

Inhalation Exposure to Isocyanates of Car Body Repair Shop Workers and Industrial Spray Painters

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As part of a large-scale epidemiological study, occupational isocyanate exposure was assessed in spray-painting environments. The aim was to assess which compounds contribute to isocyanate exposure in car body repair shops and industrial painting companies, and to identify tasks with high risk of isocyanate exposure. Mainly personal task-based samples ($n = 566$) were collected from 24 car body repair shops and five industrial painting companies using impingers with DBA in toluene. Samples were analysed by LC-MS for isocyanate monomers, oligomers and products of thermal degradation. From the 23 analysed compounds, 20 were detected. Exploratory factor analysis resulted in a HDI, TDI and MDI factor with the thermal degradation products divided over the TDI and MDI factors. The HDI factor mainly consisted of HDI oligomers and was dominant in frequency and exposure levels in both industries. Spray painting of PU lacquers resulted in the highest exposures for the HDI factor ($<LOD-2643 \mu\text{g}/\text{m}^3 \text{NCO}$), with no significant difference between the industries. Exposure variability during PU spray painting was large with a variability over time of $w_w S^2 = 9.1$ compared with between-worker variability of $b_w S^2 = 1.6$. Lower level exposure to the HDI factor was found during other painting-related tasks and even tasks without direct exposure to paint. Exposure to the TDI factor was found more regularly in car body repair shops than in industrial painting companies. Exposure levels were low ($<LOD-5 \mu\text{g}/\text{m}^3 \text{NCO}$) compared with the HDI factor and no clear contrast in levels between the tasks was observed. Exposure to the MDI factor was found incidentally during spraying and welding in car body repair shops ($<LOD-0.5 \mu\text{g}/\text{m}^3 \text{NCO}$). The results indicate that paint is the most important source and major contributor of isocyanate exposure in both industries with highest exposures during PU spraying. However, since respiratory protection is less extensively used during other tasks, lower level exposure during these other tasks may significantly contribute to the internal dose.

Keywords: isocyanate; occupational exposure; oligomers; spray painting; thermal degradation

INTRODUCTION

Isocyanates are industrial chemicals containing highly unsaturated $\text{N}=\text{C}=\text{O}$ groups which are used

in polyurethane (PU) products such as foams, paints, lacquers, inks, insulating materials, varnishes, rubber modifiers, and bonding and vulcanizing agents (Lesage *et al.*, 1992). In Western countries, these low molecular weight allergens are one of the most commonly identified causes of occupational asthma (Vandenplas *et al.*, 1993b; Bernstein, 1996; Wisniewski and Redlich, 2001) with the highest risk among spray

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painters (Di Stefano *et al.*, 2004). Despite their widespread use and serious consequences, a lack of insight in the relationship between exposure and disease still exists due to uncertainties on health endpoints, underlying mechanisms and biologically relevant exposure (Wisnewski and Redlich, 2001; Redlich and Karol, 2002). Exposure assessment is complicated by the variety of isocyanate compounds present in different occupational settings (Streicher *et al.*, 2000). Moreover, peak exposure (Bernstein *et al.*, 1993) and dermal exposure (Kimber, 1996; Kimber and Dearman, 2002) may play an important role in the development or aggravation of disease.

In the Netherlands, data on the magnitude of health risks are lacking due to the absence of occupational disease registries. A large-scale epidemiological study is being set up to evaluate isocyanate exposure, health effects and exposure-response relationships. This study mainly focuses on end users of PU lacquers in car body repair shops and industrial painting companies. Within these industries, exposure to a range of isocyanates with variable physical and chemical properties may occur. Hardeners of PU lacquers used generally contain hexamethylene diisocyanate (HDI) based compounds and isophorone diisocyanate (IPDI). To reduce the vapour hazards associated with monomeric HDI, the HDI monomer has mostly been replaced by its oligomers. Other isocyanate containing intermediates can be formed during application (Streicher *et al.*, 2000). In addition, toluene diisocyanate (TDI) and methylenebisphenyl diisocyanate (MDI) can be present in kits, glues, pastes and insulating materials used in these industries. Moreover, a variety of thermal degradation products (mono isocyanates and amino isocyanates) can be formed when cured PU products are heated (Henriks-Eckerman *et al.*, 2002; Karlsson *et al.*, 2002; Molander *et al.*, 2002), e.g. by welding and possibly by grinding and sanding of spray-painted parts.

So far, several studies have measured isocyanate exposure in spray painters (Rosenberg and Tuomi, 1984; Pisaniello and Muriale, 1989; Tornling *et al.*, 1990; Myer *et al.*, 1993; Maitre *et al.*, 1996; Carlton and England, 2000; Woskie *et al.*, 2004). However, information on the occurrence of a wide range of isocyanate compounds is not available since most studies focus on exposure to either HDI, oligomers of HDI or total NCO. Additionally, in most studies only exposure during spray painting is sampled. In the present paper, we differentiate between task-based exposures to a range of isocyanate compounds in car body repair shops and industrial painting companies. The aim of this study is to assess which compounds, including monomers, oligomers and thermal degradation products, contribute to isocyanate exposure in these industries, to identify tasks with high risk of isocyanate exposure, and to describe control measures currently in use in The Netherlands.

METHODS

Population and sampling strategy

Exposure assessment was carried out as part of an epidemiological study on isocyanate exposure and health effects in car body repair shop workers and industrial spray painters in The Netherlands. The study currently involves 520 workers from some 100 companies. Car body repair shops were enrolled using databases from the branch organization (written information on study design and a request to participate in exposure as well as health assessment part of the study was sent to 763 companies; positive response rate: 11%) and the Chamber of Commerce (written information and request to 93 companies; positive response rate: 9%). Industrial painting companies were contacted through shipyards resulting in companies specialized in painting of mainly ships and harbour equipment (telephone contact with 16 companies, positive response rate: 69%). Air measurements were performed in a random selection of these companies.

Mainly task-based personal air samples were collected. Prior to the selection of tasks, a thorough walk through survey was carried out to identify tasks involving isocyanate exposure. Some tasks with no obvious direct exposure were also included to assess possible bystander exposure. Coinciding with the personal exposure measurements, data on work circumstances, e.g. ventilation and PPE use, and product samples were collected.

