

Transferability of Aliphatic Isocyanates from Recently Applied Paints to the Skin of Auto Body Shop Workers

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Isocyanates, the essential cross-linking chemicals used to make polyurethane, are potent sensitizers and a common cause of occupational asthma. In addition, isocyanate (NCO) skin contact may contribute to the development of isocyanate asthma. Prior work has shown that unbound NCO can persist on recently spray coated auto body parts after appearing dry. The purpose of this study was to assess whether isocyanate skin exposure can result from handling such surfaces. Quantitative surface and skin wipe sampling for total NCO was performed on test panels sprayed with aliphatic isocyanate coatings, and on paired skin samples obtained from participants who had rubbed the recently dried surfaces. Surface and skin samples, obtained from 18 workers in five auto body shops, were prepared following NIOSH method 5525 (modified for skin samples), and isocyanate species derived from hexamethylene diisocyanate and isophorone diisocyanate were analyzed using high-performance liquid chromatography with ultraviolet and fluorescence detectors. Quantifiable unbound NCO species were detected on 84.2% of all sprayed surfaces sampled after initially considered dry. Only 7 out of a total of 104 (6.7%) non-compounded skin samples obtained after contact with the recently dried coatings had detectable quantities of free NCO. The 7 positive samples, all obtained at the initial sampling time (t_0), had a geometric mean of $0.016 \mu\text{g NCO cm}^{-2}$ (range: 0.002 – $0.88 \mu\text{g NCO cm}^{-2}$). Only 1 of 12 (8.3%) of skin samples obtained after compounding contained detectable free NCO. The risk of substantial human isocyanate skin exposure from contact with the dry appearing (yet not fully cured) isocyanate coatings evaluated in this study appears to be low, although other isocyanate coatings and tasks may pose a greater risk of NCO skin exposure.

Keywords asthma, auto body, clearcoat, compounding, hexamethylene diisocyanate, isocyanates, occupational skin exposure, primer

INTRODUCTION

Aliphatic isocyanates, reactive low molecular weight organic compounds that contain at least one $\text{N}=\text{C}=\text{O}$ (NCO) functional group, are one of the most commonly reported causes of occupational asthma.^(1–4) These agents are commonly used to generate ultraviolet (UV) and chemical resistant polyurethane (PU) coatings applied to products of the automotive, aerospace, and construction industries. In the auto body repair setting, isocyanates are primarily found within the cross-linking hardener component of paints applied to car surfaces.⁽⁵⁾ In the United States there are approximately 35,600 auto body refinishing shops employing almost 224,000 workers, a considerable work force with the potential for isocyanate exposures.⁽⁶⁾

Traditionally, inhalation was considered the fundamental route of worker NCO exposure, with spray painters at high risk.^(7–11) In an effort to reduce airborne isocyanate exposures, changes have been implemented in auto body shops, including ventilation controls, respiratory personal protective equipment (PPE), and the use of lower volatility isocyanates, such as the polymeric species of hexamethylene diisocyanate (pHDI) and isophorone diisocyanate (pIPDI), which now contribute over 99% of the total NCO groups found in current automotive refinishing paints.^(12–15) Nevertheless, isocyanate-induced asthma has persisted among these end users.^(1,13,16,17) NCO skin exposure may also factor into both isocyanate sensitization and the development of asthma, focusing attention on possible sources of skin exposure. Skin exposure during spray painting and mixing tasks has been documented, which is not unexpected. However, whether job tasks that do not involve direct application of uncured isocyanate products entail risk of isocyanate skin exposure is an important unanswered question, especially as workers frequently do not wear PPE during such tasks.

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After structural repair and surface preparation, auto body refinishing culminates in various painting-related procedures (e.g., paint mixing, application of coatings, untaping, dry or wet sanding of coated auto body panels, compounding, and detailing).^(11,12,18,19) In general, a series of coatings is sequentially sprayed on the car surface after each has been allowed to dry. A primer coating is first applied to the auto body surface—sometimes on the shop floor. Then when dry, the automobile is generally moved into a ventilated spray booth, if not done already, where the remaining coatings will be applied and then dried, frequently with a baking cycle around 140°F (60°C). Thereafter, a base coat is sprayed that gives the car surface its color, and finally, a protective topcoat (i.e., the clearcoat) is applied.⁽⁷⁾ While the number of coats can vary depending on the job and shop practices, these coatings, with the exception of the basecoat, usually contain an aliphatic isocyanate hardener or activator component.^(7,11,20) Drying times fluctuate depending on the given product, drying method, and subsequent task, with times typically ranging from 5 min or longer between coats to around 2 to 4 hr for tasks such as sanding, and up to 16 hr or longer for final detailing.⁽²⁰⁾

Recently coated car surfaces with which auto body workers frequently come into contact have been shown to contain unbound isocyanate (NCO) species even after appearing to have dried, raising the concern that such surfaces may be a potential source of unexpected skin exposure to isocyanates.⁽²⁰⁾ This prior investigation primarily used a qualitative method to detect surface NCO and did not evaluate worker isocyanate skin exposure. Skin isocyanate exposure assessment has proved challenging given limitations of existing methodologies, the variety of isocyanate products in use, as well as the sporadic nature of the tasks performed.^(21–23) Furthermore, although there is evidence to suggest a rapid absorption of monomeric and polymeric isocyanates deep into the stratum corneum of full thickness cadaveric skin within minutes of direct deposition of various automotive refinishing coatings, there remains uncertainty regarding NCO absorption patterns in living human skin following more subtle exposures.⁽²⁴⁾ Of note, limited studies to date have suggested that skin NCO exposure may occur not only with spray painting but also with tasks performed on dried painted surfaces, such as compounding, unmasking, or wet sanding.^(19,25)

The goal of this study was to address the important question of whether contact with surfaces that were recently coated with aliphatic isocyanate paints and appear dry can result in isocyanate skin exposure, especially as workers frequently do not wear gloves and other protective clothing while performing such non-spray painting tasks. If isocyanate species can be transferred to human skin from recently coated surfaces, then understanding the factors (e.g., curing time) and tasks (e.g., compounding) that may modify the risk of such exposure should facilitate preventive strategies.

