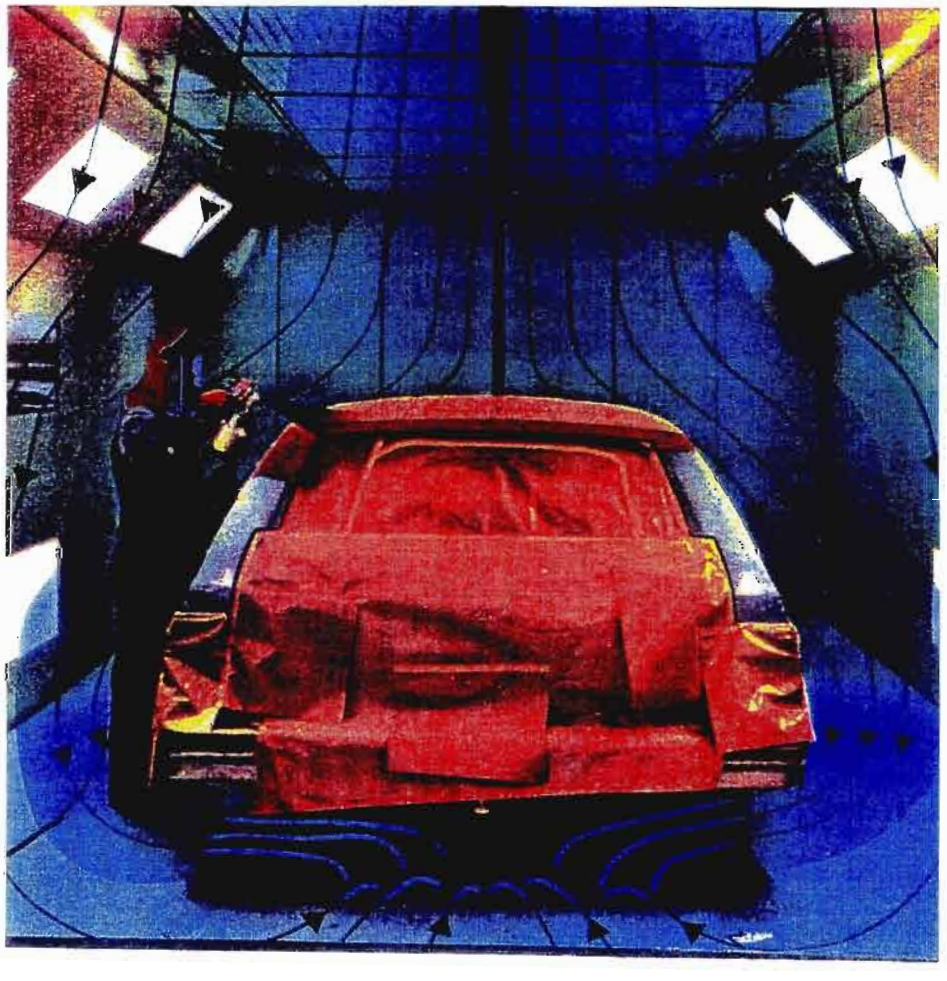
A FOLLOW-UP STUDY OF THE RESPIRATORY HEALTH STATUS OF AUTOMOTIVE SPRAY PAINTERS EXPOSED TO PAINTS CONTAINING ISOCYANATES

BERNARD W. RANDOLPH



PREFACE

This study represents original work by the author and has not been submitted in any form to another University. Where use was made of the work of others, it has been duly acknowledged in the text.
The research described in this dissertation was carried out under the supervision of Prof. U. G. Lalloo Respiratory Unit, Department of Medicine, University of Natal Medical School.