In 24 car body repair shops, a total of 475 task-based samples were taken during the following tasks: preparatory/finishing work, sanding/grinding of painted parts, mixing lacquers, spraying PU lacquer, spraying water-based color lacquer, cleaning spray gun, welding, assembly work and use of isocyanate containing glues, kits and pastes.

In five industrial painting companies, a total of 36 task-based samples were taken during the following tasks: PU spray painting, applying PU lacquer with a roller or brush, mixing lacquers, assisting a spray painter and other activities near the spray painter (bystander).

Besides task-based samples, a background office sample was taken on most measurement days (28 in car body repair shops and 2 in industrial painting companies) and stationary samples were taken when high-risk tasks were performed on the general work floor at a distance of 0.5–5 m (22 in car body repair shops and 3 in industrial painting companies).

Sampling periods were from September to December 2003 and from June to November 2004. Samples were taken on one measurement day per company except for eight car body repair shops where samples were taken on two measurement days within the same sampling period.

Air sampling and analysis

Task-based personal air samples were collected at 1 l/min using midjet impingers, containing 10 g (=11.5 ml) 0.01 M di-*n*-butylamine (DBA) in toluene, attached to the lapel (Karlsson *et al.*, 2002). During 31% of the measurements, filter back-up samples (13 mm glass fibre filters) were taken that were submerged in 10 ml DBA in toluene after the measurement day. Gillian personal sampling pumps were calibrated before and after sampling with a rotameter and average flows were used for calculations. Task-based measurement times varied between 1 and 64 min depending on task duration. When spray painting involved several layers, sampling was stopped during intermitting times. The use of impingers in combination with the volatile toluene results in limited sampling times and therefore eliminates the possibility of taking 8 h samples.

Immediately upon sampling, isocyanate groups derivatize with DBA in the impinger. After sampling, samples were stored at 4°C. Derivatization of amine groups was performed with a chloroformate reagent in a two-phase system (toluene/water) within 3 weeks after sampling, resulting in the determination of amine groups (amino isocyanates) as carbamate esters (Karlsson *et al.*, 2002).

Since on material safety data sheets, isocyanate compounds are only roughly defined (e.g. poly isocyanates, polymeric HDI), 23 product samples have been randomly collected coinciding with air sampling. These samples were qualitatively analysed for isocyanate compounds to investigate if compounds in the exposure samples are present in the products.

Compounds were separated by reversed phase high performance liquid chromatography (RP-HPLC) ionized with electrospray in the positive ionization mode and detected with tandem mass spectrometric detection (MS-MS). A total of 23 compounds were quantified in a single analytical run. Analysed compounds were HDI, IPDI, MDI, TDI, oligomers of HDI (uretidone, isocyanurate, biuret, diisocyanurate, unknown oligomer of HDI) and MDI (3-, 4- and 5-ring MDI) and thermal degradation products. Thermal degradation products included mono isocyanates: methyl isocyanate (MIC), ethyl isocyanate (EIC), propyl isocyanate (PIC), phenyl isocyanate (PhI) and the amino isocyanates of HDI, TDI and MDI—hexamethylene amino isocyanate (HAI), toluene amino isocyanate (TAI), methylenebisphenyl amino isocyanate (MAI). Only thermal degradation products containing N=C=O groups were analysed. In the present paper, all polymeric isocyanates, which are indicated with different terms (polyisocyanates, oligomers, adducts) in the literature, will be indicated as oligomers. The analysis of all compounds in a single analytical run resulted in a high and unstable background signal and limit of quantification for

isocyanic acid (ICA). Therefore, ICA was excluded from this study.

Quantification

Deuterated internal standards (derivatized with DBA) and derivatized external standards were used for calibration of monomers, monisocyanates and aminoisocyanates (Karlsson *et al.*, 2002). D9-DBA derivatized external standards were available for the quantification of biuret, isocyanurate and diisocyanurate. For uretidone and an unknown oligomer of HDI, no standards were available. Based on the structure of the molecule, it was decided to use the biuret calibration for uretidone and consequently express uretidone in biuret equivalents. The unknown oligomer of HDI was expressed in diisocyanurate equivalents. Bobeldijk *et al.* (2005) give a more detailed description of derivatization, calibration and analysis of the isocyanate compounds within the present study.

To be able to interpret the contribution of individual compounds, all concentrations are expressed in $\mu\text{g}/\text{m}^3$ NCO in air calculated as the concentration of the compound divided by its molecular weight times the number of NCO groups times the molecular weight of NCO (42): $(C_{\text{compound}}/MW_{\text{compound}}) * N_{\text{NCO}} * MW_{\text{NCO}}$.

The limit of detection (LOD) depends on compound and measurement time. The maximum LOD (calculated with the minimum measurement time of 1 min, standard volume of 11.5 ml and standard flow of 1 l/min) in this study was roughly 0.1–2.4 $\mu\text{g}/\text{m}^3$ NCO for diisocyanates, 0.03–0.2 $\mu\text{g}/\text{m}^3$ for aminoisocyanates, 0.1–2.9 $\mu\text{g}/\text{m}^3$ for monoisocyanates and 1.4–37.7 $\mu\text{g}/\text{m}^3$ for oligomers of HDI. These LOD values decrease linearly when measurement time increases.

Statistical analysis

SAS statistical software (SAS System for Windows, version 8.02; SAS Institute, Cary, NC) was used for data analysis. Due to the large proportion of samples with non-detectable concentrations, exposure distributions were (severely) truncated to the left for the majority of the individual compounds. Therefore, exposure was described by the frequency of detects and the minimum, median and maximum concentration for samples above LOD.

Because it is impossible to study exposure determinants or exposure–response relationships for all compounds separately, methods for aggregation of compounds were explored. Next to aggregation based on chemical properties, exploratory factor analysis (PROC FACTOR) was used on the presence of 19 compounds (above/below LOD) to identify clusters of compounds that occurred regularly in combination with each other during personal exposure. Only compounds that were found multiple times were

included. Factors were retained if eigenvalues were >1. Factors were identified using the factor pattern matrix after orthogonal varimax rotation. Compounds with a factor loading score >0.25 were included in a factor.

Sum measures were calculated for grouped components. These were calculated by adding up detectable levels only, resulting in a non-detectable sum measure of zero when the concentrations of all compounds were below the LOD.