METHODS

Terminology

Paint system technical data pamphlets frequently use the terms “dried” and “cured” interchangeably to mean that the sprayed auto body surface is ready for the next work task. In this study, only drying is defined in that manner. The term cured describes the state where there are no detectable unbound transferrable isocyanate species.^(20,26) The terms “unbound” and “free” are used as synonyms to describe such unreacted isocyanate (i.e., NCO) groups in chemical moieties that are not joined to the polymeric network.

Study Population and Auto Body Shops

Eighteen auto body shop workers, without previous isocyanate sensitization or current asthma, from a diverse array of five refinishing shops of varying size, work capacity, annual income, and number of employees in the New Haven, Connecticut, area were recruited to participate in the study. The project protocol was approved by the Human Investigation Committee at Yale University and informed written consent was obtained from each participant.

Recruited workers completed a questionnaire, which included items related to symptoms, medical and occupational history, and use of personal protective equipment. In total, painters sprayed 42 standard (10.5 × 15 cm) steel test panels (DuPont M-5832; Wilmington, Del.) with aliphatic isocyanate-containing coatings, comparable to their typical work, and allowed them to dry. Ten different coating types (four primers and six clearcoats) with varying NCO content routinely used in the study shops were evaluated (Table I). Each test panel was sprayed using one of the five different paint brands of primer alone (n = 12) or primer and later clearcoat (n = 30). These painted surfaces were then dried according to manufacturer / shop specifications, by either baking in a booth followed by air drying (n = 32), heating with infrared lamps then air drying (n = 6), or air drying alone (n = 4). All panels were sprayed and dried next to similar real jobs in each shop. An overview of collected surface and skin samples is shown in Table II.

Sampling of Dried Painted Surfaces at the Initial Time Point (t₀)

After test panels were sprayed and dried according to the specifications noted above, shop personnel were asked to determine the point at which each painted surface was suitably ready for handling and work (time t₀). At that time a prefabricated template cut from card stock was laid down over its given test panel about to undergo sampling. These identical templates divided their individual 10.5 × 15 cm panel into seven distinct sampling cells each of a fixed surface area (16 cm²). The template provided clear borders for each cell so that various sampling phases of the study could be performed sequentially

TABLE I. Panel Surface Coating and Drying Characteristics

Coating Type	Coating Hardener Percentage (%)	Drying Time (Min)	Baking Temperature (°F)	Drying Humidity (%)
Shop 1				
Clearcoat (slow drying)	33	120	149	50
Shop 2				
Clearcoat (fast drying)	25.6	97	140	50
Primer (fast drying)	14.3	30 to 50 ^A	140 to 150 ^A	50
Shop 3				
Clearcoat (normal drying)	33	255	130 ^B	59
Clearcoat (normal drying)	20	70	86.3 ^C	43
Primer (normal drying)	20	105	86.3 ^C	43
Shop 4				
Clearcoat (slow drying)	30	37	139.7	41.5
Primer (normal drying)	8.7	55	139.7	41.5
Shop 5				
Clearcoat (fast drying)	20	94 to 105 ^A	138 to 150 ^A	25 to 47.5 ^A
Primer (normal drying)	20	54	98.6 ^B	42

Notes: Drying temperature and relative humidity baking values were recorded from in-booth gauges, whereas surfaces dried under heating lamps and/or in the open air alone had these values recorded with a digital humidity meter thermometer whose probe was placed directly adjacent to the drying panels.

^AMultiple phases of the study were conducted using this coating.

^BHeating lamp and air dried only.

^CAir dried only.

TABLE II. Overview of Collected Study Samples

Sampling Time	Shops (n)	Painters (n)	Workers Skin Sampled (n)	Surface Wipe Samples (n = 96)		Quantitative Skin Samples (n = 145)			
				Qualitative (n = 40)	Quantitative (n = 56)	Tape-Strip (n = 125)		Wipe (n = 20)	
						Control	Test	Control	Test
Initial Time Point (t ₀)									
Clearcoat	5	5	13	12	28	9	44	4	16
Primer	4	4	8	8	10	7	20	0	0
Time Course (t ₀ –t ₃)									
t ₀ (≈0 hr post-dry)	2	2	4	4	4 ^A	4 ^A	8 ^A		
t ₁ (≈1.5 hr post-dry)	2	2	4	0	4	0	8		
t ₂ (≈3 hr post-dry)	2	2	4	0	4	0	8		
t ₃ (≈24 hr post-dry)	2	2	4	4	4	4	8		
Task-Related									
Pre-Compounding	3	3	6	6	6 ^A	0 ^B	12 ^A		
Post-Compounding	3	3	6	6	6	5	12		

^AAlso counted in initial time point (t₀) samples.

^BIdentical to/performed as initial time point (t₀) clearcoat controls.

on the same test panel in adjacent cells without disturbing the other cells.

Designated cells were then wipe sampled by the same investigator, who used fresh nitrile gloves (KC500 Kimberly-Clark Corp; Roswell, Ga.) for each sample. Wipe samples were collected for quantitative isocyanate analysis and also qualitative (colorimetric) analysis, using 5×5 cm polypropylene glycol (PPG) impregnated quantitative wipes (Colormetric Laboratories, Inc., Des Plaines, Ill.), and 2.5×3.0 cm qualitative surface SWYPEs (Colormetric), respectively, as previously described.⁽¹²⁾ Both types of sampling were performed concurrently and compared with skin samples collected following contact with the dried isocyanate paint-coated panels.

