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Evaluation of Hexamethylene Diisocyanate as an Indoor Air Pollutant and Biological Assessment of Hexamethylene Diamine in the Polyurethane Factories

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1. Introduction

Isocyanates are widely used in surface coatings, polyurethane foams, adhesives, resins, elastomers, binders, and sealants. In general, the types of exposures (inhale and dermal) encountered during the use of isocyanates (i.e., monomers, prepolymers, polyisocyanates, and oligomers) in workplace are related to vapor pressure of the individual chemical compounds (Bello *et al.*, 2002; Tury *et al.*, 2003). Isocyanates exist in many different physical forms in the workplace. The workers are potentially exposed to unreacted monomer, prepolymer, polyisocyanate, and/or oligomer species found in a given product formulation (Rosa *et al.,* 1999). They can also be exposed to partially reacted isocyanate containing intermediates formed in the course of polyurethane production (Woskie *et al.*, 2004; Tinnerberg and Sennbro, 2005). The second type of exposure might be more hazardous, as a number of isocyanates reactions are exothermic in nature and also evolve sufficient heat for the volatilization isocyanate compounds (NIOSH, 1994).

Isocyanate exposure is irritative to the skin, mucous membranes, eyes, and respiratory tract. The most common adverse health outcome associated with isocyanate exposure is asthma due to sensitization; less prevalent are contact dermatitis (both irritant and allergic forms) and hypersensitivity pneumonitis (Vandenplas *et al.*, 1992). Hexamethylene diisocyanate (HDI) is a colorless compound or may be slightly yellow liquid and is not much heavier than water (Adam *et al.*, 2002). This substance forms oily droplets in water and hydrolyses rapidly.

If isocyanates are inhaled, they are metabolised or broken down in body, eliminated and discharged through the urine. The metabolized form of Hexamethylene diisocyanate (HDI)

is hexamethylene diamine (HDA) which is an organic compound and isocyanate-derived diamines from protein which is conjugated with urine (Dalene *et al.*, 1994b, 1996; Williams *et al.*, 1999; Dalene, 2004). HDA has chemical formula of $H_2N(CH_2)_6NH_2$. The molecule is a diamine, consisted of a hexamethylene hydrocarbon chain terminated with amine.
The level of isocyanate metabolites in urine is an indicator of how much isocyanate has been absorbed and how well the pollution controllers and the prevention units are working. The levels of HDA are reported as "μmol/mol creatinine". The guidance standard value for HDA is at a level of 1 μmol/mol creatinine and each sample above the guidance standard value is an indication of exposure to contaminated environment (Williams *et al.*, 1999 and 2004).
The specific goals of this chapter are to answer the following questions:

- What are the determinants of HDI pollution level in the polyurethane factories?
- Does any correlation exist between HDI concentration from air sampling and HDA concentration from biological sampling (worker's urine sample) in the polyurethane factories?
- What is the pollution condition in terms of HDI and HDA concentration in the different selected factories?

2. Materials and methods

2.1 Polyurethane factories

In this study, five HDI polyurethane factories were selected for air sampling and biological monitoring. These factories are situated in three provinces namely T (factories coded as H_1 and H_2), K (H_3 and H_4) and M (H_5).
The main uses of HDI in the HDI factories (H_1, H_2, H_3, H_4 and H_5) are for the production of adhesives, process regulators and paints and lacquers and varnishes, as well as for the production of polishing paints and adhesives. 5 HDI polyurethane factories were selected for this study; the number of workers working in factories H_1, H_2, H_3, H_4 and H_5 were 265, 130, 320, 120 and 130, respectively.
The workers were exposed to HDI in the indoor environment. There were some workers who did not work full-time in the workplace; they worked as officers and sometimes came and went into workplaces and are identified as unexposed workers. In the HDI polyurethane factories all the exposed workers wear simple gloves and simple paper respirable mask (Model: 2600 Half-mask with elastic) when working at their workplaces in the factories.

2.2 Air sampling and analysis

There were two group workers in the polyurethane factories. The first group as office workers who had least exposure (n= 100). The second one were workers working inside factories (n= 400) and they were sufficiently exposed to HDI. Only five samples were collected from office spaces as blank samples for least exposed environment.
Sample handling and preparation include those steps taken to stabilize the sample or make the sample more compatible with the analytical procedure. Sample handling considerations actually began before sample collection. For air sampling in the field, sample pumps [low flow (SIBATA, MP302 Model) Japan] were attached to individual adsorbent tubes using 30 cm lengths of clear, inert polythene tubing suitable for low-level organic compounds. Each pump and tube assembly was calibrated using a bubble flow meter (SKC UK, UK) in order

to measure and adjust the sampling flow-rate precisely. The pumps were adjusted to provide a flow-rate of 2 L/min ~ Samples (static and personal) were taken adjacent to an operation where HDI was being handled in the factory for the periods of 2 h. On completion of field sampling, the tubes were sealed with vials end-caps and returned to the analytical laboratory. Samples were chilled to 2°C in a laboratory refrigerator and analysed within 24 h.

The first step in the analysis of a solution is derivatization of isocyanates for the separation through high-performance liquid chromatography (HPLC) for their qualitative as well as quantitative analysis. All the air samples were analyzed in the laboratory for HDI using HPLC through standard method of analysis (NIOSH, 1994)

2.3 Biological sampling and analysis

The biological sampling was carried out by collecting the workers' urine at the end of working shift; it was collected into polystyrene containers with citric acid and transferred to laboratory for GC Mass spectrometry analysis (Wu *et al.*, 1990; Williams *et al.*, 1999).

Due to the short half life (about 1.5 - 3 h) of HDA in urine, samples were collected at the end of the shift to detect any short term exposure as well as an estimation of the 8 h time weighted average exposure (Williams *et al.,* 2004).

In this study the urine samples were collected and dispatched in a similar way, frozen and sent blind to the laboratory for analysis. Based on Williams's method, subjects provided urine samples on the working day at the end of the working shift. The time of exposure and the personal protective equipment worn were recorded. For the factories securities, the samples obtained were labeled with code numbers and either the time or by sample number with other details like whether they were exposed worker, unexposed, or bystander.

2.4 Determinants of HDI pollution level

During air sampling for HDI concentration inside the factories, data for indoor relative humidity, indoor dry bulb temperature, altitude and dimension of factory were recorded. HDI was considered as dependent variable and the rest were independent variables. These independent indoor air variables were divided into two groups. Regression analysis procedure was used to state the statistical relationship between the variables and identify any meaningful relationship between those variables. Due to the fact that the number of independent variables was more than one, multiple linear regression analysis was used in the present analysis (Bahatin and Ibrahim, 2007). A multiple regression equation, which has four independent variables was used, and it can be expressed as follows:

$$Y = B_0 + B_1\,Rh + B_2\,Td + B_3\,D + B_4\,Alt + e_i \qquad (1)$$

where:

Y is the dependent variable (HDI concentration)

Rh, Td, D and Alt are independent variables (relative humidity, dry bulb temperature factory dimension and altitude,) as the predictors in this model.

