pHDI) and IPDI polymers (pIPDI) were quantified separately and added together as the total reactive isocyanate groups (total NCO), as previously described (Bello *et al.*, 2002). Advantages of the total NCO metric have been discussed previously (Bello *et al.*, 2004) and include its unambiguous meaning and its ability to express mixed polymeric isocyanate species as a single unit, which facilitate comparison between studies.

Since it is unclear whether the mass (load) on the skin or concentration is a better metric for isocyanate skin exposure, results were reported in both units: surface concentration (ng total NCO cm^{-2}) and mass (µg total NCO per sample).

Statistical analysis

Data were analyzed with SAS® (Statistical Analysis Software, Version 8.12, SAS Institute, Cary, NC, USA). Since the data obtained better fit a lognormal distribution, the geometric mean (GM) and geometric standard deviation (GSD) were used to characterize data distribution. Values at or below the limit of detection (LOD) were substituted with 1/2 LOD. Analysis of variance was used to compare skin exposure levels among different body parts, tasks and PPE types. However, large GSD values, small sample sizes and samples below LOD limited statistical analyses.

RESULTS

Analytical method performance

Detailed evaluation of the modified NIOSH 5525 method performance for aliphatic polyisocyanate species in air, such as those found in the auto body repair and refinishing industry, has been published in Bello *et al.* (2002). Provided here is the information relevant to the skin samples methodology. The method detection limit (LOD) for skin wipes was similar to air samples; ~5 ng NCO per sample (3 pmol injected) for each species (HDI and IPDI monomers and the main HDI biuret, HDI isocyanurate and IPDI isocyanurate peaks). The ultraviolet detector response of MAP-isocyanate derivatives is practically independent of the isocyanate species. The IPDI monomer could not be measured in the presence of HDI polyisocyanates due to its co-elution with HDI-derived species, but IPDI is a minor component of such paints (<1% of total IPDI-based NCO group). The calibration curves over a range of standard concentrations (10 ng to 21.4 µg NCO per sample) were linear with $R^2 > 0.995$. The relative standard deviation of each regression coefficient β (standard deviation of β/mean of β) over 5 years has been ~5%. The recovery of isocyanate species from spikes on wipes, followed by extraction in methylene chloride, has been reproducible and quantitative (data omitted), with a mean of 100 ± 5% for the HDI monomer, 90 ± 10% for HDI-derived polyisocyanate species and 80 ± 10% for IPDI-derived polyisocyanate species over a wide range of concentrations (~10 ng to 20 µg NCO per sample).

Exposure of unprotected skin

A total of 49 samples were collected from exposed skin immediately after spray painting, with over 85% of samples having a total NCO above LOD (Table 1). The highest average skin exposure levels of total NCO (ng cm^{-2}: GM and GSD) were measured for forearms (8.7 and 1.9) with lower similar levels noted for face (2.0 and 10.0) and hands (1.4 and 14.3). However, only three forearm samples were collected, and differences did not reach statistical significance. Notable are the large GSD values (>10) for hand and face distributions; the maximum measured values

Table 1. Skin exposure to aliphatic isocyanate species (ng NCO cm^{-2}) on different body parts during spraying without PPE

Spray painting (without PPE)	*n*	pHDI			pIPDI			HDI monomer			Total NCO				
		GM	GSD	% ≤LOD	GM	GSD	% ≤LOD	GM	GSD	% ≤LOD	GM	GSD	% ≤LOD	Range	GM load (ng NCO per sample)
Forearm	3	7.8	1.7	0	0.05	48.4	67	0.22	1.2	0	8.7	1.9	0	5.5–18.3	5933.1
Hand	18	1.1	17.3	22	0.2	13.6	46	0.05	7.7	56	1.4	14.3	28	0.0–34.5	300.1
Face	28	1.2	14.7	21	0.3	10.1	41	0.05	4.6	71	2.0	10.0	7	0.0–64.4	188.1
Total	49	1.3	14.6	20	0.2	12.6	45	0.05	5.5	61	1.9	10.9	14	0.0–64.4	275.8

Total NCO, total reactive isocyanate group content of the sample.

were 18.3 (ng NCO cm^{-2}) for forearm, 34.5 for hand and 64.4 for face. The GM total NCO load (in ng NCO per sample) was also highest for forearm samples (5933 ng NCO per sample) compared to hands and face, which were similar (300.1 for hands and 188.1 for face).