A quantitative surface pad was wiped within its designated test panel cell by the same gloved researcher following a standardized rubbing protocol in which the investigator used his thumb, index, and middle finger to grip the pad and firmly wipe the entirety of each cell with 10 sec of vertical strokes followed by 10 sec of horizontal strokes. The surface wipe was then deposited within its own scintillation vial containing 10 mL of derivatizing solution (5×10^{-4} M 1-9-anthracenylmethylpiperazine [MAP] dissolved in acetonitrile), sealed, and immediately placed with the other samples within a cooler containing ice packs at $\approx 38^\circ\text{F}$ (3°C) and shipped overnight to the laboratory and kept in a freezer until preparation and analysis. Bulk samples of the diisocyanate-containing hardener used in each tested product were also collected for analysis along with field blank samples of unused surface wipes.

Quantitative analysis was performed for several isocyanate species including monomeric hexamethylene diisocyanate (HDI), several higher oligomeric species of HDI commonly found in polymeric hexamethylene diisocyanate (pHDI) paints in auto body shops (e.g., uretidine dione, biuret, isocyanurate and diisocyanate),⁽²⁷⁾ and polymeric isophorone diisocyanate (pIPDI). The sum of oligomeric species of HDI was reported collectively as pHDI in $\mu\text{g NCO cm}^{-2}$. In bulk products between 65–95% of total isocyanate content in pHDI is contained in a few major analytes, including biuret, isocyanurate, and occasionally uretidine dione, among others. Total NCO was also calculated and reported as the sum of all isocyanate species (HDI, pHDI, and pIPDI) per sample.

Each qualitative surface pad was wiped within its specific test panel cell according to the same rubbing procedure employed when wiping the surface with the quantitative pad (i.e., 10 sec of vertical strokes followed by 10 sec of horizontal strokes within the given test panel cell being sampled). The SWYPE pad was inspected on development for any color change. As previously described, color intensity was rated on a 0 to 5 scale with 0 representing no color change, 1 light orange, and 5 (deep red) being the highest intensity. All color intensity scores were rated by the same investigator.⁽²⁰⁾ The sampled surface area size, wiping technique, frequency, and precautionary measures (e.g., new nitrile gloves for each sample and grid template) against cross contamination were identical between the surface quantitative and qualitative sampling procedures and were all collected on site by the same investigator.

Sampling of Skin Surfaces at the Initial Time Point (t_0)

Prior to rubbing procedures, each participant's hands (along with the investigator's) were washed in a standardized manner using soap (5 Star X-treme Hand Cleaner #5995; Scottsdale, Ariz.). After the participants' hands were completely dry, a published tape-strip sampling method⁽²⁸⁾ was performed to obtain the skin samples, which were analyzed as previously described.^(20,25) Beginning with a designated control finger, a tape-strip with dimensions 2×2.5 cm of Cover-Roll adhesive tape (Beiersdorf AG, Hamburg, Germany) was applied and smoothed upon the worker's finger tip by the freshly gloved researcher using forceps (that had been cleaned with methanol). A nontoxic washable marker was used to outline the applied tape-strip to allow for an identical placement of the subsequent tape-strip. The initial strip was left in place for 1 min, after which it was peeled away using the cleaned forceps and deposited in a vial containing 10 mL of derivatizing solution (5×10^{-4} M MAP dissolved in acetonitrile). A second tape-strip was immediately applied in the same manner and also left in place for 1 min before being removed and transferred into the same vial. Collectively, the tape-strips were used to sequentially remove two layers of stratum corneum. In an effort to minimize the risk of cross-contamination, new nitrile gloves were donned by the researcher and new forceps were used between each finger tested. In addition to the two tape-strips, which were collected from an un-rubbed finger to serve as a control, two additional tape-strips were transferred directly into the derivatizing solution without skin tape-stripping to serve as field blanks.

Following the collection of control samples (two tape-strips) for each finger, study participants were asked to contact the dried test panels with the volar aspect of their fingers. Each worker was asked to rub a particular finger upon a dried test panel that had already undergone qualitative and/or quantitative wipe surface sampling but in a cell that had not previously been sampled. In this new cell the worker rubbed for a total of 20 sec (10 sec with a vertical motion of the finger tip region, immediately followed by another 10 sec using a horizontal motion) with sufficient force to blanch the terminal perimeter of the digit. As described above, two tape-strips were then sequentially applied one after the other for 1 min each before being peeled off and deposited together in a scintillation vial for each sampled finger. This procedure was repeated using an additional finger on a separate panel cell for duplicate sampling. At the completion of the sampling, the participant's hands were again washed prior to returning to work.

Tape-stripping was the primary method used to sample workers' skin. Nevertheless, to compare dermal quantitative methodologies, a limited number of skin wipe samples ($n = 16$) were also obtained on different digits in addition to tape-strip sampling after participants rubbed the test panel as previously described. PPG impregnated 5×5 cm quantitative skin wipe pads (Colormetric) were used according to a previously published methodology.⁽²⁵⁾ First, a measurement of the length and width dimensions of each of the workers'

finger pad over which the wipe sampling would be performed was taken. After completing the 20-sec test panel rub for each previously unsampled finger, the volar area distal to the distal interphalangeal joint was wiped by the gloved investigator with 10 sec of vertical followed by 10 sec of horizontal strokes to cover the entirety of the given finger pad. The wipe samples were then immediately placed into the derivatizing solution.