B_0, B_1, B_2, B_3 and B_4 are the model coefficients.

e_i is the residual error

The values for the constant and the coefficients are determined using the least-squares method which minimizes the error as 'e' in the above regression equation. The significance level of the constant and coefficients are statistically tested using t-distribution. The R^2

(coefficient of determination) determines the direction and significance level of relation between the variables in the mathematical model and shows how much the dependent variable is affected by the independent variables. All statistical analysis was performed using SPSS software Ver.16. In this study the alpha level is 0.05 ($P \leq 0.05$) similar to other indoor air pollution studies (Marek *et al.*, 1999; Molander *et al.*, 2002; Dalene, 2004).

3. Results and discussion

3.1 Air sampling and indoor air variables

The sampling protocols described in NIOSH Method 5522 were used throughout the experiments. The psychrometric parameters (relative humidity and dry bulb temperature) and factory parameters (dimension of factory and altitude) were measured for all HDI polyurethane factories and work stations. A total of 300 air samples were collected randomly from working places inside the 5 factories for the exposed workers (20 samples per each HDI factory and for three times per working shift).
Table 1. shows the maximum, minimum and mean values of indoor air independent variables with respect to HDI concentration in the polyurethane factories. The lowest minimum HDI concentration in all the factories was 61 μg/m³ and also the highest of the maximum HDI concentration was 96 μg/m³. These values can be considered as high, when compared to NIOSH exposure limit of 35 μg/m³. The mean HDI concentration was 78.8 μg/m³, the mean indoor relative humidity was 37.7%, and the mean dry bulb temperature was 28.3°C. The size of workplace for the five polyurethane factories ranged from 5,000 to 9,800 m³ and the altitude of factories were from as low as 22 to as high as 1200 m.

Average	H_5	H_4	H_3	H_2	H_1	Factories code Variables
						HDI concentration
91.2	88	90	90	92	96	(μg/m³), Max
64.8	61	64	66	66	67	Min
78.8	76.7	77	78.7	79.8	82.2	Mean
						Relative Humidity (%),
46.8	40	45	45	52	52	Max
31.2	31	31	31	31	32	Min
37.7	34	37	37	40	40.5	Mean
						Dry bulb temperature (°C),
31.8	30	32	32	32	33	Max
24	23	24	24	24	25	Min
28.3	27.1	28.7	28.7	27.8	29.3	Mean
7460	9800	9000	7400	6100	5000	Dimension of factory (m³)
882	22	890	1100	1200	1200	Altitude (m)

Table 1. Values of indoor air variables in the HDI polyurethane factories

It has been summarized and stated in Table 1. that several factories show variable concentration of diisocyanates, with respect to relative humidities of each factory. The highest mean value HDI concentration was 82.2 μg/m³ which corresponds to the highest mean relative humidity of 40.5% inside of factory H_1. Factories H_1 and H_2 were located in T province. Factory H_2 had the second highest mean HDI concentration and also the second highest mean relative humidity (79.8 μg/m^3 and 40%, respectively). Factory H_5 had the lowest mean value HDI concentration which was 76.7 μg/m^3. Factory H_5 was situated in M province and this factory had the lowest mean relative humidity of 34%.

3.2 Relationship of HDI and indoor air variables

In this study, the data (n = 100) of psychrometric parameters (indoor relative humidity and dry bulb temperature) and factory parameters (factory dimension and altitude) were collected and used to predict HDI pollution level. Correlation analysis was carried out after checking the normality assumptions for both variables, all parameters are strongly correlated with HDI concentration where $P < 0.05$. The calculated R^2 values for RH is 0.5461 (R^2= 0.739^2), Td is 0.77 (R^2=0.88^2), D is 0.8767 (R^2= -0.887^2) and Alt is 0.7225 (R^2= 0.85^2). Since all parameters are strongly correlated, all of them are put in the regression model. Table 2. showed the regression model summary where it can be seen that 83.7% of the HDI concentration can be attributed to any or all the independent variables (relative humidity, dry bulb temperature, dimension and altitude) (R^2 = 0.837).

Model	r	R^2	Adjusted r^2
	0.915	0.837	0.83

Predictors: (Constant), Altitude (m), Dimension of factory (m^3), Relative humidity (%), Dry bulb temperature (ºC)

Table 2. Regression model summary of HDI

The results of the summary imply that all or some of parameters (altitude, dimension of factory, relative humidity and dry bulb temperature) can be significant predictors of HDI concentration in the polyurethane workplaces.
Table 3. below reports an analysis of variance for HDI concentration in the polyurethane factories. From the table, it can be seen that *F* is 121.9 which is significant at $P < 0.05$. We can conclude that the regression model predicts the concentration level of HDI significantly well.

Model		Mean Square	F	P value
	Regression	1155.895	121.934	0.0001
	Residual	9.48		
	Total			

Predictors: (Constant), Altitude (m), Dimension of factory (m^3), Relative humidity (%), Dry bulb temperature (˚C), Dependent Variable: HDI concentration (μg/m^3)

Table 3. Regression model for HDI polyurethane factories factors

Since the results of regression model test in Table 1.3 illustrate that the independent variables are significant predictors of HDI concentration, we can employ equation 1.1 to stand for the different psychrometric and factory parameters in order to measure the predictive regression correlation between the parameters and HDI concentration.
Table 4. shows the results of regression analysis between HDI concentration and polyurethane indoor air parameters. Both indoor relative humidity and dry bulb temperature can be seen to be significant predictors of HDI pollution ($P< 0.05$). Both of these parameters fall under the

psychrometric parameters group. The other two parameters (factory dimension and altitude) are the factory parameters and both are not significant (P>0.05).

Model		Coefficients		T	P-value.
		B	SE		
	(Constant)	43.267	17.837	2.426	0.017
	Relative humidity (%)	0.367	0.071	5.182	0.0001
	Dry bulb temperature (˚C)	1.112	0.399	2.785	0.006
	Dimension of factory (m^3)	-0.001	0.001	-1.479	0.142
	Altitude (m)	0.003	0.002	1.475	0.144

Dependent Variable: HDI concentration (μg/m^3)

Table 4. Result of regression analysis between HDI concentration and polyurethane indoor air parameters

The independent variables (relative humidity and dry bulb temperature) were reproduced for the model to find the regression coefficients for HDI pollution in the polyurethane factories. The coefficients with respect to the constant, relative humidity and the dry bulb temperature as well as the collinearity statistics are shown in Table 5.