Since the compounds in the 'HDI factor' were the most dominant in both frequency and concentration, this factor was selected for more detailed analyses. Within-worker ($_{ww}S^2$) and between-worker ($_{bw}S^2$) variance components for exposure to the HDI factor during PU spray painting were obtained by PROC MIXED with worker as a random component and no fixed components. Mixed effect models were also used to assess the following fixed effects: company type, lacquer type and water-based clear coat lacquer. In all mixed effect models, worker was considered a random effect and a compound symmetric covariance structure was assumed. The between-worker variance components were used to estimate the range within which 95% of the individual mean exposures fall: $_{bw}R_{0.95} = \exp[3.92 * (_{bw}S)]$. Analogously, a $_{ww}R_{0.95}$ was calculated within which 95% of the estimates for an individual fall (Rappaport, 1991). For the mixed model analyses, exposure levels were (natural) log-transformed and non-detectable values were

substituted by the lowest LOD/2 in the factor (LOD of HDI).

RESULTS

Task description and control measures

Table 1 gives an overview of the location in which tasks were performed and control measures used during the measurements.

Car body repair shops. In the spray departments, 1–8 spray cycles occurred that each consisted of sanding/grinding of the car (parts), masking, spraying base coat (PU), color coat (water-based) and clear coat (PU) and de-masking. Occasionally, a PU colour top coat was used. One company had just started to use newly developed water-based clear coats.

For each coat the lacquer was mixed, sprayed on in multiple layers and spray guns were cleaned by the same worker. The use of HVLP spray guns is widespread in Dutch car body repair shops (>90%). Spray booths were equipped with downdraft ventilation except for one company (4%), which had cross-draft ventilation. In 75% of the companies, base coat was sometimes sprayed outside the spray booth in a spray bay with local exhaust ventilation. To accelerate curing, inside the spray booth, cars were heated with warm air for 30–60 min. Outside the booth, small IR or UV heaters were used in 75% of the companies. Automated gun cleaning machines were

Table 1. Workplace characteristics and control measures

	Location	Inhalatory protection ^a (yes/no)	Local exhaust ventilation (yes/no)
Car body repair shops			
Use of PU kit, glue, paste	General work floor	None	None
Preparatory/finishing work	Spray department	11% Filtering mask	None
Sanding, grinding	General work floor/spray department	35% Dust mask	42%
Mixing	Mixing room	17% Filtering mask	82%
Spray painting PU-based lacquer	Base coat: 44% spray booth, 56% spray bay Clear/2-component coat: 100% spray booth	97% Filtering mask	100%
Spray painting water-based lacquer	Spray booth	100% Filtering mask	100%
Gun cleaning	Mixing room	46% Filtering mask	70%
Welding	General work floor	11% Welding mask	17%
Assembly work	General work floor	None	None
Industrial painting companies			
Spray painting PU lacquer	77% Hall, 23% outside	86% Filtering mask	Hall: 30% Outside: none
Applying PU lacquer with brush or roller	8 % Hall, 92% outside	20% Filtering mask	None
Mixing	67% Hall, 33% outside	67% Filtering mask	None
Spray assistant	Hall	100% Filtering mask	None
Near spray painter	Hall	None	None

Overview of task-based use of respiratory protection and local exhaust ventilation during the measurements in car body repair shops and industrial painting companies based on data collected during the measurements.

^aNo supplied air masks were observed in this study.

encountered in 75% of the companies, but cleaning always involved manual handling also. Usually, spray painters alternate daily or weekly between spraying inside the booth and activities outside the booth (sanding, masking, de-masking, incidentally spraying base coat). In this study, preparatory and finishing work includes (de-)masking, spraying of non-PU coats and polishing. Questionnaires among 186 workers in spray departments indicate that the amount of time a worker spends on actual spraying is very limited and varies greatly. A mean spraying time inside the booth of 37 h per month (SD = 37) and spraying time outside the booth of 9 h per month (SD = 18) were reported. This results in a mean spraying time per day of 111 min inside the booth and 27 min outside the booth in case of 20 working days per month. Preparatory work like masking and de-masking and also waiting between different layers and coats makes up most of the working day.

The general work floor was always connected to the spray department. On the general work floor, metal sheet workers and mechanics incidentally performed tasks with possible isocyanate exposure, i.e. welding and using isocyanate containing glues, kits and pastes. All other activities with no obvious source of isocyanate exposure were classified as assembly

work. Sanding was done in both the spray department and on the general work floor.

Industrial painting companies. Most industrial painting companies had sandblasting departments that were not included in the study since they comprised a separate group of workers in an isolated area. Painted objects varied from ships to small parts of a crane. Consequently, a paint job lasted longer (7 man-hours) and mixing and gun cleaning was performed less frequently (1–2 per day) than in car body repair shops. All PU lacquers encountered were color top coats. In addition to (airless) spray guns, rollers and brushes were used to apply lacquers. Painters worked alone or with an assistant who conducted supportive tasks. Objects were painted in a hall or outdoors. Lacquers were mixed in the same area in which often also other workers (bystanders) were present. Sampling of long paint jobs was truncated at 30–45 min since the use of impingers limits sampling time.

Isocyanate compounds

A total of 566 air samples were collected from 29 companies. In the samples, 23 isocyanate compounds were analysed of which 20 could be detected. Table 2 gives an overview of the distribution of

Table 2. Overview of personal and stationary samples in car body repair shops and industrial painting companies

Task description	Type P/S	Sampling time (min) Median (range)	<i>N</i> samples	<i>N</i> workers	<i>N</i> companies
Car body repair shop workers					
Use of PU kit, glue, paste	P	4 (2–18)	11	9	7
Preparatory/finishing work	P	6 (2–64)	18	14	12
Sanding, grinding	P	11 (2–30)	48	36	19
Mixing	P	3 (1–23)	101	48	24
Spray painting PU lacquer	P	7 (1–40)	148	51	24
Spray painting water-based lacquer	P	11 (3–34)	27	17	14
Gun cleaning	P	3 (1–13)	77	41	24
Welding	P	12 (1–46)	29	21	17
Assembly work	P	23 (10–43)	16	15	13
Office	S	39 (20–113)	28	—	21
Near drying with portable IR/UV lamp (1–5 m)	S	28 (15–61)	16	—	13
Near spraying (1–5 m)	S	24 (12–97)	4	—	4
Near mixing (1–5 m)	S	2 (—)	1	—	1
Near welding (1–5 m)	S	10 (—)	1	—	1
Industrial spray painters			41	15	5
Spray painting PU lacquer	P	25 (7–33)	13	6	4
Applying PU lacquer with brush or roller	P	25 (7–41)	12	5	3
Mixing	P	8 (4–10)	3	3	3
Spray assistant	P	30 (27–40)	4	2	1
Near spray painter (1–100 m)	P	30 (16–31)	4	3	2
Office	S	— (24–26)	2	—	2
Near spraying	S	13 (13–26)	3	—	2