Sampling of Surface and Skin over Time (t_0 – t_3)

Two of the shops involved in the initial time point (t_0) sampling were selected for additional surface and skin sampling over time. A primer was tested at one of the shops, while a clearcoat was evaluated at the other. Once the coatings were considered to have dried, two different auto body shop workers at each site underwent quantitative skin tape-strip sampling in duplicate (two different fingers) at four different time intervals (i.e., at approximately $t_0 = 0$ hr, $t_1 = 1.5$ hr, $t_2 = 3$ hr, and $t_3 = 24$ hr post-dry time) (Table II). Corresponding quantitative surface sampling was also performed at each time point for both products in duplicate to assess the relationship between the presence of unreacted surface aliphatic diisocyanates and transfer to human skin.

Sampling of Surface and Skin After Compounding Tasks

Transfer of free NCO species to human skin was assessed prior to and following the common shop task of compounding by quantifying free NCO on surfaces that had been compounded and on the fingers of workers who had contacted the compounded surfaces. Compounding, commonly performed late in the automotive refinishing process, involves buffing the dried outermost layer of clearcoat with polishing paste and could involve skin contact with dried yet incompletely cured isocyanate species.⁽⁵⁾ Two workers from three shops performed compounding for a period of approximately 2.5 min on their respective test panels that had been previously sprayed with clearcoat and allowed to dry. Quantitative and qualitative surface wipe sampling and paired duplicate skin tape-strip samples from two fingers of each worker were obtained after rubbing the compounded surface using the above 20-sec protocol, which also included control finger samples. Samples were all processed and analyzed as described above.

Sample Analysis

All study quantitative samples (i.e., surface quantitative wipe, skin tape-strip, and skin wipe) were prepared using the previously described NIOSH method 5525 with analysis performed via high performance liquid chromatography with ultraviolet and fluorescence detectors (HPLC/UV/FLD).⁽²⁹⁾ Good recovery has been observed for individual species of aliphatic polyisocyanates from spiking aluminum foil and wipe media, in excess of 80% for HDI and pHDI and 75% for pIPDI species.^(20,25,29) Tape-strip recovery of HDI has been reported to be in excess of 99%.⁽²⁸⁾

Statistical Analysis

Tests for normality, descriptive statistics, t-tests, and multivariate regression analyses were performed with SAS version 9.2 statistical software (SAS Institute, Cary, N.C.). Given that the data fit a lognormal distribution, the geometric mean (GM) and geometric standard deviation (GSD) were used to characterize data distribution. Surface quantitative sample data was used to construct a model in which the dependent variable was the ln of surface total NCO (μg). To achieve the most parsimonious model in the multivariate regression analysis, a backward elimination strategy was employed whereby all collected study variables were initially present then extracted one at a time based on their extent of failure to reach a p-value of 0.05. Significance for all statistical tests performed in the study analysis was assessed based on an α of 0.05. In addition, individual sample values for polymeric hexamethylene diisocyanate (pHDI) $\leq$ the limit of detection (LOD) were substituted with $\frac{1}{2}$ LOD as done previously.⁽²⁵⁾

RESULTS

Sample Coating Products and Panel Preparation Characteristics

Ten different coatings were evaluated. The percentage of aliphatic diisocyanate contained within each varied as the hardener component of these products differed from one another. Overall the ratio of NCO-containing hardener for both product types (i.e., primers and clearcoats) ranged from 8.7 to 33.3%. The percent hardener ranged from 8.7 to 20.0% in the primer mixtures, and from 20.0 to 33.3% in the clearcoat mixtures. Average primer drying time (deemed by shop personnel) was 59 min (range: 30–105 min). For primers, the average total time between paint application and the execution of worker skin sampling was 151 min (range: 54–385 min). The clearcoats had an average drying time of 110 min (range: 37–255 min) with an average total time between clearcoat application and skin sampling being 192 min (range: 75–355 min). Average drying conditions for sprayed test panels included: 0.5 hr at 143.7°F (62°C) when baked, 0.33 hr at 119.5°F (49°C) when heated with infrared lamps, and 2.8 hr at 81.3°F (27°C) when air dried. The mean relative humidity during the drying period was 47.9% (range: 25–59%).

Surface and Skin Sampling at the Initial Time Point (t_0)

Unbound NCO species were detected in 32 of the 38 (84.2%) quantitative wipe samples obtained from surfaces sprayed with isocyanate-containing coatings that appeared fully dried at the initial time point (t_0) (Table III). Surfaces last sprayed with clearcoats ($n = 28$) showed significantly ($p < 0.008$) higher levels of free NCO cm^{-2} (geometric mean of 0.139 μg NCO cm^{-2}) than those whose outermost coating was primer ($n = 10$; geometric mean of 0.063 μg NCO cm^{-2}).

A total of 100 skin samples were obtained from the auto body shop workers at t_0 (immediately after the painted surface appeared dry) (Table II). Ten different coatings (primers

TABLE III. Aliphatic Isocyanate ($\mu\text{g NCO cm}^{-2}$) Detected on Surfaces and Skin (Time t_0)

Coating Type	Surface Quantitative Wipes (n = 38)										Skin Quantitative Samples (n = 80)						
	pHDI			pIPDI			HDI Monomer			Total NCO ^A			Tape-Strips			Wipes	
	GM	% > LOD	GM	% > LOD	GM	% > LOD	GM	% > LOD	Range	n	% > LOD	n	% > LOD	n	% > LOD		
	(GSD)		(GSD)		(GSD)		(GSD)										
Clearcoat	28	0.038 (38.7)	75	0.393 (3.2)	57	0.003 (7.3)	82	0.139 (18.4)	86	<0.001–3.268	44	5	16	13			
Primer	10	0.043 (19.7)	80	0.158 (1.3)	40	0.001 (6.1)	60	0.063 (17.1)	80	<0.001–0.439	20	15	0	0			
All Samples	38	0.039 (31.5)	76	0.327 (3.0)	53	0.002 (7.4)	76	0.113 (17.7)	84	<0.001–3.268	64	8	16	13			

Note: $\frac{1}{2}$ LOD was used for pHDI in calculations if the individual sample value was $\leq$ LOD (0.005 $\mu\text{g NCO}$).