Model		Coefficients		t	P value	Collinearity Statistics	
		B	SE			Tolerance	VIF
	(Constant)	27.771	2.638	10.528	0.0001		
	Relative humidity (%)	0.368	0.067	5.454	0.0001	0.592	1.689
	Dry bulb temperature (ºC)	1.492	0.119	12.588	0.0001	0.592	1.689

Dependent Variable: HDI concentration (μg/m^3)

Table 5. Collinearity statistical model coefficients

The Variance Inflation Factor (VIF) measures the impact of collinearity among the variables in a regression model. Myers (1990) suggests that a value of more than 10 means there is a concern to worry about collinearity. Menard (1995) suggests tolerance (or 1/VIF) below 0.2 indicates a potential collinearity problem. For the current work, the suggestion by Myers (1990) is used and it can be seen in Table 1.5 the VIF values are well below 10 and the tolerance is above 0.2 indeed. Therefore, it can be safely said that there is no collinearity within the current data.

The two factory predictor variables (dimension of factory and altitude) were found to be not significant in the model. They were eliminated for making a new regression model based on relative humidity and dry bulb temperature. By replacing Y, X_1 and X_2 with HDI, Rh (relative humidity) and Td (dry bulb temperature), respectively and eliminating X_3 (factory dimension) and X_4 (altitude) and also substituting the relevant coefficients from Table 5., Equation 2, can be written as follows:

$$HDI = 27.77 + 0.368Rh + 1.492Td \quad (2)$$

Equation 2 implies that relative humidity and dry bulb temperature affect diisocyanates pollutant concentration in the work places. The background HDI concentration was about 27.77μg/m³ as indicated by the value of the constant in the regression equation.

3.3 HDI concentration determinants

Figure 1. shows the relationship between HDI concentration and psychrometric parameters (relative humidity and dry bulb temperature) in five polyurethane factories based on equation 1.2.

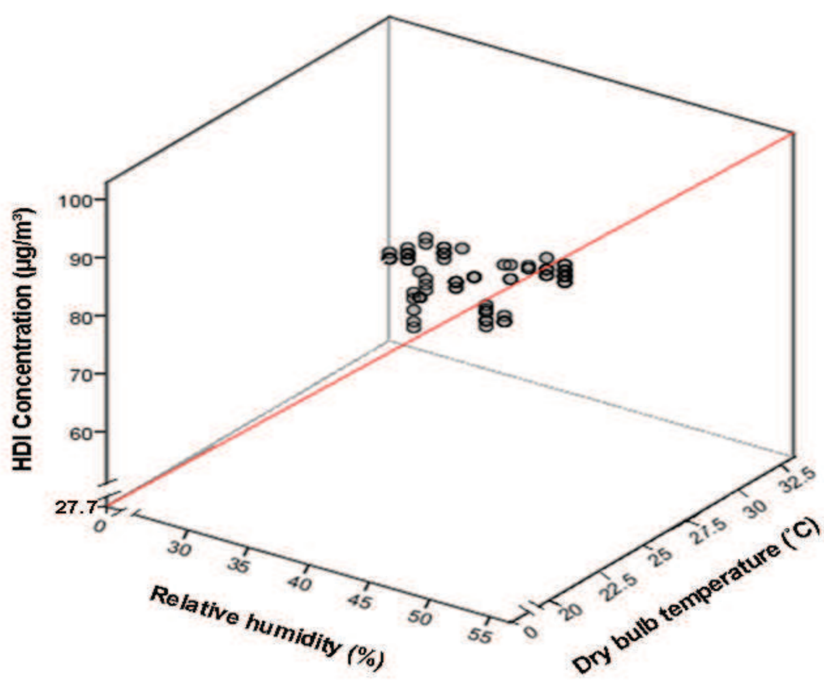


Fig. 1. Relationship between HDI concentration and psychrometric parameters (relative humidity and dry bulb temperature)

Both indoor air relative humidity and dry bulb temperature are significantly contributing to the variability of the HDI concentration ($R^2 = 0.837$) and both factors also show a straight positive relationship with the HDI concentration. This means that as the indoor relative humidity or the dry bulb temperature increases, the HDI concentration also increases.

As for the effects of relative humidity on isocyanate concentration, Ludwig and Urban (1996) observed that reactions of isocyanate groups with OH groups during cross-linking are inversely proportional to the relative humidity of the environment. They explained that the presence of competing reactions between water and isocyanate, hinder the degree of cross-linking between them. Abram and Bowler (2005) studied the effect of relative humidity on the curing and dielectric properties of the polyurethane-based composites. They have found that a polyurethane factory at 87% relative humidity (RH) gave more noticeable effect as compared to one at 37.7% RH. The electromagnetic properties of the polyurea/polyurethane-based composites studied were found to be strongly influenced by the presence of water vapor during the curing process, as evidenced by the significant difference in the real relative permittivity of samples cured in different RH environments.

This difference was caused primarily by water uptake into the polymer matrix. The RH alters the dielectric properties of the composite material due to its strong polar nature and high value of real relative permittivity. In this study, the RH was in the range of 31 to 52%. The working range for RH in this study is lower than that reported by Abram and Bowler (2005) for the noticeable effects (87% RH). Hence the effect of RH is expected to be not as significant as to the effects of temperature.

The mean isocyanate concentration in this study was 78.87µg/m^3 (0.079mg/m^3). This is comparable to an investigation conducted in southern Australian auto body shops which reported a geometric mean concentration of 0.07 mg/m^3 isocyanates (range <0.01–3.5 mg/m^3 NCO) (Pisaniello and Muriale, 1989). Swedish auto body shops exposures during spray painting showed higher values between 0.26 and 1.1 mg/m^3 (Torling *et al.*, 1990). A survey of Oregon auto body shops measured a geometric mean concentration of 0.35 mg/m^3 isocyanate with a maximum of 4 mg/m^3 isocyanate (Janko *et al.*, 1992). Maître *et al.* (1996) have reported an arithmetic mean level of 0.33 mg/m^3 isocyanate (range 0.05–0.65 mg/m^3) in a French isocyanates spray factory. These findings suggest that the measurements in this research are comparable to other related literatures. However comparison of such results is quite difficult because of the sampling time, sampling method and manufacturing process were totally different (Maître *et al.*, 1993).

Previous studies often involved isocyanate exposure levels in auto body shops (Pisaniello and Muriale, 1989; Torling *et al.*, 1990; Woskie *et al.*, 2004) and up to date little work has been done to evaluate the determinants of isocyanate concentration levels in factories producing polyurethane foams with respect to HDI and indoor air quality variables. The current work points to psychrometric factors (indoor air temperature and relative humidity) as important predictors of HDI within the factories. Woskie *et al.* (2004) have pointed out that for small, low volume auto body shops as a consistent predictor of higher exposures especially during the colder months when buildings were closed up and general ventilation was reduced. However in this research dimension or size of the factories along with the altitude were seen to be not significant as HDI pollution determinants. Large size factory has difficulty in interpretation. For instance, Woskie *et al.* (2004) in a work based on auto body shops pointed that 'large shop' might mean more activities or jobs per day or a larger less cramped work area with greater general dilution ventilation.