P, personal sample; S, stationary sample.

personal and stationary samples over the branches, tasks, workers and companies. In many samples, most of the compounds were below the LOD. In both car body repair shops and industrial painting companies, the most dominant compounds, in frequency and concentration, were HDI oligomers and to a lesser degree HDI monomers (Table 3). IPDI and 2,4-TDI were found regularly in car body repair shops but levels were low compared to HDI and its oligomers. Measurements indicate that exposure to MDI-related compounds occurred only to a limited extent. Most mono isocyanates and amino isocyanates were found infrequently and in low concentrations in both industries. Yet in car body repair shops, these products of thermal degradation were encountered relatively more frequently and in a larger variety than in spray-painting companies. The most dominant thermal degradation products were MIC, 2,4-TAI and 1,6-HAI.

On 180 filter samples that were collected, oligomers of HDI were the most dominant compounds.

Frequencies of detectable oligomers were lower (5–18% of filters) and levels were a fraction of levels found in the impinger samples. Thermal degradation products were also detectable, with frequencies and levels more comparable to levels in impingers. Since detectable frequencies and levels on filters were low, filter samples have not been collected in later sampling periods and the results are not presented in the present paper.

In 23 hardener product samples collected coinciding with paint-related tasks, the following compounds were detected: HDI (26% of samples), IPDI (13%), IPDI-isomer (13%), uretidone (22%), isocyanurate (74%), biuret (34%), diisocyanurate (61%) and unknown oligomer of HDI (39%). In four samples (17%), no isocyanates were detected. These four samples were all base coat hardeners. Product samples have not been analysed quantitatively. Since the water-based clear coat hardener also contained a variety of the above compounds, the application of this hardener was assigned 'application of PU lacquer'.

Table 3. Descriptive statistics of personal samples in car body repair shops and industrial painting companies

Compound	Car body repair shop workers <i>N</i> = 475		Industrial spray painters <i>N</i> = 36	
	<i>n</i> > LOD	Median (range)	<i>n</i> > LOD	Median (range)
Mono isocyanate				
MIC	51	0.05 (0.01–3.1)	6	0.05 (0.01–0.65)
EIC	1	0.54 (—)	0	—
PIC	6	0.43 (0.04–0.54)	0	—
Phi	8	0.04 (0.01–0.48)	0	—
Amino isocyanate				
2,4-TAI	14	0.04 (0.001–0.59)	7	0.01 (0.004–0.04)
4,2-TAI	5	0.02 (0.003–0.54)	0	—
2,6-TAI	8	0.05 (0.001–0.74)	0	—
1,6-HAI	43	0.21 (0.02–1.82)	14	0.19 (0.02–3.95)
4,4-MAI	7	0.03 (0.02–0.10)	0	—
Diisocyanate				
2,4-TDI	63	0.07 (0.005–1.16)	0	—
2,6-TDI	3	0.67 (0.27–2.88)	0	—
1,6-HDI	183	0.44 (0.002–15.5)	34	0.11 (0.01–28.8)
4,4-MDI	3	0.02 (0.02–0.06)	0	—
IPDI	44	0.08 (0.004–1.72)	0	—
IPDI isomer	26	0.23 (0.01–1.10)	0	—
Oligo HDI				
Uritidone	77	1.29 (0.12–47.5)	19	3.2 (0.07–61.9)
Isocyanurate	213	13.29 (0.02–892)	21	5.31 (0.06–1931)
Biuret	142	8.11 (0.06–306)	28	2.78 (0.11–552)
Diisocyanurate	90	24.27 (0.84–149)	11	4.21 (0.65–577)
Unknown poly HDI	92	10.58 (0.26–79.9)	4	1.06 (0.42–5.89)
Oligo MDI				
Three ring MDI	0	—	0	—
Four ring MDI	0	—	0	—
Five ring MDI	0	—	0	—

Number of detectable samples and minimum, median and maximum concentration (in $\mu\text{g}/\text{m}^3$ NCO) for the samples above the LOD for all analyzed compounds.

Factor analysis

To explore correlation in the occurrence of different isocyanates, exploratory factor analysis was performed on binary variables for each compound (above/below LOD) that was found more than once (19 compounds). This yielded three factors that explained 84.5% of the total variance (Table 4). HDI-based compounds loaded on factor 1: 'HDI factor', TDI-based compounds loaded on factor 2: 'TDI factor' and MDI-based compounds loaded on factor 3: 'MDI factor'. IPDI loaded on both the HDI and TDI factors. Since theoretically IPDI is more likely to coincide with paint-related compounds from the HDI factor and since the factor loadings were slightly higher on the HDI factor, we choose to assign IPDI isomers to the HDI factor. Monoisocyanates loaded on the TDI factor or MDI factor. PhI loaded on both factors and was assigned to the TDI factor for further analyses. Assignment of PhI to the MDI factor in any of the further analyses did not influence the results.

Sum concentrations for the personal and stationary samples were calculated for different groups of compounds to give insight into concentrations based on different aggregation methods. Exposure measures were aggregated according to the three

factors: chemical structure (monomers, oligomers and thermal degradation products), and a total NCO measure was calculated (Table 5).

Tasks

The task-based frequency of detectable samples and exposure range (samples above LOD) of each factor for all personal samples is presented in Fig 1.

Exposure to the HDI factor was found frequently during paint-related tasks. Frequency of detectable samples was higher in the industrial painting companies. PU spray painting resulted in the highest exposures with industrial spray samples in the high range of car body repair spray samples. Other paint-related tasks, without aerosol formation, like mixing and cleaning the spray gun resulted in lower exposures to the HDI factor. Besides spray assistants, other workers in the same area were also exposed.

Exposure to the TDI factor was found regularly. However, compared to the HDI factor, levels are lower and less contrast in levels between tasks was observed. Exposure to the MDI factor was found incidentally during welding and spraying of non-PU lacquers. Levels were lower than levels of the TDI factor.