B. W. Randolph

14 December 1997

B. W. RANDOLPH

PUBLICATIONS

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ORAL PRESENTATIONS

Papers on the initial and follow-up studies on hexamethylene diisocyanate were presented at local and international conferences by the author at the following venues:-

- XIth South African Pulmonology Society Congress, Transkei, (April 1993).
- Zeneca 11th Annual Clinic Research Day, Dept. of Medicine, University of Natal. (August 1993).
- Society of Public Health Inspectors, Singapore (November 1994).
- Second International Occupational Hygiene Association Conference, Hong Kong (November 1994).
- Asian Pacific Conference on Occupational Health and Safety, (held under auspices of ICON International Commission on Occupational Health), Brisbane, Australia, (September 1995).
- 25th International Congress on Occupational Health, Stockholm, Sweden, (September 1996).
- XIVth South African Pulmonology Society Congress, Windhoek, Namibia, (September 1997).
- Zeneca 15th Annual Clinic Research Day, Dept. of Medicine, University of Natal, (October 1997).

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1. The South African Medical Research Council for their research grant which enabled me to undertake this follow-up study.

2. Technikon Natal for financial assistance and the granting of special study leave in order to collect the final data from the spray painting establishments.

3. Langet Laboratories for the assistance with the analysis of the samples of hexamethylene diisocyanate taken from the spray booths.

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4. Mr E. J. Steytler ex Principal Inspector of Occupational Safety, Department of Labour, Durban for his idea in initiating this type of study in the Durban area. From his practical insight and long experience in dealing with the health hazards associated with spray painting, I was able to draw up an overall strategy on the method of handling this type of project.

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ABSTRACT

In order to evaluate the respiratory health status of spray painters exposed to paints containing hexamethylene diisocyanates (HDI) and to obtain more insight into the relationship between occupational exposures to isocyanates and chronic obstructive airway diseases, a follow up study on 33 of an original cohort of 40 randomly selected workers was undertaken. The original investigation was conducted by the author in 1989.

The subjects were studied using a standardised American Thoracic Society (ATS) approved respiratory health questionnaire, baseline pre and post shift spirometry and ambulatory peak flow monitoring. Bronchial hyperresponsiveness tests using histamine (PC_{20}) were performed. Immunological tests including IgE, RAST (HDI), and house dust mite evaluations were also made. The subjects were stratified into exposed (n=20), partially exposed (n=5) and no longer exposed (n=7) groups. One subject was excluded from the group analysis because of his indeterminate isocyanate exposure. Warehouse assistants (n=30) in a non-exposed occupation were used as controls. The worker's compliance with safety regulations and the employers provision of safety requirements was assessed by means of a questionnaire. The environmental conditions in the workplace were measured by the evaluation of the isocyanate concentrations at the worker's breathing zone. Spray booth efficiency was measured using measurements of airflow velocities and airflow patterns within the booth. Longitudinal changes in respiratory health status was assessed by comparison with baseline data studied in 1989.

The exposed group showed the largest mean cross-shift declines of 297 ml (± 83.8) in forced expiratory volume in one second (FEV_1). The decline in the partially exposed group was 282 ml (± 102.7) and 54 ml (± 140) in the no longer exposed group. The results of the first study, when compared with the second study, showed a mean cross-shift decline in FEV_1 of 130.5 ml. (± 203) (p=0.0002) and 297ml. (± 323) (p=0.0001) respectively. Furthermore, of the spray painters examined, 10 (25%) showed clinically significant cross-shift declines in FEV_1 viz. decreases >250 ml in the first study (n=40) compared with 9 (45%) in the second study (n=33). In contrast to the HDI exposed spray painters, a closely matched control group (n=30) showed a mean cross-shift increase in FEV_1 of 17.4 ml (± 63.04). Only 2 subjects had a diagnosis of asthma which was made in childhood and not related to occupation. The mean annual baseline decline in FEV_1 was greatest in the exposed group 41.25 ml (25% showed a decline greater than > 90 ml per annum). These values exceeded the predicted annual declines for both smokers and non smokers due to age. The decline in the no longer exposed group was 7.85 ml per annum.