^ATotal NCO = calculated by individual sample as the sum of HDI, pHDI, and pIPDI species.

TABLE IV. Isocyanate (μg NCO) Content Among Positive Skin Samples ($n = 7$)

Sample Type	Coating Type	HDI Monomer	Selected pHDI Species			pIPDI	Total NCO (per sample)	Total NCO (μg NCO cm^{-2})
			Dione	Biuret	Isocyanurate			
Tape-strip $n = 5$	Pr	ND	ND	ND	0.003	0.004	0.007	0.001
	Pr	ND	ND	ND	0.011	ND	0.011	0.002
	CC	ND	ND	ND	0.003	ND	0.008 ^A	0.002
	CC	0.078	0.015	0.041	3.254	ND	4.394 ^B	0.879
	CC	0.062	0.030	0.026	2.736	ND	3.942 ^C	0.788
Wipe $n = 2$	CC	ND	0.008	0.008	0.080	0.027	0.218 ^D	0.032
	CC	ND	ND	ND	0.005	0.012	0.017	0.002

Notes: CC = clearcoat, Pr = primer, ND = non-detectable ($\leq$ LOD). HDI: LOD 0.001–0.004 μg NCO depending on sample matrix. Dione, biuret, and isocyanurate: LOD 0.001–0.004 μg NCO depending on sample matrix. pIPDI: LOD <0.001 μg NCO.

^ASample contains other pHDI species equal to 0.005 μg NCO.

^BSample contains other pHDI species equal to 1.006 μg NCO.

^CSample contains other pHDI species equal to 1.088 μg NCO.

^DSample contains other pHDI species equal to 0.950 μg NCO.

and clearcoats) were each sampled by at least two different auto body workers, with duplicate tape-strip skin samples taken from each person for every product (64 tape-strip skin samples). Sixteen quantitative skin wipe samples were also obtained to compare methodologies (Table II). For the skin samples obtained at t_0 only 5 out of 64 (8%) tape-strip samples and 2 out of 16 (13%) wipe samples had positive isocyanate species (Table III). All control samples were negative. Thus, only 7 out of 80 total (8.7%) skin samples obtained immediately after contact with the coatings shortly after they appeared dry were positive for quantifiable free NCO on the skin.

Substantial variability was observed among the seven positive skin samples. The two skin samples with the greatest total NCO were tape-strip samples and were collected from a single participant after contact with a clearcoated surface. Of note, the baked and dried test panel corresponding to these two samples had a 37-min drying time that was the lowest of any panel evaluated in the study. The other five positive skin samples (three clearcoats and two primers) had lower levels of total NCO detected and no obvious patterns (e.g., extremes in drying times, type of coating or skin sampling method) to account for their variability (Table IV).

Multivariate regression to identify predictive factors for surface NCO level (Table V) yielded an R-squared value of 0.92. Significant predictors of surface NCO level were painting temperature, humidity, type of coating, type of drying, and isocyanate hardener ratio. Two interactions were identified as statistically significant, namely, the interaction of temperature and humidity, as well as the interaction between type of coating and hardener ratio. For both clearcoat and primer, lower hardener ratio yielded higher levels of NCO; this effect was greater for primer than clearcoat (Figure 1). An interaction was also noted between humidity and temperature. Although for lower humidity, increasing temperature resulted in lower surface NCO levels; at higher humidity, increasing temperature resulted in higher surface NCO levels (Figure 2).

Surface and Skin Sampling over Time (t_0 – t_3)

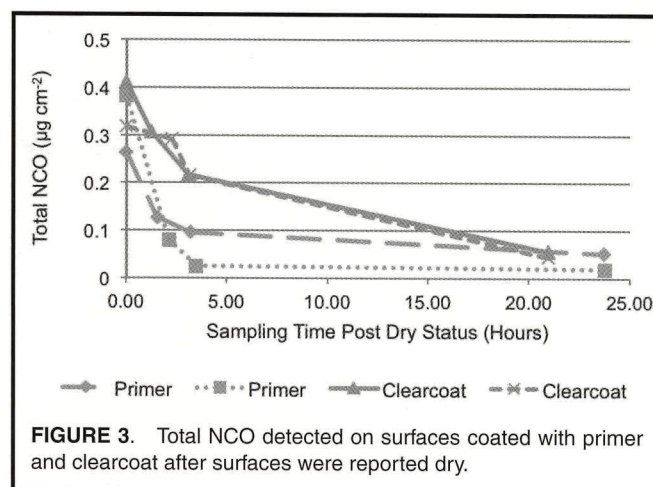
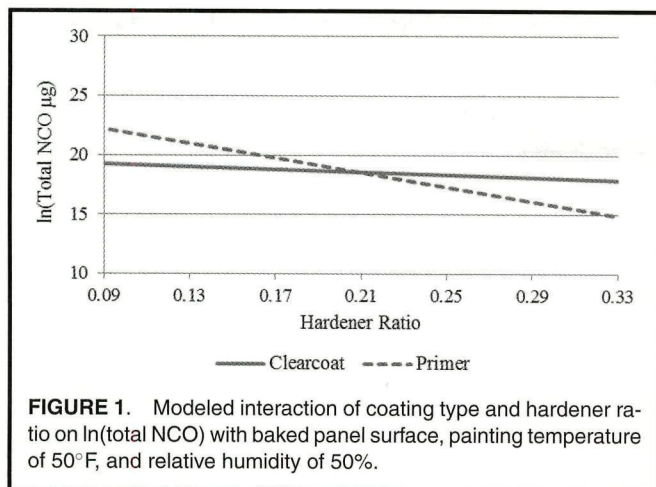
Levels of free NCO detected on the surface of the painted panels decreased significantly ($p < 0.001$) over time for all paints tested (Table VI), with the primers curing more quickly than the clearcoats (Figure 3). At approximately 24 hr post-drying, levels of total NCO were low, yet still contained