Table 4. Clusters of correlating compounds and percentage of explained variance as determined by factor analysis (factor loadings after orthogonal varimax rotation between brackets)

HDI factor 44.1% ^b		TDI factor 27% ^b		MDI factor 13.4% ^b	
Biuret	(0.85)	2,6-TAI	(0.77)	4,4-MDI	(0.77)
Diisocyanuraat	(0.80)	4,2-TAI	(0.66)	4,4-MAI	(0.66)
Uritidone	(0.77)	2,4-TAI	(0.54)	PIC	(0.33)
Unknown polyHDI	(0.73)	PhI ^a	(0.52)	PhI ^a	(0.51)
Isocyanurate	(0.70)	2,6-TDI	(0.40)		
1,6-HDI	(0.69)	MIC	(0.33)		
1,6-HAI	(0.55)	2,4-TDI	(0.28)		
IPDI ^a	(0.43)	IPDI ^a	(0.30)		
IPDI isomer ^a	(0.38)	IPDI isomer ^a	(0.33)		

^aPresent in multiple factors.

^bPercentage of variance explained.

Table 5. Descriptive statistics of sum measures in personal samples in car body repair shops and industrial painting companies

Compound	Car body repair shop workers <i>N</i> = 475		Industrial spray painters <i>N</i> = 36	
	<i>n</i> > LOD	Median (range)	<i>n</i> > LOD	Median (range)
HDI factor	256	8.55 (0.002–1124)	35	6.67 (0.01–2643)
TDI factor	111	0.07 (0.001–5.38)	11	0.02 (0.004–0.65)
MDI factor	12	0.10 (0.02–0.54)	0	—
TDP ^a	103	0.12 (0.001–4.64)	17	0.17 (0.01–3.95)
Monomers	217	0.42 (0.002–15.5)	34	0.11 (0.01–28.8)
Oligomers	217	27.92 (0.02–1122)	29	14.21 (0.12–2614)
Total	293	5.13 (0.01–1124)	35	6.68 (0.01–2643)

Number of detectable samples and median (range) concentration (in $\mu\text{g}/\text{m}^3$ NCO) for the samples above the LOD for sum concentrations.

^aTDP, thermal degradation products.

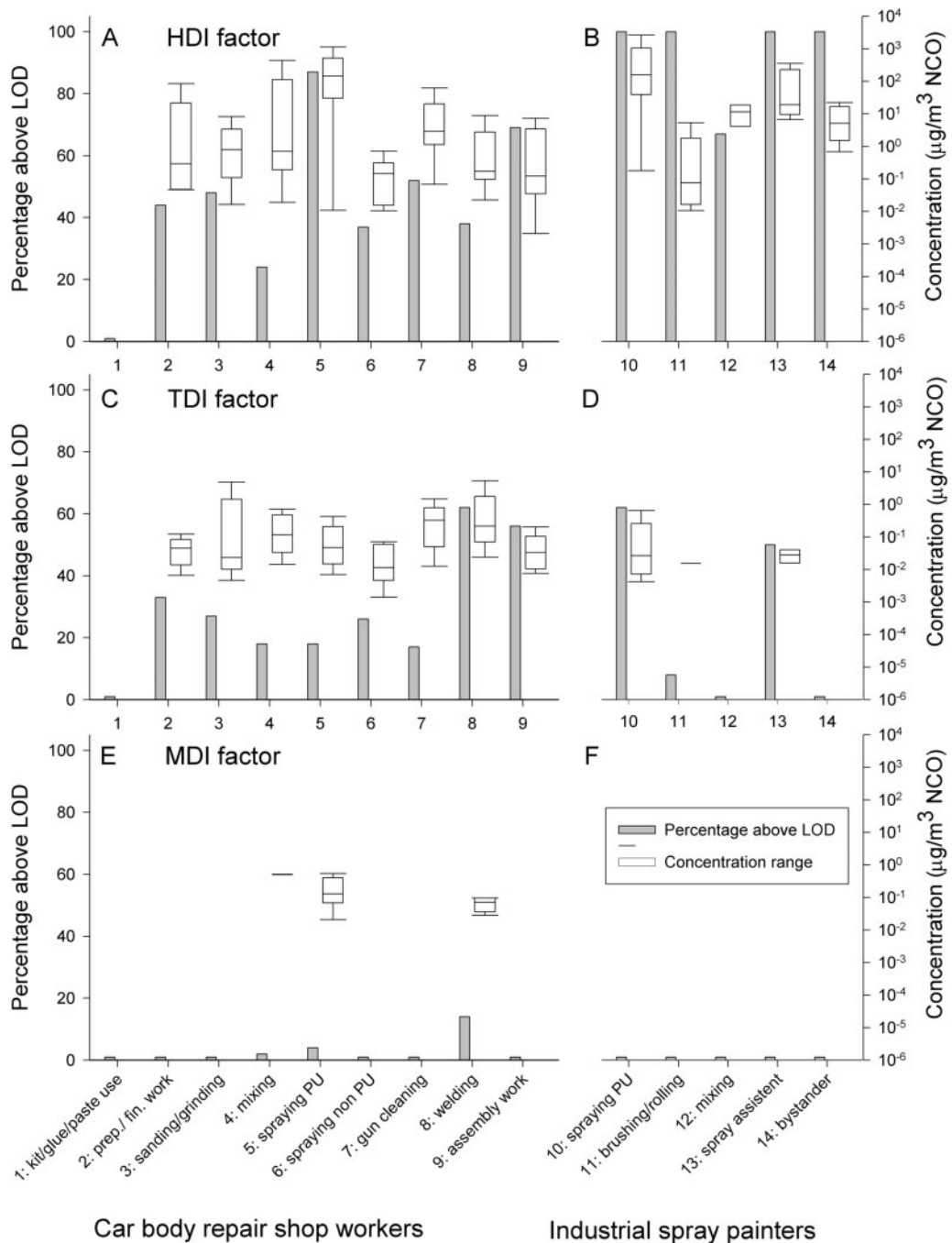


Fig. 1. Task-based personal exposure to the sum concentrations of the HDI factor (A and B), TDI factor (C and D) and MDI factor (E and F) for car body repair shop workers (A, C and E) and industrial spray painters (B, D and F). Grey bar = percentage above LOD, white box plot = exposure range for samples above the LOD in µg/m³ NCO (minimum, P₂₅, median, P₇₅, maximum).