Immunological tests showed no correlation with declines in FEV_1. This study demonstrates the difficulties in correlating immunological status with clinical and lung function findings in workers exposed to HDI, as a means of predicting occupational asthma. Although measurements in cross-shift declines in FEV_1 appear to be a suitable predictor of occupational asthma, in some cases it was found that the forced expiratory flow rate ($FEF_{25-75\%}$) was a more sensitive predictor of early changes in the small airways.

The mean isocyanate concentration in the spray painter's breathing zone was 14.65 mg/m^3 (± 12.219), exceeding the current South African Occupational Exposure Limit - Control Limit (OEL-CL) of 0.07 mg/m^3 for isocyanates.

Fifty per cent of the subjects suffered from eye irritation and 40% had dermatitis of the hand. This was expected since none of the spray painters wore goggles or gloves. Whilst no subject had evidence of clinical asthma related to spray painting, a large proportion demonstrated significant cross- shift changes in lung function implying short- term adverse effects of exposure. In addition longitudinal declines in lung function which was worse in those who continued spray painting in the follow-up study, is of major concern. The lack of cases of clinical or occupational asthma may be due to the healthy worker effect.

Recommendations include, routine spirometric lung function testing of all spray painters, the use of high volume-low pressure spray guns and the wearing of positive pressure airline masks complying with the South African Bureau of Standards (SABS) safety standard. In terms of current legislation it was further recommended that spray booths be regularly monitored, including the measurement of HDI concentrations, airflow velocities and airflow patterns within the booth and the implementation and enforcement of stricter control measures. Workers demonstrating excessive declines in both cross-shift and longitudinal spirometry, require special attention.

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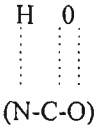
TABLE OF ABBREVIATIONS

ACGIH	American Conference of Governmental Industrial Hygienists
ATS	American Thoracic Society
BHR	Bronchial hyperresponsiveness
COSHH	Regulations for the Control of Substances Hazardous to Health 1988 (UK)
ECCS	European Community Coal and Steel reference values
FEF	Forced Expiratory Flow measured in litres per second
FEF_{25-75}	Forced average mid-expiratory flow in the middle half of the vital capacity, measured in litres per second
FEV_1 / FVC%	$\frac{\text{Forced expiratory volume in one second}}{\text{Forced vital capacity}} \times 100$
FEV_1	Forced expiratory volume in one second (measured in litres)
ΔFEV_1 %	$\frac{\text{Measurement of } FEV_1 \text{ before exposure - } FEV_1 \text{ after exposure}}{FEV_1 \text{ before exposure}} \times 100$ (White 1989)
FVC	Forced vital capacity measured in litres.
HDI	Hexamethylene diisocyanate and 1,6 diisocyanatohexane
HDI- BT	Biuret trimer of hexamethylene diisocyanate
HPLC	High Performance Liquid Chromatography
HSE	Health and Safety Executive, UK
HVLP	High volume low pressure
HWE	Healthy worker effect
IARC	International Agency for Research on Cancer
Ig E	Immunoglobulin E
IgG	Immunoglobulin G
IPDI	Isophorone di-isocyanate
kUa/ l	Kilo international units per litre
MDI	4.4 Diphenylmethane di-isocyanate
mg/ m^3	Milligrams per cubic metre
mg/ml	Milligrams per millilitre
mol.wt	Molecular weight

NIOSH	National Institute for Occupational Safety and Health (USA)
N=C=O	Chemical group containing nitrogen, carbon , oxygen
NPF	Nominal Protection Factor
OEL-CL	Occupational Exposure limit-Control Limit
OESSM	Occupational Exposure Sampling Strategy Manual
OSHA	Occupational Safety and Health Administration (USA)
PC_{20}	Provocation concentration 20
PEF	Peak expiratory flow
PEFR	Peak expiratory flow rate measured in litres per minute
ppm	Parts per million
RAST	Radioallergosorbant test
SABS	South African Bureau of Standards
SAS	Statistical Software Package
STEL	Short-term Exposure Limit
TDI	Toluene di-isocyanate
THDI	Trimeric hexamethylene diisocyanate
TLV	Threshold limit value
TWA	Time weighted average
ug/m^3	Micrograms per cubic metre
VC	Vital capacity measured in litres