TABLE V. Multivariate Regression Model Parameter Estimates for Factors Predicting $\ln(\text{Total NCO } \mu\text{g})$ Surface Contamination at Time t_0

Parameter	Estimate	Standard Error	t Value	p Value
Baked surface	6.42	0.59	10.90	<0.001
Clearcoated surface	–5.20	2.05	–2.53	0.017
Temperature during painting ($^{\circ}\text{F}$)	–0.76	0.09	–8.02	<0.001
Humidity during painting (%)	–0.98	0.18	–5.50	<0.001
Coating hardener ratio (% isocyanate)	–30.55	8.74	–3.49	0.002
Coating type (CC = 1) and hardener ratio interaction	24.94	10.63	2.34	0.026
Painting humidity and temperature interaction	0.013	0.002	5.88	<0.001

TABLE VI. Aliphatic Isocyanate ($\mu\text{g NCO cm}^{-2}$) Detected on Surfaces and Skin over Time (t_0 - t_3)

	Quantitative Surface Wipes										Quantitative Skin Samples			
	pHDI			pIPDI			HDI Monomer						Total NCO	
	n	GM (GSD)	% > LOD	GM (GSD)	% > LOD	GM (GSD)	% > LOD	GM (GSD)	% > LOD	GM (GSD)	% > LOD	n	% > LOD	
t_0 ($\approx$ 0 hr post-dry)	4	0.156 (1.2)	100	0.181 (1.3)	100	0.001 (11.1)	50	0.339 (1.2)	100	0.263–0.411	8	13		
t_1 ($\approx$ 1.5 hr post-dry)	4	0.070 (2.0)	100	0.101 (1.9)	100	0.002 (1.8)	100	0.174 (1.9)	100	0.080–0.306	8	0		
t_2 ($\approx$ 3 hr post-dry)	4	0.024 (5.9)	100	0.071 (2.4)	100	0.001 (2.8)	100	0.104 (2.7)	100	0.026–0.217	8	0		
t_3 ($\approx$ 24 hr post-dry)	4	0.005 (2.3)	100	0.032 (1.7)	100	0.001 (2.7)	75	0.040 (1.6)	100	0.020–0.056	8	0		



detectable isocyanate species (Table VI). Of the 32 skin samples obtained from the auto body workers after rubbing the painted surfaces (8 at each time point) only 1 skin sample (3.1%) showed detectable free NCO. This sample was obtained at time t_0 included in the 7 positive skin samples noted above. Thus, no free NCO was detected on skin samples obtained at times after t_0 .

Overall, only 7 out of the 104 (6.7%) total skin samples obtained in the non-compounding phases of the study were positive for free NCO, and these 7 were all obtained around t_0 , shortly after the surface was deemed dry.

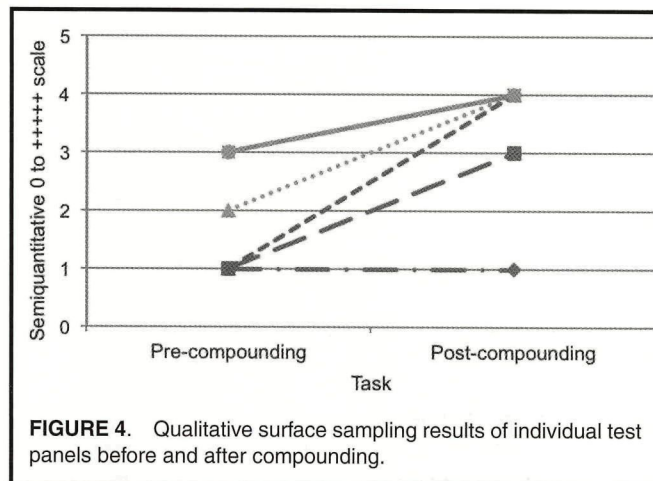
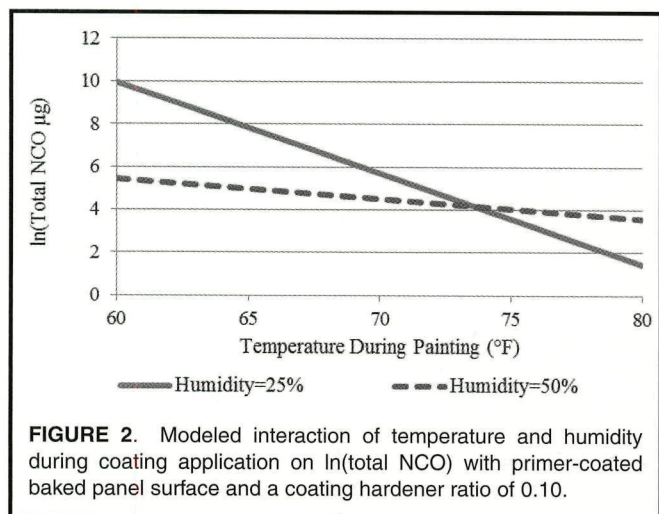
Compounding Surface and Skin Sampling

The presence of free NCO species on human skin was evaluated following the routine shop task of compounding dried surfaces that had been coated with clearcoat. The painted surfaces were sampled before and after compounding, both qualitatively and quantitatively (Table II). Six workers were recruited from three shops and performed compounding using their standard procedure and products for a period of approx-