The current work admittedly has limitations but may be a useful initiative in estimating possible HDI pollution situation in the polyurethane workplaces based on indoor air temperature and relative humidity. It can hopefully help to provide a basis to prioratise future exposure evaluation and intervention efforts and reduce the workers to exposure to isocyanates which are well known as asthmagens and respiratory irritants.

3.4 Biological monitoring

The aims of the present investigation regarding biological monitoring are to: (i) show the relationship between air pollution and exposed worker health; (ii) characterize worker diisocyanate exposure and examine the relative negative impact of pollution and inhalation routes in HDI polyurethane factories.

3.4.1 Subject individual characteristics

Individual exposure data as well as information regarding each individual were extracted, pooled, and entered into SPSS, V. 16 software for statistical analysis. The sample size for biological monitoring was 50 workers. At the end of the shift, workers took a shower and changed clothes before going to the factory's medical service in order to give urine samples. All samples were collected in polystyrene bottles containing 10 g citric acid, and stored at 4 °C until analysis. A negative ion chemical ionization mass spectrometry was used to determine the urinary HDA.

Table 6. describes the mean age of workers, who work in the HDI polyurethane factories was 34.5 years. The mean duration of work history was 4.9 years and the mean weight of the workers was 69.6 kg.

	N	Mean	SD	Min	Max
Age (year)	50	34.48	7.465	24	47
Weight (kg)	50	69.64	12.348	50	88
Work history (year)	50	4.74	2.94	2	13

Table 6. Characteristics of subjects

Table 7. shows that 54% of total workers, working in the HDI factories were categorized as smokers and also the same percentage of HDI workers had some symptoms [sore eyes, running nose, sore throat, coughing, wheezing (asthma) and chest tightness] relevant to diisocyanates exposure.

Variables	N	Percent
Smoking	27 – Smoker	54
	23 - None	46
Symptoms of disease	27- with	54
	23- without	46

Table 7. Frequency and percentage of smokers and symptoms of disease

Table 1.8 shows the age, weight and years of the services of the workers in the HDI factories. The information is presented in terms of the ranges, frequency and percentage.

Variables	Range	Frequency	Percent
Age (year)	20-30	19	38
	31-40	16	32
	41-50	15	30
Weight (kg)	40-60	20	40
	61-80	11	22
	81-100	19	38
Years of services (year)	0-5	35	70
	6-10	10	20
	11-15	5	10

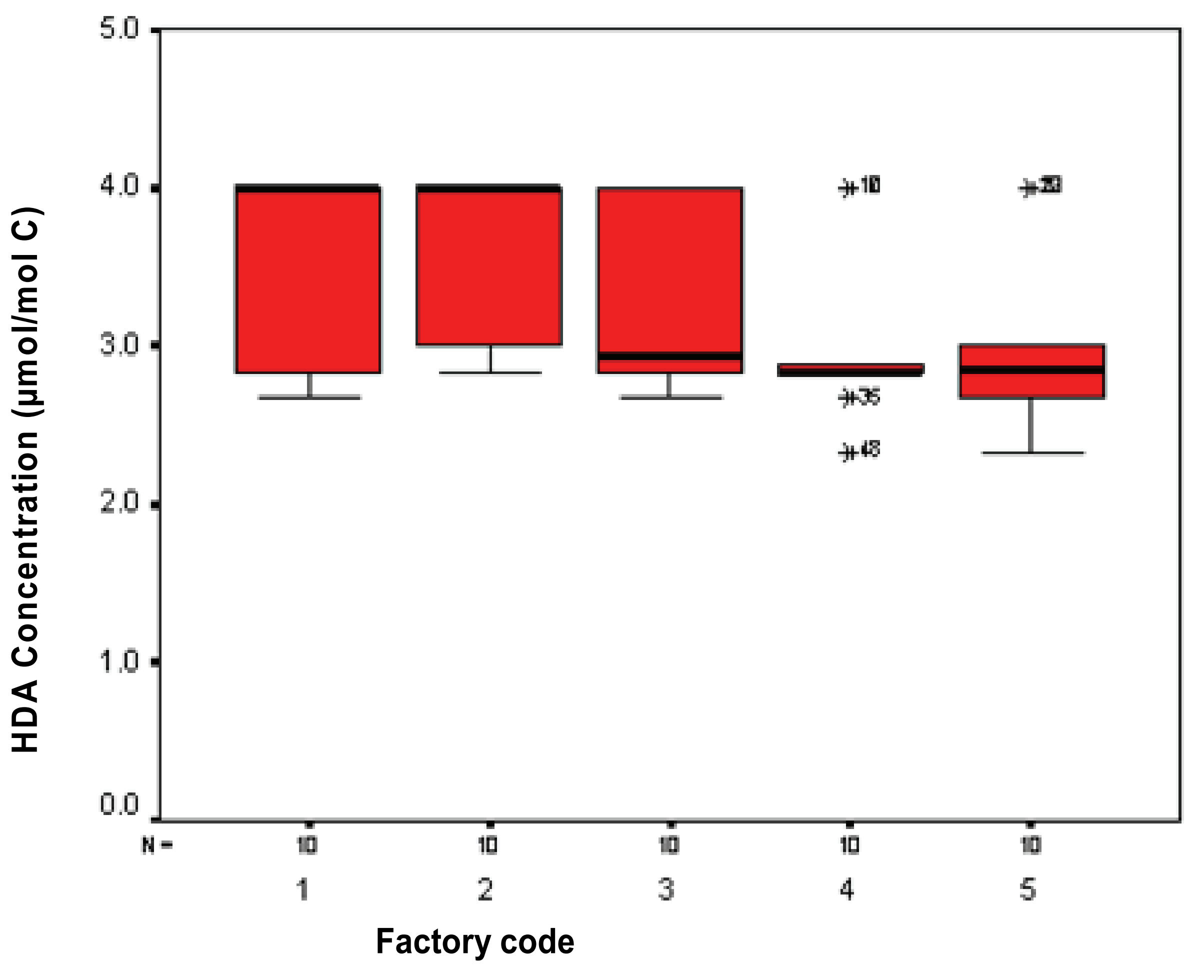
Table 8. Statistical data for the age, weight and years of services of the workers

3.4.2 Urinary concentration of HDA in the factories

Table 9 shows the descriptive statistics of urinary hexamethylene diamine (HDA) in different factories. The maximum concentration of HDA measured from worker's urine in the HDI polyurethane factories was 4 µmol/mol creatinine and the mean value was in the range of 3.01 to 3.58 µmol/mol creatinine for all factories. The urine results for all of the workers indicated high exposure with respect to HDI, because of the lowest concentration of HDA in their urine was 2.33 µmol/mol creatinine.