DEFINITIONS

aliphatic	An organic (substance) containing straight or branched chain arrangements of carbon atoms.
aromatic	An organic (substance) usually containing one or more benzene ring structures. In some substances, typical "aromatic" chemical properties are also conferred by other ring structures.
breathing zone	Imaginary globe of two foot radius surrounding the head. (Plog, 1988)
crosslinking	Formation of bridges between different polymer chains.
cross-shift	Measurements taken at the beginning of the shift, before exposure to isocyanates and again at the end of the shift, after the exposure to isocyanates.
IDLH	Immediately dangerous to life or health: the maximum level from which one could escape within 30 minutes without any escape impairing symptoms or irreversible health effects.
isocyanates	The isocyanate group (N=C=0), including hexamethylene di-isocyanate HDI; toluene di-isocyanate TDI.; methylene di-isocyanate M.DI.
lung function	A test conducted and evaluated in accordance with the American Thoracic Society's (ATS) recommendations using a Vitalograph Alpha.
lung function variables	Includes VC, FVC, FEV_1, FEV_1/VC, FEV_1/FVC, PEF and FEF
LC_{50}	Lethal Concentration Fifty. A calculated concentration of a substance in air, exposure to which, for a specified length of time, is expected to cause the death of 50% of the entire defined experimental animal population.

LD_{50}	Lethal Dose Fifty. A calculated dose of a substance which is expected to cause the death of 50% of an entire defined experimental animal population. It is determined from exposure to the substance by any route other than inhalation of a significant number from that population.
monomer	A substance which is capable of conversion into a polymer.
Polymer	A high molecular weight substance, natural or synthetic, which can be represented as a repeated small unit (monomer).
Co-polymer	A co-polymer contains more than one type of monomeric unit.
Polyol	A substance containing several hydroxly groups. A dial trial, and tetrol contain 2, 3 and 4 hydroxyl groups respectively.
Polyurethane	Polymeric substance containing many urethane linkages  Abbreviated as Pu.
Prepolymer	A polyurethane reaction intermediate made by reacting isocyanate with a polyester or polyether, in which one component is in considerable excess of the other.
spray booth	A pre-constructed or purpose made unit fitted with means of mechanical extraction for the specific removal of contaminants which are found in the overspray.
spray painter	An employee applying spray paint by means of a compressed air gun which emits a fine mist vapour or aerosol of paint.
study A	Refers to the initial study.
study B	Refers to the follow-up study.
TCL_0	Concentration low. The lowest concentration of a substance, if a substance is introduced by any route other than inhalation over any given period of time and reported to produce any toxic effects in humans.

TLV-STEL The concentration to which workers can be exposed continuously for a short period of time without suffering from:-

1) irritation
2) chronic or irreversible tissue damage
3) narcosis of sufficient degree to the likelihood of accidental injury, impair self rescue, or materially reduce work efficiency (ACGIH, 1989/90).

It is further defined as a 15-minute TWA exposure which should not be exceeded at any time during a work day even if the 8-hour TWA is within the TLV-TWA. Exposures above the TLV-TWA up to the STEL should not be longer than 15 minutes and should not occur more than four times per day. There should be at least 60 minutes between successive exposures.

TLV-TWA The time weighted average concentration for a normal 8-hour work day and a 40-hour work week to which nearly all workers may be repeatedly exposed day after day without adverse effect. (ACGIH, 1989/90)

Urethane The chemical group

(N-C-O)

Also a corruption of polyurethane

CHAPTER ONE
INTRODUCTION

1.1 INTRODUCTION TO ISOCYANATES

It is well established that the isocyanate family of chemical compounds have a range of negative impacts on human health. Of particular concern is the ability of isocyanates to cause progressive declines in lung function with chronic exposures (Peters and Murphy 1970). Numerous papers have been published on the health effects of toluene diisocyanate (TDI) used in the manufacture of foam products but in comparison, relatively few studies have been done on HDI found in automotive spray painting.