A *t*-test showed that in car body repair shops, task-based sampling time is significantly ($P = 0.004$) longer for detectable (any compound) samples (mean: 9.9 min) than for non-detectable samples (mean: 6.4 min). In industrial painting companies, the only non-detectable task-based sample (any compound) was collected during a shorter sampling time

(3.8 min) than the other samples (range: 7.0–40.8 min).

Figure 2 shows exposure levels to the HDI factor during PU spray painting for each worker in both industries ($n = 57$). Variation within workers was large while the range is similar for workers. Variance components obtained by a mixed model confirmed

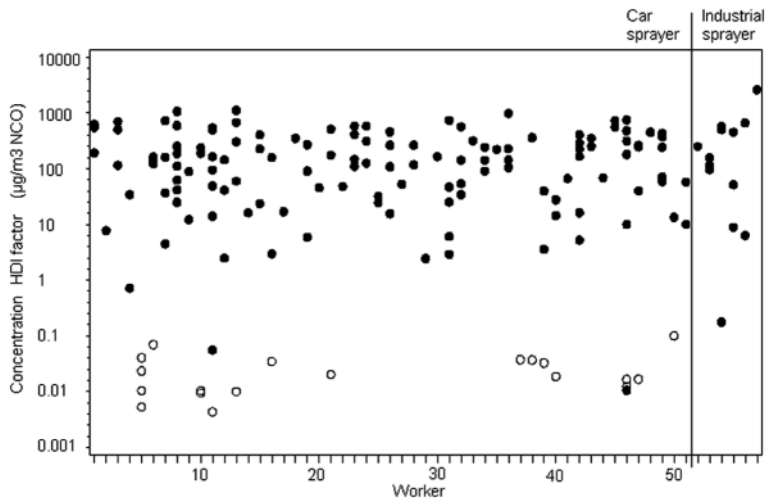


Fig. 2. Scatter plot of the concentrations of the HDI factor (y-axis) during (repeated) spray painting of PU lacquer measurements for each worker (x-axis). Open circle, non-detectable (= all compounds below LOD); filled circle, detectable.

a high within-person variance of 9.1 compared with a between-person variance of 1.6. This results in a range within which 95% of the estimates for an individual fall (${}_{ww}R_{0.95}$) of 140 000 and a range within which 95% of the individual mean exposures fall: (${}_{bw}R_{0.95}$) of 145. Including company type, lacquer type and water-based clear coat simultaneously into the model as fixed components showed that lacquer type is the only significant predictor of exposure level during PU spraying. Spraying PU color top coat and PU clear coat both lead to significantly different exposure levels compared with spraying PU base coat ($P < 0.01$). Company type (car body repair shop or industrial painting company) and the use of water base clear coats did not have a significant effect on exposure levels. The corrected (for the company type and water-based clear coat) geometric mean levels and 95% confidence intervals are $71 \mu\text{g}/\text{m}^3$ (11–457), $79 \mu\text{g}/\text{m}^3$ (12–504) and $4.6 \mu\text{g}/\text{m}^3$ (0.6–35) for spraying PU color top coat, clear coat and base coat, respectively. Including all fixed effects into the model resulted in a reduction of 11% for the within-worker variance component (${}_{ww}R_{0.95} = 68\ 000$) and 19% for the between-worker variance component (${}_{bw}R_{0.95} = 82$).

Stationary samples

Results of stationary samples are summarized in Table 6. Detectable exposure in offices was found in 64% of car body repair shops and 100% industrial painting companies. Exposures to all factors in car body repair shops and the HDI and TDI factor in industrial painting companies were in the same range, and levels were very low compared with personal samples. Stationary samples near spray painting and drying of paint showed mainly exposure to the HDI factor. Two samples taken near mixing and near

welding did not show any detectable isocyanate levels (data not shown).

Comparison with exposure limits

Currently, in The Netherlands an occupational exposure limit (OEL) exists for monomers only. None of the samples in this study was above the short-term exposure limit (STEL) of $70 \mu\text{g}/\text{m}^3$ NCO for HDI. For oligomers, no exposure limits exist in The Netherlands. Bello *et al.* (2004) give a summary of existing airborne OELs worldwide. Bayer Corporation has established a Manufacturer's Guideline Limit, which was later adopted by the Oregon State OSHA, as a 15 min STEL of $220 \mu\text{g}/\text{m}^3$ NCO for the sum of biuret and isocyanurate only. The frequency of samples above this limit in the present study was 1% during mixing and 26% during spraying in the car body repair shops. In industrial painting companies, the frequency of samples above this limit was 46% during PU spraying and 25% during assisting spray painters. The United Kingdom health and safety executive (UK-HSE) combines all monomers and polyisocyanates into a 15 min STEL single isocyanate standard of $70 \mu\text{g}/\text{m}^3$ NCO. The frequency of samples above this limit for total NCO was 6% for preparatory/finishing work, 1% for mixing and 54% for PU spray painting in car body repair shops, and 69% during PU spray painting and 25% during assisting a spray painter in industrial painting companies.

DISCUSSION

The aim of this study was to assess which compounds contribute to isocyanate exposure in car body repair shops and industrial painting companies, and to identify tasks with a high risk of isocyanate exposure. This is the first study in which the occurrence of

Table 6. Descriptive statistics of sum measures in stationary samples in car body repair shops and industrial painting companies

	Car body repair shops						Industrial painting companies								
	Office $n = 28$			Near spray painting $n = 4$			Near drying $n = 16$			Office $n = 2$			Near spray painting $n = 3$		
	$n > LOD$	Median (range)		$n > LOD$	Median (range)		$n > LOD$	Median (range)		$n > LOD$	Median (range)		$n > LOD$	Median (range)	
HDI factor	10	0.04 (0.001–0.13)		3	10.47 (0.07–10.48)		12	0.49 (0.01–2.67)		1	0.005		3	20.79 (3.01–31.57)	
TDI factor	16	0.03 (0.004–0.25)		1	0.01 (—)		5	0.01 (0.01–0.03)		2	(0.02–0.06)		0	—	
MDI factor	1	0.009 (—)		0	—		0	—		0	—		0	—	
TDP ^a	15	0.03 (0.004–0.25)		0	—		5	0.01 (0.01–0.03)		2	(0.02–0.06)		0	—	
Monomers	8	0.01 (0.001–0.05)		3	0.11 (0.01–0.20)		10	0.05 (0.01–0.23)		1	0.004		3	0.17 (0.11–0.29)	
Oligomers	7	0.09 (0.01–0.10)		3	10.27 (0.07–10.36)		8	0.50 (0.23–2.61)		0	—		3	20.62 (2.91–31.28)	
All compounds	18	0.04 (0.004–0.35)		3	10.47 (0.08–10.48)		13	0.48 (0.01–2.68)		2	(0.03–0.06)		3	20.79 (3.01–31.57)	

Number of detectable samples and median (range) concentration (in $\mu\text{g}/\text{m}^3$ NCO) for the samples above the LOD for sum concentrations.