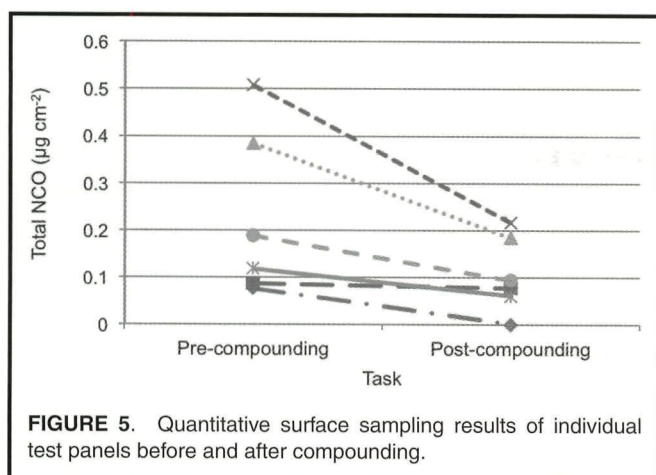
imately 2.5 min on their respective test panels that had been previously sprayed with clearcoat and allowed to dry. A total of 24 tape-strip samples were obtained, 12 before and 12 after rubbing the compounded surface using the 20-sec rubbing technique previously described (Table II).

Paired qualitative and quantitative wipe sampling both showed detectable levels of free NCO on all six test panel surfaces before compounding (Figures 4 and 5 and Table VII). The pre-task levels of unbound NCO detected quantitatively on the six surfaces decreased following compounding (from geometric mean 0.176 to 0.042 $\mu\text{g total NCO cm}^{-2}$), but this change was not statistically significant ($p = 0.157$) using the student's t-test. However, all but one of the six qualitative SWYPE samples showed an increase in the surface levels of unbound NCO following compounding relative to the baseline samples prior to the task (Figures 4 and 5 and Table VII).

Only 1 out of 12 (8.3%) skin samples obtained after compounding was positive for free NCO. All 12 skin samples obtained before the compounding task were negative for free NCO (Table VII).



Quantitative Surface Wipes														
pHDI						pIPDI		HDI Monomer		Total NCO		Quantitative Skin Samples		
	n	GM (GSD)	% > LOD	GM (GSD)	% > LOD	GM (GSD)	% > LOD	GM (GSD)	% > LOD	GM (GSD)	% > LOD	Range	n	% > LOD
Pre-compounding	6	0.036 (19.8)	83	0.141 (1.5)	33	0.003 (4.0)	83	0.176 (2.2)	100	0.077–0.508	12	0		
Post-compounding	6	0.005 (42.3)	50	0.075 (1.4)	33	0.001 (6.9)	50	0.042 (11.6)	83	<0.001–0.217	12	8		



DISCUSSION

Residues of aliphatic isocyanates were quantified on recently painted test panel surfaces beginning when the paint products were deemed dry and the amount of unbound NCO recovered from the painted surfaces declined over time. Notably, the presence of unbound NCO on the skin of workers who had touched the coated surfaces, after they were deemed dry but contained detectable free NCO, was detected in only 6.7% of all the skin samples analyzed. These positive skin samples were all obtained after hand contact with coated surfaces at the earliest time point (time t_0) when the product was considered dry and these skin samples had relatively low levels of total free isocyanate. None of the 24 skin samples obtained at later time points after the surfaces appeared dry (i.e., 1.5 to 24 hr) showed detectable amounts of free NCO, and only one of the quantitative skin samples obtained after compounding showed any detectable unbound NCO.

Previously published data showed detectable unbound isocyanate species on freshly painted auto body surfaces for hours to days after appearing dry, raising concern that such surfaces could be a source of unsuspected isocyanate skin exposure.⁽²⁰⁾ This prior investigation predominantly involved qualitative surface sampling of NCO sprayed car parts with quantitative sampling of only two auto body surfaces over time. The current study, which involved more extensive quantitative sampling of coated surfaces, confirmed that free NCO levels went down over time but could still be detected on surfaces up to 24 hr after appearing dry. Clearcoat surface samples collected at t_0 had a geometric mean of $0.139 \mu\text{g total NCO cm}^{-2}$, similar to the previous study's findings (GM of $0.109 \mu\text{g NCO cm}^{-2}$).⁽²⁰⁾ The quantitative samples taken 24 hr after appearing dry in the current study were also comparable to similar previously reported 24-hr surface samples (GM of $0.051 \mu\text{g NCO cm}^{-2}$ and $0.015 \mu\text{g NCO cm}^{-2}$, respectively).

Although not the primary focus of the study, the multivariate analysis identified several predictive factors for surface total NCO levels, including painting temperature, humidity, and coating hardener ratio, as well as several interactions between these variables. In one, a higher hardener ratio yielded lower

levels of total NCO, particularly for primer coatings, which is consistent with the hardener's function of promoting the curing process. The modeled interaction between temperature, humidity, and total NCO levels is more complex. In general, humidity may potentially affect drying in multiple ways: by attenuating the evaporation rate of the coating components, such as solvents, or by expediting the polymerization process of the free NCO species. While such factors are known to alter isocyanate reactivity, data evaluating their impact on curing times and NCO levels in real world settings, are not readily available.

In addition to the persistence of free isocyanate groups on automotive surfaces, the present investigation was also motivated by a prior study from our group that had demonstrated detectable free NCO on the skin of a small number of auto body workers performing tasks such as compounding, untaping, and sanding.⁽²⁵⁾ These tasks are not typically performed with gloves and protective clothing, raising concerns that such workers were at risk for unsuspected skin exposure to isocyanates. However, the more extensive quantitative skin sampling data presented here showed minimal isocyanate skin exposure from contact with dry, recently spray painted surfaces, including skin samples taken after compounding. Other tasks such as wet sanding were not evaluated in this study.