Twin-pack paints containing HDI were first introduced into South Africa during the early 1980's and are currently in widespread use in the automotive spray painting industry (Randolph *et al,* 1997). The importance of exposures to isocyanates has now been recognised by the Compensation Commissioner in that it has been included on the third schedule of occupational asthma (Compensation for Occupational Injuries and Diseases Act 1993).

1.2 WHAT ARE ISOCYANATES ?

Isocyanates are chemical compounds that contain the chemical group nitrogen, carbon and oxygen (N=C=O). Chemicals in this group are highly reactive with certain chemical compounds including human body proteins. Isocyanates are organic compounds and there are three types, monoisocyanates, diisocyanates, and polyisocyanates. They are used principally in the production of other industrial chemicals. Commercial interest in isocyanates is based on their reaction with other compounds to form polyurethane products including flexible and rigid foams, solid elastomers, adhesives and surface coatings (IAPA 1984). This study specifically addresses hexamethylene diisocyanates used in surface coatings.

The Bayer Catalogue (Bayer Edition 1.5.1977:1) lists the types of isocyanates which can be found on the market in the form of twin pack paints. This includes the following group of monomeric diisocyanates:

Toluene diisocyanate - TDI

Hexamethylene diisocyanate - HDI

Isophorone diisocyanate - IPDI

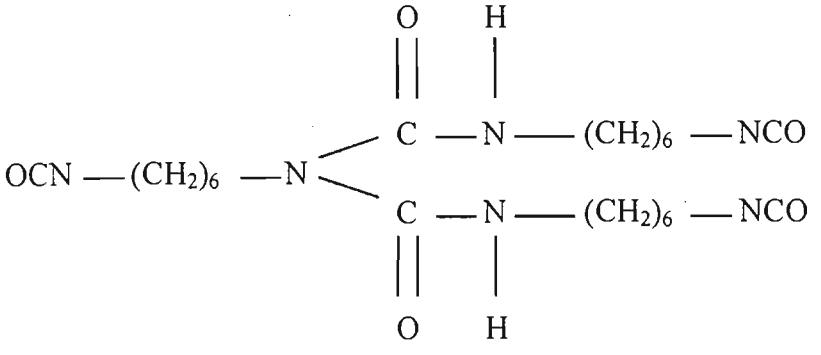
4:4 Diphenylmethane diisocyanate - MDI

1.2.1 Chemical and Physical Properties

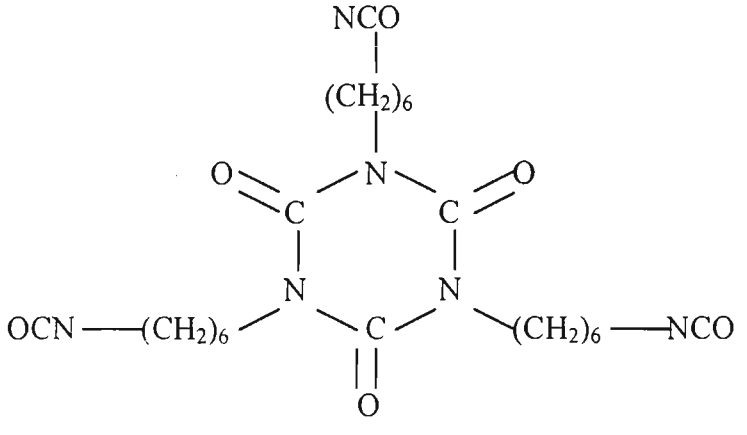
Polyurethane coatings containing 1,6 - hexamethylene diisocyanate (HDI) based polyisocyanate activators have several outstanding qualities such as durability, colour stability, resistance to abrasion and chemicals and a high resistance to temperature extremes. The properties of aliphatic HDI are in contrast to the aromatic isocyanates methylene diphenyl diisocyanate (MDI) and toluene diisocyanate (TDI).