Factory code	**Mean**	**SD**	**Minimum**	**Maximum**
H_1	3.52	0.630151	2.67	4
H_2	3.58	0.540577	2.83	4
H_3	3.30	0.604230	2.67	4
H_4	3.01	0.547881	2.33	4
H_5	3.01	0.553021	2.33	4

Table 9. Descriptive statistics of hexamethylene diamine (HDA) in different factories (n= 10)



Note: Guideline value: 1 µmol/mol creatinine (Williams et al., 1999)

Fig. 2. HDA concentrations in different factories

Figure 2. indicates different HDA concentration compare to different factories because there are some factors that affected on workers exposure in the different work area, for example working process, space of work station, etc.

3.4.3 HDI and HDA relationship in the factories

Fifty male workers in the five polyurethane factories, in an age range of 20-50 years, participated in the present investigation. They were engaged in injection glue device, painting sprayer and varnishing. Based on the diisocyanates biomonitoring method (Rosenberg *et al.*, 1986; Skarping *et al.*, 1995; HSE, 2005), the urine samples were collected at the end of exposure. This is due to the urinary half-life is about 2 hours and results reflected after 2 – 4 h exposure. Table 1.10 shows the HDA values in the urine associated with HDI concentration for the 50 workers. Air samples taken near the gluing operation contained high concentration of HDI (83.1 to 92.7 μg/m^3) as compared to the other operations. The workers at the gluing operations also showed high urinary HDA concentration of between 2.88 to 4 μmol/mol creatinine. Workers involved in other operations had lower HDA concentration in their urine and also they had lower values of HDI exposure. The lowest HDI exposure was in varnishing operation (62.24 μg/m^3) where the HDA value was found to be also the lowest at 2.33 μmol/mol creatinine but the value is also above the guideline value of 1 μmol/mol creatinine (Williams *et al.*, 1999).

Subject Frequency	Operation	HDI (μg/m^3)	HDA (μmol/molC)
4	Gluing	92.7	4
4	Gluing	90.1	2.88
3	Gluing	87.62	2.88
3	Gluing	85.67	2.88
3	Gluing	83.1	4
4	Paint sprayer	80.57	2.88
3	Paint sprayer	79.29	2.88
3	Varnishing	78.38	2.88
3	Paint sprayer	74.67	2.88
3	Paint sprayer	68.5	3
4	Paint sprayer	67.72	2.83
3	Varnishing	66.94	2.83
3	Paint sprayer	65.33	2.67
3	Paint sprayer	64.11	2.67
4	Varnishing	62.24	2.33

Table 10. Exposure to HDI and excretion of HDA in workers urine (n=50)

Table 11. shows the correlated results between HDI concentration in the air and HDA in the urine sample taken from workers. It can be seen that HDI concentration in the air is directly related to HDA concentration in the urine of workers with a Pearson correlation coefficient at $r = 0.857$ and the significance value is less than 0.001. This means that, as the HDI concentration in the air in factories increase, the HDA level in the urine of workers also increase.

The regression model summary for HDI and HDA is shown in Table 12. It indicates that the value of R^2 is 0.735. This means that the exposure to HDI pollution in the factories account for 73.5% of the level of HDA in the workers' urine.

Table 12. shows the F-test in the regression analysis; it is a relationship test between HDI in air samples and HDA in urine samples. For these data F is 133.247, which is significant at $P< 0.05$. Thus the regression model predicts the exposure to HDI pollutant significantly well.

		HDA Concentration	HDI Concentration
Pearson Correlation	HDA Concentration	.	0.857
	HDI Concentration	0.857	1
Sig. (2-tailed)	HDA Concentration	.	0.0001
	HDI Concentration	0.0001	.
N	HDA Concentration	50	50
	HDI Concentration	50	50

Correlation is significant at the 0.05 level.

Table 11. Generalized correlation HDI concentration and HDA

Model		Sum of Squares	F	P value
	Regression	13.161	133.247	< 0.0001
	Residual	4.741		
	Total	17.903		

(Constant), HDA Concentration, HDI Concentration

Table 12. Generalized regression model for HDI and HDA

The regression model used in this study is a simple linear model in the form of

$$Y = B_0 + B_1 X_1. \tag{3}$$

From Table 13, B_0 is -0.62 and B_1 is 0.051.

Since B_0 is rather small in magnitude, the B_0 value can be ignored but B_1 is significant in model ($P< 0.05$). The predictive relationship for HDI and HDA can be suggested in a linear regression equation ($R^2= 0.735$) as shown in Equation 4:

$$HDA = 0.051\ HDI \tag{4}$$

where

HDA is dependent variable

HDI is independent variable

Model		Coefficients		T	P value
		B	SE		
	(Constant)	-0.62	0.341	-1.818	0.075
	HDI Pollution	0.051	0.004	11.543	0.0001

a Dependent Variable: HDA Concentration

Table 13. Generalized regression model coefficients for HDI and HDA

Figure 3. shows the graph for the relationship between factory air HDI concentration and urine HDA concentration of the workers. The graph shows a linear relationship between HDI and HDA. No background HDA was detected in the workers and the graph validates HDA as an initial indicator of a preceding exposure of workers to HDI with $R^2 = 0.735$.

In a related research conducted by Maitre *et al.* (1993) focusing on biological monitoring of occupational exposure among nine (9) workers; they were exposed to toluene diisocyanate (TDI) in TDI-based polyurethane production. The study has validated the use of urinary