As expected, polymeric HDI species were the main contributor of the total NCO content and the smallest number of non-detectable samples (∼20%). The GM concentrations of pHDI (1.1–7.8 μg NCO cm^{-2}) were more than four times higher than for pIPDI (0.05–0.3 μg NCO cm^{-2}). The HDI monomer contributed ≤1% of the total NCO groups, which is consistent with its content in the bulk product.

Isocyanate contamination of unprotected skin during various tasks is summarized in Table 2, demonstrating skin contamination during most spraying, mixing and paint-related tasks. A large number of different tasks and paint products were sampled, limiting the number of samples obtained for each task. The number of samples below the LOD varied by task, with skin samples for mixing and compounding being all above LOD, spraying 10–29% ≤LOD and for other tasks 20–50% ≤LOD. The large GSD values for most tasks and small sample sizes limited statistical analyses. However, several findings are notable. The overall GM (GSD) isocyanate skin values were highest for spray painting and paint mixing tasks [1.9 (10.9) and 1.7 (8.4) ng NCO cm^{-2}, respectively]. The highest GM (GSD) was for mixing primer [5.2 (31.5)], but only three samples were obtained for this task. The maximum measured values were as high as 64.4 ng NCO cm^{-2} for spraying sealer and 59.8 for mixing primer.

Of note, isocyanate skin exposure was also common with paint-related tasks that did not involve spraying or mixing, but involved hand exposure to recently applied paint, such as compounding, untaping and wet sanding of primer, tasks typically not performed with PPE. Skin exposure levels for these paint-related tasks were in the range of 0.2–0.8 ng NCO cm^{-2}, with the highest exposure measured during wet sanding (67.3 ng NCO cm^{-2}). Non-paint-related tasks, such as taping, body filling, mechanical work and office work, had the lowest isocyanate skin exposures.

Skin exposure under PPE

Isocyanate skin exposure data under PPE during paint spraying, stratified by PPE type, are summarized in Table 3. A total of 40 samples were collected, 20 of which were from under respirators, 17 from under gloves and only 3 samples from under clothing. Workers used their regular PPE, most commonly latex gloves (88%), and negative pressure half face-piece cartridge respirators (100%). The GM total NCO under all PPE was ∼1.0 ng NCO cm^{-2} (GSD of 3–6), with similar GM total NCO skin exposure levels under the different types of PPE. Several

Table 2. Skin exposure to aliphatic isocyanate species (ng total NCO cm^{-2}) by task without PPE

Task	*n*	GM	GSD	% ≤LOD	Range	GM load (ng NCO per sample)
Spraying						
Primer	7	0.8	15.5	29	0–27.6	133.7
Sealer	10	1.9	11.6	10	0–64.4	239.5
Clear[a]	32	2.3	10.2	13	0–50.7	337.8
Total	49	1.9	10.9	14	0–64.4	275.8
Mixing						
Primer	3	5.2	31.5	0	0.1–59.8	840.5
Sealer	6	0.9	4.6	0	0.2–7.1	241.4
Clear	4	1.7	8.1	0	0.1–14.4	323.6
Total	13	1.7	8.4	0	0.1–59.8	352.4
Paint related						
Compounding	3	0.5	10.5	0	0–2.8	68.0
Untaping	10	0.6	9.5	20	0–6.7	120.8
Dry sanding	4	0.2	7.4	50	0–2.4	45.5
Wet sanding	10	0.8	10.8	20	0–67.3	170.6
Non-paint-related[b]	53	0.1	4.8	32	0–7.6	16.6

Total NCO, total reactive isocyanate group content of the sample.
[a]Includes hand, forearm and face samples; all other categories include only hand samples.
[b]Non-paint-related tasks include cleaning, taping, body filling, mechanical work, cutting/welding, office and supervising.

findings are notable. For one, over 90% of skin samples taken from under PPE were above the LOD. The maximum value of 47.0 ng NCO cm^{-2} was collected under a respirator. The overall GM total NCO levels under PPE (1.0 ng NCO cm^{-2}) were generally lower than samples collected without PPE (1.9 NCO cm^{-2}; Table 1), but the differences were not large. Findings were similar when expressed as GM total NCO loads.

Isocyanate skin exposures under PPE, stratified by task for spraying (40 samples) and mixing (3 samples), are shown in Table 4. Samples were taken under gloves for all tasks except for spraying clear coat, which also included 20 samples under respirator and 3 samples under clothing. The small number of painting tasks sampled with primer and sealer (three each) make any comparisons difficult. However, the lowest isocyanate skin exposures under PPE were detected for painting tasks using primer coating, GM 0.2 ng NCO cm^{-2} (GSD 10.0).