Their popularity in the international car refinishing industry, as in the case of the South African market, is undisputed. The typical polyurethane paint system has two components, polyol with pigments, solvents and additives, and a second component containing polymeric isocyanates in an appropriate solvent. The two forms of HDI polymers currently in use are the biuret trimer (HDI-BT) and the isocyanurate of HDI (-IC) (Janko *et al,* 1992).

These products are manufactured by Mobay Corporation and sold under various trade names. The most important are the biuret types Desmodur N-75, Desmodur N-100 and N-3200 and the isocyanurate types, Desmodur N-3390 and Desmodur N-3300). The molecular structure of these types is shown in Figure 1.1.



Biuret trimer of HDI



Isocyanate of HDI

Figure 1.1: Biuret and isocyanurate of hexamethylene diisocyanate.

The physical properties of monomeric diisocyanate have been summarised in Table 1.1 below.

Table 1.1: The physical properties of monomeric diisocyanates.

Isocyanate Group	mol. wt.	Boiling Point (^{0}C/torr)	Melting Point (^{0}C)	Vapour Pressure p at 25^0 C (mbar)	(torr)	Converted to saturation concentration at 25^0 C (ppm)	(mg/m^3)
Toluene diisocyanate, (TDI isomer mixture)	174.2	Approx. 250/760 120/10	< - 14	$3x10^{-2}$	$2.25x10^{-2}$	29	210
1,6 Hexamethylene diisocyanate, HDI	168.2	127/10	- 67	$1.4x10^{-2}$	$1.05x10^{-2}$	13	95
Isophorone diisocyanate, IPDI	223.3	170/20	approx. - 63	$0.67x10^{-3}$	$5x10^{-4}$	0.67	6
4,4 Diphenyl methane diisocyanate, MDI	250.3	156-158/1	38-39	$0.12x10^{-3}$	$0.9x10^{-4}$	0.12	1.21

(Source: Bayer Edition 1.5.1977:1)

1.2.2 Polyurethane Paints

1.2.2.1 Twin-pack polyurethane paints

The important polyurethane paints are the two-pack types. One component consists of a polyester, polyether or acrylic resin with free hydroxyl groups and the other a polyisocyanate. They offer a system which provides a highly resistant finish on drying at ambient temperature. The common isocyanates used in coatings are toluene diisocyanate (TDI) and hexamethylene diisocyanate (HDI). These isocyanates are never used as such but in the form of additives or polymers in which the content of original isocyanate is kept to a minimum (below 1%) (Croners Handbook, 1993: Occupational Hygiene).

1.2.2.2 One-pack air drying polyurethane paints

These paints are of two types:

a) a prepolymer containing free isocyanate which is moisture cured in the atmosphere and presents a similar hazard to the twin-pack polyurethane paints.

b) an isocyanate is reacted with a fatty oil or alkyd and cures by autosaclation. It presents no isocyanate hazard.

In this study all the paints were either from the twin-pack or from a prepolymer as in (a) above. Both the twin-pack paints and the one-pack paint, require dilution in order to facilitate application. This is achieved by adding a solvent which has the effect of changing the viscosity of the paint. Solvents are applied in the ratio of 2:1.

According to the Bayer technical data sheet, immediately after production and after short-term storage, Desmodur N75 (R) contains less than 0.5% monomeric hexamethylene diisocyanate (HDI). However prolonged storage at room temperature or at an elevated temperature for several days (+50^{0}C), HDI monomer may rise to a maximum of 0.9%. The technical data sheet concludes, from the health point of view, there is a slight risk of irritation through inhalation (Bayer, 1986).

1.2.3 Additives

Bayer also emphasised that spray mists contain other substances such as pigments, solvents, resins and other additives. A typical 2K topcoat formulation will consist of a pigmented base and a curing agent/ thinner pack. A pigmented base consist of the following:-

Hydroxyl bearing Acrylic resin 55 - 80%
Pigment 2 - 40%
Additives e.g. Silicone solution < 0.5%
Solvents balance up to 100%
Curing agents consist of Desmodur N or similar products (containing the isocyanate).