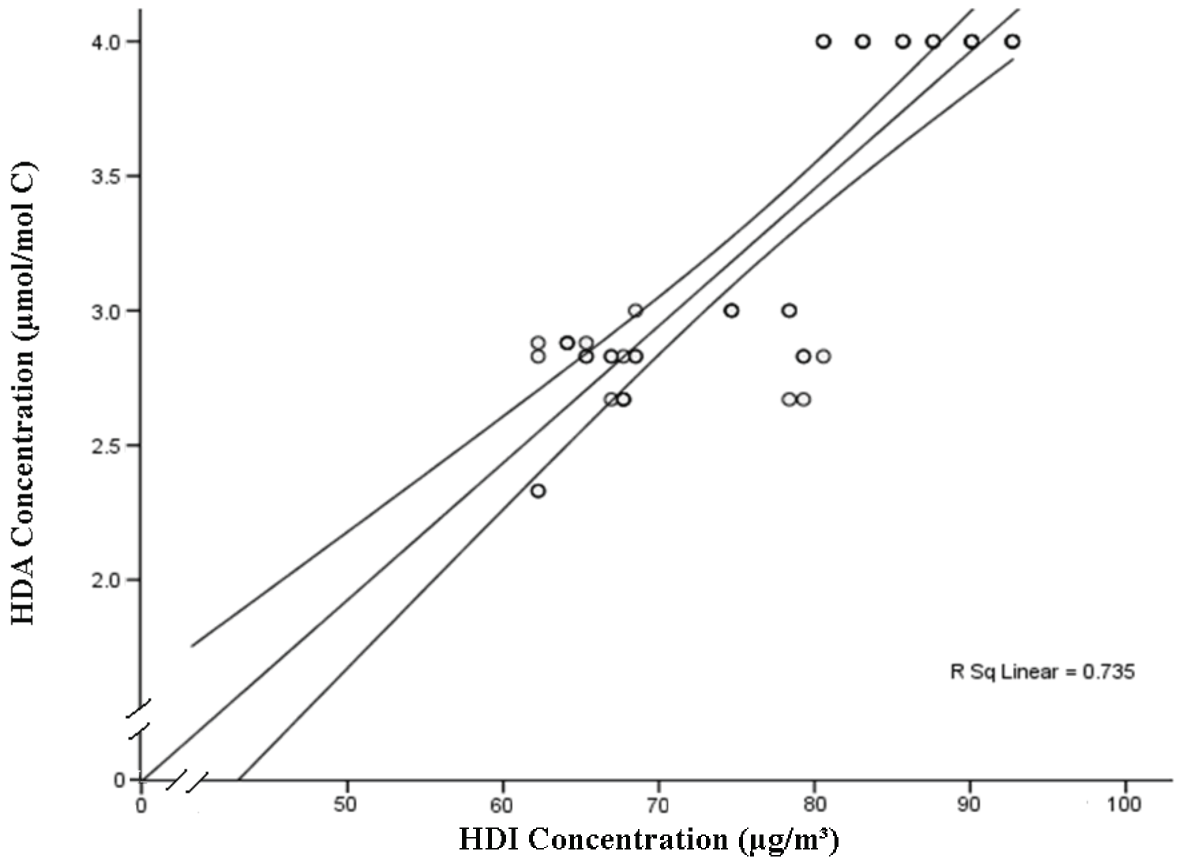


Fig. 3. Relationship between air HDI concentration and urinary HDA concentration

toluene diamine (TDA) as an indicator of preceding exposure to TDI. Their TDI exposure level was 9.5 to 94 µg/m³, and TDA concentrations varied from 6.5 to 31.7 µmol/mol creatinine. TDI and TDA were found to be linearly related and no background TDA was detected. It was noted that the workers in the research carried out by Maitre *et al.* (1993) did not wear personal protective equipment and there was also no ventilation system. That possibly explains the higher values of TDA and TDI. The workers were also engaged in different jobs (injection molding, mold stripping, cutting and gluing foam). Some were directly exposed and some were indirectly exposed to isocyanates.

In glue injection, the concentration of exposure to HDI in the air was higher than the working area near the paint spraying area or varnishing. In the other study, a high levels exposure has also been found by Lesage *et al.* (2001) at isocyanate injection workplace. The concentrations of HDA detected in this study are less than those found in the other studies (Brorson *et al.*, 1990; Maitre *et al.*, 1993). Brorson *et al.* (1990) have reported a mean value of HDA by the end of the shift was 20 µmol/mol creatinine after 7.5 h exposure to 25 µg/m³ HDI. Whereas Maitre *et al.* (1993) have measured a value of 12 µmol/mol creatinine for HDI exposure at the same concentration from a separate survey of workers.

In a developing country, the above situations reinforced the reasons why Kakooei *et al.* (2006) had expressed the importance of studying indoor air pollution in such industries. For the imported technology and the machinery used without suitable application of adequate engineering controls and proper safe work practice together with the levels of training and awareness can cause great exposure to air pollutants and may result in more occupational health problems than in the developed countries.

In a similar study that has been conducted by Cocker (2007) the urine samples which were also analysed for the diamine metabolites of hexamethylene diisocyanate had detectable levels with 22 μmol/mol creatinine. This value was much higher than that the maximum urinary concentration of the current study (4 μmol/mol creatinine).

Comparison of obtained results with previous work was difficult; because of the sampling time, sampling method, and manufacturing process were totally different. The present study detected a straight correlation between the isocyanate concentration in the air and its biological results in the workers' urine. The obtained biological results from the present conducted research was lesser than that of the results reported by Lesage *et al.* (2001) that was related to manufacturing of foam plants.

The obtained results from the analysis of worker's urine showed that all of the workers were exposed via isocyanates in their workplaces based on guidance value for HDA. This implies that the high level of metabolites concentration in the urine of the workers can be attributed to the polluted situation of the workplaces. The concentrations of diisocyanates metabolite detected in the polyurethane workers were higher than the guidance value (>1 μmol/mol creatinine). However, this result is low compared to work performed by Brorson *et al.* (1990) where it was reported that the mean value of isocyanates metabolite at the end of working shift was 20 μmol/mol creatinine. Similarly, Maitre *et al.* (1996) have measured a value of 12 μmol/mol creatinine for diisocyanates exposure at the same concentration from a survey of workers.

The result of present investigation showed that the HDA concentration was also less than the research conducted by Tiljander *et al.* (1989) in US polyurethane factories for methylene diamine (5-30 μg/l in urine) and it was similar to results that have been reported by Selden *et al.* (1992).

The results of present study showed that biological monitoring can be a useful tool to assess isocyanate exposure in this group of exposed workers in the polyurethane factories. This work is comparable to the biological monitoring work done by Williams *et al.* (1999) when assessing exposure from use of isocyanates in motor vehicle repair-shop. They have noted that urinary biological monitoring has the potential to measure a worker's body burden received by all routes of exposure (oral, inhalation and dermal). However biological monitoring does not determine the route of exposure which means exposure could have been through any of the three methods although inhalation is the most likely route given the lack of published evidence for the absorption of isocyanates through the skin (Williams *et al.*, 1999).

Tinnerberg and Sennbro (2005) have cautioned that both air and biological monitoring methods have limitations. They have discussed that the exposures are complex and different in various environments. In their studies, biological monitoring has been used as a standard method to survey the exposure to aromatic diisocyanates and air monitoring to assess peak exposures and to find emission sources. They have also found that by using biomarkers it was easier to collect and analyse more samples as the sampling was not as time-consuming as air monitoring. Analyzing urine may be simple however in this study, it was also noted that the workers were quite reluctant to give their urine possibly due to urinary analysis is often associated to drug screening tests.

3.4.4 HDI work-related disease risk assessment

Diisocyanate work-related disease risk assessment is defined as an estimate of daily human exposure to diisocyanates pollution (HSE, 2005). Risk assessment is derived whilst adequate data exist to identify the high risk factors in the polyurethane factories. Eventually, it is important to comprehend how HDI interact with humans, with other species and physical

environment. The risk assessment regression model summary where about 89.5% of the HDI risk can be attributed by any or all the independent variables (age and weight of workers, smoking, years of services and HDI pollution level) ($R^2 = 0.895$, Adjusted $R^2 = 0.883$).
A multiple linear regression analysis was performed to evaluate individual factors for developing asthma induced by diisocyanates (Table 14.). Two factors were statistically related to risk of work-related disease of diisocyanate at the 0.05 significance level. These were: (*a*) weight of exposed workers, (*b*) HDI pollution. None of them had experienced previous incidents of exposure to diisocyanates.