The overall GM (GSD) exposure under PPE after mixing was 6.9 (5.3) ng NCO cm^{-2}, higher than for overall spray painting [1.0 (5.2)], but only three skin samples were obtained under PPE for mixing. The skin sample for mixing primer was one of the highest, with 32.4 ng NCO cm^{-2}. The GM total NCO loads for spraying and mixing tasks under PPE (Table 4) overall showed similar findings to levels expressed as concentration.

DISCUSSION

Methods for isocyanate skin sampling and quantitative analysis are limited. This article describes a method developed to quantify isocyanate skin exposures, especially polyisocyanates, based on quantitative analysis of sampling wipes, and application of this method in the SPRAY study. NIOSH 5525 method, previously modified by us to optimize air sampling of aliphatic polyisocyanates (Bello *et al.*, 2002), was further modified to enable analysis of skin samples.

The method showed good recovery of analytes, particularly the more difficult to analyze polyisocyanate species from the wipes, and identified and quantified various isocyanate types, HDI monomer and HDI- and IPDI-based polyisocyanates, in a single sample. The LOD for different isocyanate species on skin samples was nearly identical to air samples, largely due to the good resolution achieved with the pH gradient. The quantitative method is >100 times more sensitive than qualitative wipes (Liu *et al.*, 2007). This modified NIOSH 5525 method can also be used to analyze skin samples collected using alternate protocols such as tape strips with minor additional modifications. However, the quantitative skin methodology requires time-intensive-specialized laboratory analysis that limits the amount of sampling possible. Another limitation is that the removal efficiency of isocyanates from human skin is unknown and difficult to evaluate in humans due to ethical and logistic reasons. Our prior testing on non-porous aluminum foil indicated that with PPG, one wipe removed 70–80% of isocyanates (Bello *et al.*, 2005).

This methodology was used to quantitate isocyanate skin exposures in auto body shop spray painters

Table 3. Skin exposure to aliphatic isocyanate species (ng NCO cm^{-2}) on different body parts under PPE during spray painting

PPE type	*n*	pHDI			pIPDI			HDI			Total NCO				
		GM	GSD	% ≤LOD	GM	GSD	% ≤LOD	GM	GSD	% ≤LOD	GM	GSD	% ≤LOD	Range	GM load (ng NCO per sample)
Clothing/suit	3	0.2	24.5	33	0.6	2.9	0	0.03	8.1	67	1.0	3.2	0	0.3–2.4	155.7
Glove	17	0.7	5.6	6	0.3	5.9	11	0.02	2.6	76	1.0	5.2	6	0.0–12.2	150.8
Respirator	20	0.6	8.3	20	0.5	4.2	10	0.03	3.2	70	1.1	6.0	10	0.1–47.0	102.4
Total	40	0.6	7.5	15	0.4	4.5	8	0.04	3.2	73	1.0	5.2	8	0.0–47.0	124.6

Total NCO, total reactive isocyanate group content of the sample.

and body technicians. Isocyanate skin exposure was commonly found following a number of different tasks, including mixing and spraying aliphatic isocyanate paints. Less expected was the finding that isocyanate skin exposure was also common with paint-related tasks involving recently applied dried paints, such as wet sanding or compounding, tasks routinely performed without PPE. These data are consistent with our recent finding that full curing of painted car parts can take up to several days, with free isocyanate species present on dried but not fully cured surfaces (Bello *et al.*, 2007b).

A key finding is the extent of isocyanate skin exposure detected under PPE (primarily latex gloves and cartridge respirators). Although comparison of the skin exposure data with and without PPE should be interpreted with caution since the samples were not paired, the extent and frequency of isocyanate skin exposure detected under all PPE types are notable. These findings do not appear to be due to regular cross-contamination of skin. Workers washed hands before the task (as did the investigator prior to sampling), new latex gloves were used for all tasks and the cartridge respirators had been fit tested, as previously reported (Liu *et al.*, 2006, 2007). However, some skin contamination while removing PPE, such as cartridge respirator, cannot be ruled out. Of note, extensive isocyanate skin contamination under gloves is consistent with Pronk *et al.* (2006), who recently reported greater aliphatic isocyanate exposure under gloves in similar workers performing similar painting tasks (discussed below). Further investigation of the effectiveness of different PPE is warranted.