1.2.3.1 Pigments

The pigments consist of titanium dioxide (white), carbon black, phthlo green, pallogen red, iron oxide, scarlet chrome, and yellow oxide (AECI fax (041) 424-012 dated 7 September 1989). According to the published literature, no adverse comments regarding possible health risks from pigments have been noted.

1.2.3.2 Solvents

Solvents include xylene, butyl acetate, Solvesso 100 + 160, ethoxy propyl acetate and butyl cellosolve acetate (AECI fax (041) 424-012 dated 7 September 1989). In general, paint solvents have a numerically high Occupational Exposure Limit (OEL) compared with isocyanates. The author in the initial study found the concentration of solvents to be significantly lower than their respective OEL's.

1.3 AUTOMOTIVE BODY REPAIR SHOP

There are six standard steps in the repair and refinishing of a damaged or rusted car bodies.
The process is similar from premises to premises, with the exception of the spray booth which could be one of three basic design types as described in 1.3.2.

1.3.1 The six basic steps in automotive body repair

The six basic steps are outlined by Collinson (1983) in his paper on automotive repairs:-

i) Dented areas of metal are hammered out to the correct shape. Areas badly corroded or severely damaged are cut out and replaced with new sheet metal and spot welded to the existing body.

ii) De-rusting is done with a disc grinder or small air powered abrasive blasting equipment.

iii) The remaining small imperfections are filled with body putty and sanded down to a smooth even contour by hand, or power sanded using 320 grit paper. The body is masked using adhesive tape. The body of the vehicle is then de-dusted using an air-line hose and finally wiped over with a solvent cloth to remove all traces of oil or grease.

iv) It is then primed in the spray booth and after drying for thirty minutes the vehicle is removed from the booth and the surface is sanded down using 400 grit paper.

v) The area is cleaned of all dust and rubbing-down compound.

vi) Finally, it is then sprayed with two or three coats each 20-30 minutes apart so as to allow drying. This is done so as to completely cover the primer coat.

It must be emphasised that the operation of de-dusting the vehicle causes a substantial amount of dust to become airborne and this is the greatest problem in the application of polyurethane paint. Dust particles finding their way into the spray booth could ruin the top coat finish, so the vehicle preparation area should be physically separated from the spray painting operation. It is thus very difficult for back-yard operators to work out in the open. The author is aware that in some instances because of the dust problem, domestic garages without adequate mechanical ventilation systems are used.

1.3.2 Basic Spray Booth Designs

There are three basic design types currently in use in South Africa; horizontal flow, vertical side and vertical down draught booths.

1.3.2.1 Horizontal Flow Booth

These booths are designed to allow the airflow in a horizontal direction. Air is drawn through the filter material situated in the front door panel and is extracted from the booth via the air outlet ducts on the opposite rear wall. Booths with horizontal air flow take advantage of the momentum of the spray mist and can be successfully used for painting small to medium sized vehicles. With larger vehicles it may not be possible to maintain adequate airflow on all sides of the object being painted. One major disadvantage of this type is that the spray mist is occasionally found in the spray painters "breathing zone" (plate 1.1, 1.2 and 1.3).