Model		**Coefficients**		**t**	**P value.**
		B	SE		
	(Constant)	0.201	0.171	1.178	0.245
	HDI Pollution	0.631	0.112	5.612	0.0001
	Age	-0.030	0.031	-0.972	0.336
	Smoking	-0.049	0.095	-0.512	0.611
	Weight	0.218	0.087	2.509	0.016
	Years of services	0.046	0.040	1.134	0.263

Dependent Variables: Symptoms of HDI work-related disease

Table 14. Regression summary model for HDI work-related disease risk assessment

Risk assessment of exposure to diisocyanates among 50 workers increased with HDI pollution with potentially higher exposure with trends in TWA concentrations with regard to individual parameters (workers' weight and HDI pollution) (Redlich and Meryl, 2002).
For HDI work-related disease risk assessment were assessed for possible risk factors experiencing an exposure to diisocyanate through inhalation. The assessment was based on determining the total risk set at the time of each event and accumulating evidence across events in favor or against specific associations. The likelihood of HDI work related disease risk assessment was not statistically related to age, history of work, or current level of cigarette smoking and years of services in the factory. In this study significant associations were found for diisocyanates concentration (expressed as a TWA) and workers' weight and HDI pollution. There was a strong correlation between symptoms of HDI work-related disease and the two independent variables (workers' weight and HDI pollution), as summarized in Table 15.

Model		**Sum of Squares**	**F**	**P value**
	Regression	1412.599	117.938	< 0.0001
	Residual	105.401		
	Total	1518.000		

Predictors: (Constant), HDI pollution, workers' weight. Dependent Variable: Symptoms of HDI work-related disease

Table 15. Summarized model for isocyanates risk assessment

Under ascertainment is less likely among long term workers at the factories because of the asthmatic people who continue to work in exposed areas often develop increasingly severe symptoms, but surprisingly, there is no significance between years of services and incidence of work-related disease for diisocyanates workers. The result of this study is similar to the other research conducted by Diem *et al.* (1982) and Weill *et al.* (1981). The present study detected the effects of weight of the workers on HDI work-related disease and the results were similar to the study conducted by Lange *et al.* (1998).

4. Conclusion

Both indoor air relative humidity and temperature significantly contribute to the variability of the HDI concentration ($R^2 = 0.837$) and both factors also showed a linear relationship with the HDI concentration. The relationship between HDI and relative humidity and indoor air temperature was found through multiple linear regression according to equation 1.2.

$$HDI = 27.77 + 0.37\ Rh + 1.49\ Td \qquad (2)$$

It was also shown that urinary HDA is detectable following HDI exposure. Urinary HDA concentration of the workers was found to be linearly related to HDI concentration of the air in the factories as correlated by following relation:

$$HDA = 0.051\ HDI \text{ with } R^2 = 0.735. \qquad (4)$$

The HDI work-related disease risk assessment of the present study showed that two personal and work condition variables were correlated with Symptoms of HDI work-related disease in the polyurethane factories (workers' weight and HDI pollution).
Finally, this study has shown that air monitoring together with biological monitoring can be used to estimate the HDI pollution situation as well as the exposure to workers of polyurethane factories. Such a study at polyurethane factories having more than 100 workers in a factory is not known till to date. Future research should focus among others on HDI exposure in relation to outdoor psychrometric factors, ventilation or application of adequate engineering controls, respiratory protective equipment, behavioral issues, the levels of training and awareness, occupational health background as well as the usage of other possible biomarkers of HDI.

5. References

Abram, E R. and Bowler, N. (2005) Effect of relative humidity on the curing and dielectric properties of polyurethane-based composites. This paper appears in: *Electrical Insulation and Dielectric Phenomena, 2005. CEIDP '05. 2005 Annual Report Conference on Publication* Date: 16-19 Oct. 2005

Adam, V. Wisnewski., Qing, L., Jing-Jing, M., Nadine, M. and Carrie, A R. (2002) Effects of hexamethylene diisocyanate exposure on human airway epithelial cells: in vitro cellular and molecular studies. *Environ Health Perspect.* 110 (9): 901–907.

Bahattin, M., and İbrahim, K. (2007) The Relation Between Meteorological Factors and Pollutants Concentrations in Karabük City. G.U. *J Sc.* 20 (4): 87-95

Bello, D., Streicher, R P. and Woskie, S R. (2002) Evaluation of the NIOSH draft method 5525 for determination of the total reactive isocyanate group (Trig) for Aliphatic Isocyanates in auto body repair shops. *J Environ Med.* 4:351–360.

Brorson, T., Skarping, G. and Nielsen, J. (1990a) Biological monitoring of isocyanates and related amines. II. Test chamber exposure of humans exposed to 1,6-hexamethylene diamine as the trifluoroethyl chloroformate derivative. *Int Arch Occup Environ Health.* 62: 385-389.

Cocker, J. (2007) Biological monitoring for isocyanates. *Occupational Medicine*. 57: 391–396.

Dalene, M., Skarping, G. and Brorson, T. (1996) Chromatographic determination of amines in biological fluids with special reference to the biological monitoring of isocyanates and amines. IV. Determination of 1, 6-hexamethylenediamine in human urine using capillary gas chromatography and selective ion monitoring. *J Chromatogra A.* 516: 405– 413.

Dalene, M., Skarping, G. and Tinnerberg, H. (1994b) Biological monitoring of hexamethylene and isophorone isocyanate by the determination of hexamethylene and isophorone diamine in hydrolysed urine using liquid chromatography and mass spectrometry. *Analyst.* 119: 2051–2055.

Dalene, M. (2004) Determination of airborne isocyanates as di-*n*-butylamine derivatives using liquid chromatography and tandem mass spectrometry. *Anal Chim Acta.* 534, 263–269.

Diem, J E., Jones, R N. and Hendrick, D J. (1982) Five year longitudinal study of workersemployed in a new toluene diisocyanate manufacturing plant. *Am Rev Respir Dis*. 126: 420–428.

HSE. Health and Safety Executive. (2005) Methods for the determination of hazardous substances; MDHS 25/3. Organic isocyanates in air. *Sudbury UK*: Health and Safety Laboratory.

Janko, M., McCarthy, K., Fajer, M. and van, Raalte, J. (1992) Occupational exposure to 1, 6-hexamethylene diisocyanate- based polyisocyanates in the State of Oregon, 1980–1990. *Am Ind Hyg Assoc J.* 53:331–338.

Kakooei, H., Shahtaheri, S J. and Karbasi, H A. (2006) Evaluation of workers' exposure to methylene diphenyl diisocyanate (MDI) in an automobile manufacturing company, Iran. *Int J Occup Saf Ergon*. 12(4): 443-449.

Lange, P., Parner, J. and Vestbo, J. (1998) A 15-year follow-up study of ventilatory function in adults and asthma. *N Engl J Med.* 339:1194–1200.