^aTDP, thermal degradation products.

a wide range of individual isocyanate compounds, including monomers, oligomers and products of thermal degradation has been assessed separately on a large scale.

From the 23 analysed isocyanate compounds, 20 can be detected. The results indicate that despite their relatively low vapour pressure, oligomers of HDI are present more frequently and exposure levels are higher than for all other compounds in both car body repair shops and industrial painting companies. The dominance of oligomers of HDI over HDI can be explained by the replacement of the monomer by its oligomers. This is also found in other studies on isocyanate exposure during spray painting (Rosenberg and Tuomi, 1984; Tornling *et al.* 1990; Goyer, 1995). No IPDI is found in industrial painting companies suggesting that IPDI is merely present in car lacquers. In the United States, IPDI and its oligomers appear to be increasingly used in auto body coatings (Sparer *et al.*, 2004; Woskie *et al.*, 2004). In this study, IPDI oligomers were not analysed. However, material safety data sheets indicate that IPDI oligomers are present in part of the different brands and types of lacquers used in The Netherlands and may constitute 2.5–12.5% while IPDI monomer may constitute <2.5%.

HDI monomer levels in the present study do not exceed the current Dutch exposure limit. Nevertheless, exposure to oligomers of HDI occurs in much higher concentrations and exposures above the exposure limits of Oregon State OSHA (USA) and HSE (UK) are found during paint-related tasks. However, the validity of these OEL's is under debate and further clinical, epidemiological and animal research is needed to elucidate disease mechanisms and clarify exposure–response relationships before more reliable exposure limits can be constructed (Bello *et al.*, 2004).

Exploratory factor analysis reveals that, in practice, compounds with the same mother compounds tend to cluster. This is not surprising, for clustering of compounds is likely to be determined by the exposure source. Since the clusters give informative insight into exposure sources and task-based exposure patterns, it was decided to use the three factors in task-based analyses. When comparing different tasks, it should be noted that a longer sampling time is associated with detectable samples. Therefore, the comparison of levels is preferred over frequencies.

The HDI factor contains all compounds that were found in product samples and 1,6-HAI. Since this compound is not found in any of the product samples, it may be formed during the application of lacquers. The dominance of the HDI factor in both frequency and levels shows that paint is, not surprisingly, the most important source and major contributor of isocyanate exposure in both car body repair shops and industrial painting companies. In addition, this factor

is mainly present during paint-related tasks. Exposure patterns for the HDI factor are similar for car body repair shops and industrial painting companies with highest levels during PU spray painting. In industrial painting companies, levels during PU spray painting are in the higher range of the levels found in car body repair shops. In industrial painting companies, higher exposure levels during PU spray painting were anticipated, for working conditions are less controlled by ventilation. Surprisingly, the mixed effect model indicates that not company type but the use of base coats probably accounts for the lower exposure levels during PU spray painting found in car body repair shops. Additionally, no significant effect was seen for the use of a new water-based clear coat, which indeed still contains isocyanates. The presence of (low level) exposure to workers outside the direct vicinity of the spray painter, as well as detectable isocyanate levels in stationary samples suggest regular bystander exposure. Sources of bystander exposure might be PU spray painting, curing outside the spray booth or the opening of the spray booth door.

The TDI and MDI factor contain, in addition to mono isocyanates, TDI and its amino isocyanates, and MDI and its amino isocyanates, respectively. Since TDI and MDI are never found during the use of kits, glues and pastes (in which these compounds are present) but are found in combination with thermal degradation products, the exposure source for these factors is probably a thermal degradation process. Mono isocyanates can be formed by thermal degradation of multiple monomers explaining PhI loading on both factors. Very little contrast in exposure to these two factors is observed between the tasks. Moreover, in the office samples, exposures in the same range are found as in the personal samples. Therefore, it is not clear whether the exposure source of thermal degradation products is welding or whether other, unidentified, activities may contribute. However, the relatively lower abundance and variety of thermal degradation products in industrial painting companies suggest that less processes of thermal degradation are present in this industry. Since for thermal degradation products comparable frequencies and levels were found in impingers and on filters, the TDI and MDI factors are underestimated relatively more than the HDI factor by excluding filters.

Accumulating exposure to different isocyanate compounds into NCO sum measures is general practice. However, while health surveys, specific inhalation challenges and animal studies suggest that oligomers, thermal degradation products and diisocyanates have similar health effects (Vandenplas *et al.*, 1992, 1993a; Simpson *et al.*, 1996; Jakobsson *et al.*, 1997; Petsonk *et al.*, 2000; Littorin *et al.*, 2002; Lastbom *et al.*, 2003), animal studies indicate that relative potencies of different isocyanate compounds are variable (Pauluhn, 2000; Pauluhn *et al.*, 2002; Lee

et al., 2003; Pauluhn, 2004). Although with the number of different compounds, the use of a sum measure or possibly a marker compound is inevitable, it is desirable to also have information on the compounds behind these measures.

A shortcoming of the present study is that only short-term task-based samples have been taken. Short-term levels are more strongly influenced by exposure peaks than 8 h levels, resulting in high variability in exposure levels. During spray painting, within-worker variability ($_{ww}S^2$) is large compared with between-worker variability ($_{bw}S^2$) suggesting that variability in task-based exposure during spray painting over time is more prominent than differences in mean exposures between workers. However, next to true variability over time, this component also constitutes of sampling and analysis error. Measured concentrations can vary greatly with the location of the sampler on the body (Goller and Paik, 1985) and by spraying direction and orientation. Additionally, even when the individual analysis error per compound is <20%, when nine compounds are added up, the resulting error can be substantial. Kromhout *et al.* (1993) give an overview of within- and between-worker components of 8 h occupational exposure to chemical agents from different job titles throughout industry.