There are a number of potential explanations for this paucity of free NCO documented on skin sampling, which differs from our prior study,⁽²⁰⁾ in which the majority of skin wipe samples showed detectable levels of free NCO. The prior study included a relatively small number of skin samples from workers performing non-spray painting tasks. Also, the prior study did not include baseline comparison samples obtained prior to task execution, and the workers did not all first wash their hands in a standardized manner, as was done in this study. In the current investigation, the predominantly negative skin sampling results could not be attributed to painted surfaces containing no detectable NCO, as the corresponding surfaces were also sampled quantitatively and shown to contain free total NCO levels, comparable to previously reported surface levels.^(20,25)

Of note, compounding was the only end user work task that was investigated in this study. In our prior study evaluating isocyanate skin exposure in auto body workers using quantitative analysis, 8 of the 10 samples collected after untaping and 8 of the 10 samples taken post wet sanding had detectable levels of total NCO,⁽²⁵⁾ with these samples having the highest total NCO levels of any of the non-spraying or non-mixing tasks evaluated, higher than the three positive compounding samples. Although the greatest potential for NCO skin exposure among auto body shop workers most likely occurs during spray painting and mixing, the risk associated with other tasks such as wet sanding warrants further exploration.

An unexpected and interesting finding was the incongruence between paired qualitative and quantitative isocyanate sampling results obtained from the same coated surfaces immediately preceding and following compounding. A decrease in total free NCO was detected quantitatively, but an increase

in free NCO using the qualitative SWYPEs, comparing levels before and after compounding, was observed. It is possible that thermal degradation or products other than monoisocyanates are generated during compounding, and were detected by the qualitative SWYPE but could not be quantified using the current HPLC methodology, and thus, also would not have been detected on the quantitative skin samples obtained post compounding.

Strengths of this study include on-site sampling in auto body shops, and the use of actual workers, equipment, paints, and procedures. Ten different primers and clearcoats were tested in an attempt to sample a representative number of products. Standardized hand washing was implemented, and importantly, skin samples were obtained before and after contact with the coated surfaces. In addition, the surface rubbing was performed by auto body shop technicians who were not the painters who sprayed the coatings to be tested, so the risk of skin contamination by overspray from painting was minimized. All field sampling was carried out by the same study personnel using a set methodology with all sampling and scoring tests performed by a single investigator. Laboratory analyses were performed using validated and sensitive methods to detect individual isocyanate species; field blanks and bulk and control samples were also collected to help rule out the presence of any cross-contamination. Furthermore, paired surface and skin quantitative wipe HPLC analysis were employed; also, two methods to sample skin (tape-stripping and wipe sampling) were used for comparison and showed similar results (i.e., little or no detectable free NCO).

Some study weaknesses exist that were largely unavoidable. Of note, the number of samples below LOD limited statistical analyses. While the predominance of skin samples below LOD likely reflects limited isocyanate skin exposure, nevertheless, falsely negative results could have occurred for several reasons. One thought is that the recovery of NCO from the field skin tape-strips or wipe samples could theoretically have been suboptimal. Yet this possibility seems unlikely given that the recovery of total NCO from skin tape-strips and wipe samples was comparable to previously reported values for quantitative wipes.^(20,25,29) Furthermore, the similar no or low detectable amounts with both methods suggests that recovery, even if not ideal, was adequate. All methods used to detect isocyanate species rely on free NCO, so rapid reaction of these groups with moisture or skin proteins could lead to low levels of free NCO being detected in the skin tape-strip or wipe samples. Every effort was made to perform all sampling as soon as the sprayed test panels were considered dry at t_0 , as well as immediately after the rubbing protocol and compounding task, to minimize the possibility of false negative results. Nevertheless, limited study manpower and participant work obligations resulted in some panels continuing to dry while sampling occurred on others or waiting for workers to become available, so that the sampling times were delayed in some cases. In addition, although there were benefits to having sampling conducted by a single investigator scoring the qualitative colorimetric surface SWYPEs in the peri-compounding phase of the study,

the possibility of subjective bias could not be completely prevented. Finally, the shop painters' determinations that parts were dry were partially subjective, which nevertheless benefited the realism of our investigation.

Adherence to a strict pre-sampling hand washing and drying protocol, while a strength of the study, was not the workers' usual practice and may have resulted in excessive removal of natural layers of stratum corneum from the hands that could have interfered with either the transfer of NCO from the painted surfaces and/or facilitated the absorption or reactivity of NCO, thus leading to a poorer recovery of NCO species. Although speculative, the careful hand washing protocol differed between the current study and our prior published data showing detectable free NCO on the majority of skin wipe samples, including non-spray tasks.

Finally, while attempts were made to sample representative aliphatic isocyanate coatings used in auto body shops and under typical work conditions, there are numerous different products in use under a range of working conditions that could impact the risk of skin exposure to free NCO, yet only a few tasks and products were sampled here.

Despite these caveats, the risk of isocyanate skin exposure to workers from car parts that appear to be dry most likely is relatively small. Our data also suggest that this risk could potentially be reduced even further by ensuring additional drying time before contact with recently coated surfaces, especially those painted with clearcoat. In addition, it may also be advantageous to ensure that workers wear appropriate PPE (i.e., nitrile gloves) during tasks that involve skin contact with potentially uncured NCO species, as prior evidence suggests that latex glove material has poorer barrier efficacy against isocyanates and solvents commonly used in sprayed auto body coatings, relative to nitrile rubber.^(30,31)

CONCLUSION

Although quantifiable unbound NCO groups were detected on the majority of surfaces that were recently painted with aliphatic isocyanate coatings and appeared dry, the data presented here demonstrate limited transfer of free NCO from these surfaces to the skin of workers who handled such coated surfaces. Thus, risk of isocyanate skin exposure from direct skin contact with recently painted and dried car surfaces appears to be low under the circumstances evaluated, with the greatest risk of skin exposure for auto body workers likely occurring during mixing and spray painting tasks.

Whether other shop tasks (e.g., wet sanding or untaping) can result in the transfer of free NCO from auto body surfaces to human skin warrants future investigation.

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