Lesage, J., Carlton, G., Streicher, R. and Song, R. (2001) Erratum to "comparison of sampling methods for monomer and polyisocyanates of 1,6-hexamethylene diisocyanate during spray finishing operations. *Appl Occup Env Hyg* Jan; 16(1):11- 17.

Ludwig, B W. and Urban, M W. (1996) Quantitative determination of isocyanate concentration in crosslinked polyurethane coatings. J Coating Techn. *Available from Word Wide Web*: *www.superiortire.com*

Maitre, A., Berode, M., Perdrix, A., Romazini, S. and Savolainen, H. (1993a) Biological monitoring of occupational exposure to toluene diisocyanate. *Int Arch Occup Environ Health*. 65:97–100.

Maitre, A., Berode, M., Perdrix, A., Stoklov, M., Mallion, JM. and Savolainen, H.(1996) Urinary hexane diamine as an indicator of occupational exposure to hexamethylene diisocyanate. *Int Arch Occup Environ Health.* 69:65-68.

Marek, W., Potthast, J., Marczynski, B., Mensing, T. and Baur, X. (1999) Subchronic Exposure to Diisocyanates Increases Guinea Pig Tracheal Smooth Muscle Responses to Acetylcholine. *Respiration*. 66:156–161.

Menard, S. (1995). Applied logistic regression analysis. Sage university paper series on quantitative applications in the social sciences. 07-106, Thousand Oaks, CA: Sage.

Molander, P., Levin, J O. and Ostin, A. (2002) Harmonized Nordic strategies for isocyanate monitoring in workroom atmospheres. *J Environ Monit.* 4: 685–687.

Myers, R. (1990). Classical and modern regression with applications (2nd ed.). Boston, MA: Duxbury.

NIOSH. (1994) Determination of airborne isocyanate exposure. NIOSH manual of analytical methods (Chapter K, 4th ed). Cincinnati, OH: US Department of Health and

Human Services, Public Health Service, Centers for Disease Control and Prevention, National institute for occupational safety and health, *DHHS* (NIOSH) publication no. 94-113.

Pisaniello, D.L. and Muriale, L. (1989) The use of isocyanate paints in auto refinishing—a survey of isocyanate exposures and related work practices in South Australia. *Ann Occup Hyg*. 33: 563–572.

Redlich, C and Meryl, K. (2002) Diisocyanate asthma: clinical aspects and immunopathogenesis. *International Immunopharmacology.* 2: 213– 224.

Rosa, J K, and Samuel, P T. (1999) An Approach to Area Sampling and Analysis for Total Isocyanates in Workplace Air. *AIHA.* 60. 200-207.

Rosenberg, C. and Savolainen, H. (1986) Determination of occupational exposure to toluene diisocyanate by biological monitoring. *J Chromatogr.* 367:385–392.

Selden, A., Berg, P., Jakobsson, R. and Laval, J. (1992) Methylene dianiline: assessment of exposure and cancer morbibity in power generator workers. *Int Arch Occup Environ Health.* 63:403–408.

Skarping, G., Dalene, M. and Littorin, M. (1995) 4, 4'-methylenedianiline in hydrolysed serum and urine from a worker exposed to thermal degradation products of methylene diphenyl diisocyanate elastomers. *Int Arch Occup Environ Health.* 67: 73–77.

Tiljander, A., Skarping, G. and Dalene, M. (1989) Chromatographic determinations of amines in biological fluids with special reference to the biological monitoring of isocyanates and amines. III. Determination of 4, 4-methylenedianiline in hydrolysed human urine using derivatization and capillary gas chromatography with selected ion monitoring. *J Chromatogra A.* 479:145–152.

Tinnerberg, H. and Sennbro, C J. (2005) Assessment of exposure to aromatic diisocyanates air or biological monitoring. In *IOHA* Pilanesberg, Page 61-64.

Torling, G., Alexandersson, R., Hedenstierna, G. and Plato, N. (1990) Decreased lung function and exposure to diisocyanates (HDI and HDI-BT) in car repair painters: observations on re-examination 6 years after initial study. *Am J Ind Med.* 17: 299–310.

Tury, B., Pemberton, D. and Bailey, R E. (2003) Fate and potential environmental effects of methylenediphenyl diisocyanate and toluene diisocyanate released into the atmosphere. *J Air Waste Manage Assoc.* 53: 61-66.

Vandenplas, O., Malo, J C., Cartier, A., Perrault, G. and Cloutier, Y. (1992) Closed-circuit methodology for inhalation challenge tests with isocyanates. *Am Rev Respir Dis*; 145:582-7.

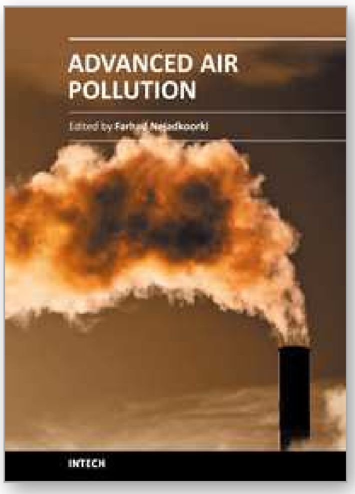
Weill, H., Butcher, B. and Dharmarajan, V. (1981) Respiratory and immunologic evaluation of isocyanate exposure in a new manufacturing plant. Cincinnati, OH: Department of Health and Human Services (NIOSH). (Publ No 81–125.)

Williams, E., Brown, Allen. H., Green, Mery., Karol, H. and Yves, C E. (2004) Immobilized cholinesterase to detect airborne concentrations of hexamethylene diisocyanate (HDI*). Toxicol App Pharmacol.* 73(1), 105-109.

Williams, N R., Jones, K. and Cocker, J. (1999) Biological monitoring to assess exposures from use of isocyanates in motor vehicle repair. *Occup Environ Med.* 56, 598–601.

Woskie, S R., Sparer, R J. Gore, M., Stowe, D., Bello, Y., Liu, F., Youngs, C., Redilich, E. and Cullen. (2004) Determinants of Isocyanate Exposures in Auto Body Repair and Refinishing Shops. *Ann Occup Hygin*. 48(5), 393-403.

Wu, W S., Stoyanoff, R E., Szklar, R S., and Gaind, V S. (1990) Application of tryptamine as a derivatizing agent for airborne isocyanate determination: Part 3. Evaluation of total isocyanates analysis by high performance liquid chromatography with fluorescence and amperometric detection. *Analyst.* 115, 801–807.



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Leading air quality professionals describe different aspects of air pollution. The book presents information on four broad areas of interest in the air pollution field; the air pollution monitoring; air quality modeling; the GIS techniques to manage air quality; the new approaches to manage air quality. This book fulfills the need on the latest concepts of air pollution science and provides comprehensive information on all relevant components relating to air pollution issues in urban areas and industries. The book is suitable for a variety of scientists who wish to follow application of the theory in practice in air pollution. Known for its broad case studies, the book emphasizes an insightful of the connection between sources and control of air pollution, rather than being a simple manual on the subject.