There are few other published human isocyanate skin exposure data to compare our results to. Our current findings are consistent with our earlier report (Liu *et al.*, 2007), demonstrating isocyanate skin exposure using less sensitive qualitative colorimetric SWYPES. As noted, Pronk *et al.* (2006) estimated isocyanate exposure on spray painters hands using a whole glove isocyanate extraction method, with median isocyanate loads in the range of 30–200 μg total NCO, levels about two to three orders of magnitude higher than the data reported here. Fent *et al.* (2006) reported HDI monomer skin levels for a single auto body shop spray painter not wearing gloves or protective clothing using tape stripping, reporting HDI GM (0.84–8.4 ng NCO) over 10 cm^2 sampled area. Possible reasons for these quantitative differences include different sampling protocols (skin area sampled, sampling technique), analytic method used (liquid chromatography/mass spectrometry versus HPLC) and work practices. Glove extraction and tape stripping methods may provide higher yields than skin wipe sampling, but no comparative studies are available, and the glove method is limited to hand sampling. Thus, the current data provide the first extensive quantitative analysis of workplace isocyanate skin

Table 4. Skin exposure to aliphatic isocyanate species (ng total NCO cm^{-2}) under PPE by task

Task	*n*	GM	GSD	% ≤LOD	Range	GM load (ng NCO per sample)
Spraying						
Primer	3	0.2	10.0	33	0–2.4	37.5
Sealer	3	2.8	3.8	0	1.0–12.2	238.4
Clear[a]	34	1.1	4.8	6	0.1–46.9	130.8
Total	40	1.0	5.2	8	0–46.9	124.6
Mixing						
Primer	1	32.4	—	0	—	5487.6
Clear	2	3.2	4.0	0	1.2–8.4	533.9
Total	3	6.9	5.3	0	1.2–32.4	1160.9

Total NCO, total reactive isocyanate group content of the sample.
[a]Includes samples under gloves, clothing/suit and respirators; other categories include only samples under gloves.

exposure we are aware of, including evaluation of a range of different job tasks, PPE used, body regions and types of aliphatic isocyanate paints. The finding of extensive isocyanate skin exposure with and without PPE is consistent with the limited available data.

There are several limitations of this study that should be noted. For one, the overall SPRAY study design was observational in nature, and factors such as the paints used and PPE worn were determined by the work practices in each shop, which were variable, and could not be modified or standardized by the research team. This study design, as well as limited resources for skin sampling and logistical issues, prevented a more 'experimental' design (such as paired pre-/post-task sampling). Thus, it was not possible to meaningfully evaluate the numerous variables (e.g. brand paints used, length of task, use of PPE and shop ventilation) that could impact on isocyanate skin exposure, further complicated by the frequently sporadic nature of isocyanate skin exposure.

Although, as noted above, the quantitative method is sensitive and specific for detection of aliphatic isocyanates; isocyanate skin exposures may have been underestimated due to several factors, including sampling inefficiencies, isocyanate reactivity and skin absorption of isocyanates, although data available are limited. Skin wipe sampling efficiency may be affected by the wipe pad, coating agent, method of skin wiping and other factors. Losses of isocyanates due to chemical reactions, such as with water and skin proteins (Ulrich, 1997; Wisnewski *et al.*, 2000) and curing reactions with polyols, could all result in under-detection of skin exposure, as the method depends on the detection of unreacted NCO groups (Bello *et al.*, 2005, 2006). Isocyanate skin absorption could also result in under-detection of skin exposure and is likely affected by factors such as type of isocyanate, solvent co-exposures and disruption of the skin barrier, but information is very limited (Creely *et al.*, 2006; Callard and Harper, 2007; Bello *et al.*, 2008). Thus, timing of skin sampling may be a critical factor. Sampling in this study was performed promptly at the end of each task to reduce the impact of these factors.

The biological significance of the isocyanate skin exposure reported here is a critical question beyond the scope of this study. Animal studies demonstrate that isocyanate skin exposure is an efficient means of inducing systemic sensitization and Th2-like immune responses (Herrick *et al.*, 2002; Pauluhn, 2008; Bello et al., 2007a). Human studies investigating the health impact of isocyanate skin exposures are very limited. Further investigation of the health impact of isocyanate skin exposure as well as strategies to prevent such exposure are needed and should be facilitated by the development of quantitative isocyanate skin methods.

CONCLUSIONS

A quantitative method for skin sampling and analysis of aliphatic polyisocyanates was developed and evaluated. Using this method, widespread aliphatic isocyanate contamination of exposed skin was documented in auto body shop workers following spray painting and paint-related tasks. Isocyanate skin exposure was also commonly detected under PPE (gloves, cartridge respirators and protective clothing), questioning the efficacy of PPE commonly used in these auto body shops. The health effects of human isocyanate skin exposure remain unclear and warrant further research. However, it is prudent to increase workers' awareness of isocyanate skin exposure and develop and implement better strategies to reduce such exposures.

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