Although the $_{bw}R_{0.95}$ of 145 in the present study falls well within the reported range, the $_{ww}R_{0.95}$ of 140 000 is higher than the maximum $_{ww}R_{0.95}$ of 10 000 for 8 h measurements. Measurement time probably accounts for this difference. Conversely, the mix of tasks performed on different days and by different workers will introduce variability in full shift exposure levels that is not captured by task-based exposure measurements.

Despite the introduction of large variability, task-based sampling has many advantages like a more direct understanding of the sources of high exposure, exposure levels can be estimated for a whole range of task combinations and increased efficiency of the sampling campaign by focusing on high-risk tasks (Seixas *et al.*, 2003). In addition, although the relative importance of intensity, duration and frequency of exposure in relation to disease development and aggravation is not well understood, new exposure standards for isocyanates appear to be aimed at short-term high-level excursions rather than chronic low-level exposure (Sparer *et al.*, 2004). Short-term exposure peaks, which may be an important contributor to disease development or aggravation, are more easily identified using task-based measurements. However, when caused by an unusual or unforeseen exposure source like an incident or maintenance, peak exposure can also be missed by task-based sampling.

Another restriction of the present study is that only exposure outside the respirator has been measured. Sampling inside a facemask is complicated because

of interference with the worker and respirator. A study by Rosenberg and Tuomi (1984) indicates that if a combination of a charcoal and dust filter is used $\sim 100\%$ of the HDI and biuret is absorbed, and in case of a charcoal filter $\sim 100\%$ of the HDI and 70% of biuret is absorbed (Rosenberg and Tuomi, 1984). This results in protection factors from 2 to 5 (Torning *et al.*, 1990). However, the validity of these figures may be questionable since they are based on a small-scale study that may be outdated. A re-evaluation is justified. Possibly, exposure during cleaning of the spray gun, mixing or even tasks without direct exposure to isocyanates may result in higher actual exposures due to the absence of protection of inhalation filtering devices. Biomonitoring might give more informative insight into actual internal dose.

Additionally, the low response rate for car body repair shops may introduce selection bias. A small questionnaire on the reply form that was completed by 41 non-participating and 116 participating companies revealed that there was no difference in the presence of a spray booth. However, non-participating non-branch members were small (mean: 1.4 workers, SD = 0.8) compared with non-participating branch members (mean: 6.6 workers, SD = 3.3), participating non-branch members (mean: 8.6 workers, SD = 9.5) and participating branch members (mean: 9.5 workers, SD = 7.1). This implies that indications exist that the population is somewhat biased towards larger companies. However, no obvious effect of shop size on exposure levels could be observed.

Comparing isocyanate levels and frequency of detects between different studies is problematic. The field of isocyanate sampling and analysis is an active area of research for a number of reasons. New calibration standards are required because of the shift from monomers to oligomers and the new focus on thermal degradation products; decreasing exposure limits bring about the need for more sensitive methods; the high reactivity of isocyanates demands for a derivatization step immediately upon sampling; both aerosols and vapours need to be collected efficiently (Streicher *et al.*, 1994; Molander *et al.*, 2002; Streicher *et al.*, 2002). Consequently, several methods based on different reagents, sample collection and analysis methods have been and still are used resulting in variable compounds being measured, measurement times, LODs and units. The method used in the present study was chosen because of the efficiency of impingers to collect paint aerosols, and its ability to differentiate between and quantify isocyanate compounds including thermal degradation products. However, aspiration characteristics of impingers are much less described than aspiration characteristics of filter samplers.

Sparer *et al.* (2004) give a thorough summary of PU spray-painting levels of previous isocyanate sampling studies converted to the $\mu\text{g}/\text{m}^3$ NCO

metric. Despite differences in methods, conditions and analysed compounds, exposure to total NCO during spray painting in the present study ($<\text{LOD}-1124 \mu\text{g}/\text{m}^3$ NCO in car body repair shops and $0.2-2643 \mu\text{g}/\text{m}^3$ NCO in industrial painting companies) is in the same range as the summarized results. Because of the large proportion of non-detectable samples, it is only possible to compare exposure ranges.

Limited studies give task-based estimates for other tasks in car body repair shops or other spray-paint industries. An Australian study found exposures $\sim 1 \mu\text{g}/\text{m}^3$ NCO (never exceeding $2 \mu\text{g}/\text{m}^3$ NCO) during mixing and gun cleaning, and $6-19 \mu\text{g}/\text{m}^3$ NCO during sanding of painted cars (Pisaniello and Muriale, 1989). In a recent study, in the United States exposures of $<\text{LOD}-108.7 \mu\text{g}/\text{m}^3$ NCO for near spray activities, $<\text{LOD}-118.3 \mu\text{g}/\text{m}^3$ NCO for mixing and $<\text{LOD}-36.1 \mu\text{g}/\text{m}^3$ NCO for sanding are reported (Woskie *et al.*, 2004). In the present study, which is the first to assess non-spraying tasks in Europe, levels are mostly in the same range as the latter. A small-scale study on airborne thermal degradation products in car body repair shops showed exposure (sampled in impingers) to MIC, HDI, TDI and MDI ($<0.5-4 \mu\text{g}/\text{m}^3$ NCO) during welding and no exposure during grinding (Karlsson *et al.*, 2000). These compounds and levels are consistent with the compounds and levels found in the present study.

When comparing the present study with other studies where hygiene conditions have been described, it seems that hygiene conditions are more controlled in the present study (Pisaniello and Muriale, 1989; Sparer *et al.*, 2004). Spray booths with down draft ventilation systems, which result in lower exposure levels (Goyer, 1995; Sparer *et al.*, 2004), are widespread. All booths are manufacturer-built and filters are changed when pressure drops. Spraying of base coats outside the booth is always done in a spray bay with local exhaust ventilation. Surprisingly, exposure levels during PU spraying and other paint-related tasks do not seem to be lower than those reported in the other studies. In addition, no significant difference in exposure levels between car body repair shops and industrial spray painters, where hygiene conditions were also less controlled, could be demonstrated. This indicates that ventilation may not be an important determinant of isocyanate exposure.

Work in progress involves a more detailed evaluation of the exposure data to study exposure determinants and the effect of control measures as well as the exploration of the application of these data in combination with questionnaire data on job title and daily activities to estimate exposure in the epidemiological study.

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