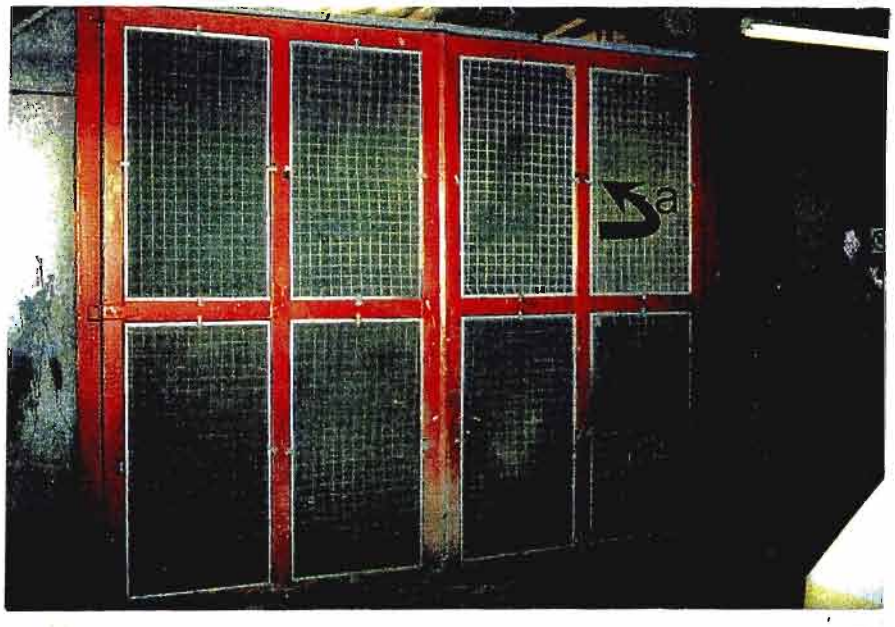


Plate 1.1: Front elevation booth showing air inlet filters at high (a) and low (b) to give an even distribution to air flow.

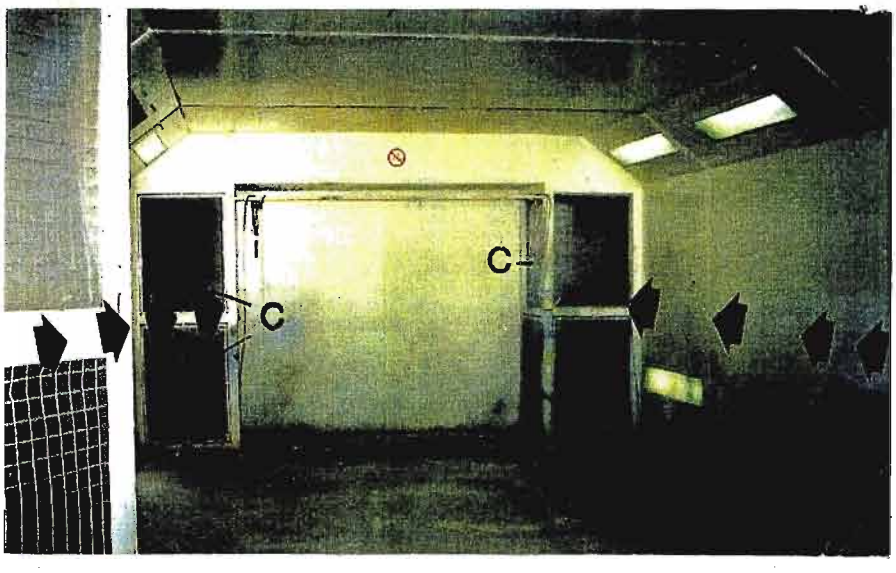


Plate 1.2: Inside view indicating air outlet filters (c) prior to discharge to the vertical duct system and then to the atmosphere. Note: Arrows indicate direction of horizontal air flow.

Plate 1.3: Showing position of vehicle in booth. Note: The horizontal flow spray booth is not an efficient system as air is frequently drawn into the spray painters "breathing zone" whilst working in the front and at the sides of the vehicle.

Plate 1.1, 1.2 and 1.3: Horizontal Flow Spray Booth.

1.3.2.2 Vertical Side Draught Booth

In this booth the air is forced through the ceiling of the spray booth and directed downwards onto the object being sprayed. The spray mists are then discharged through the sides of the booth via a duct. This design permits greater protection for the worker in comparison with the horizontal flow booth, in that the spray mists are carried, at all times, in a downward direction away from the spray painter's breathing zone before being discharged through a filter at the sides (plate 1.4 and 1.5).

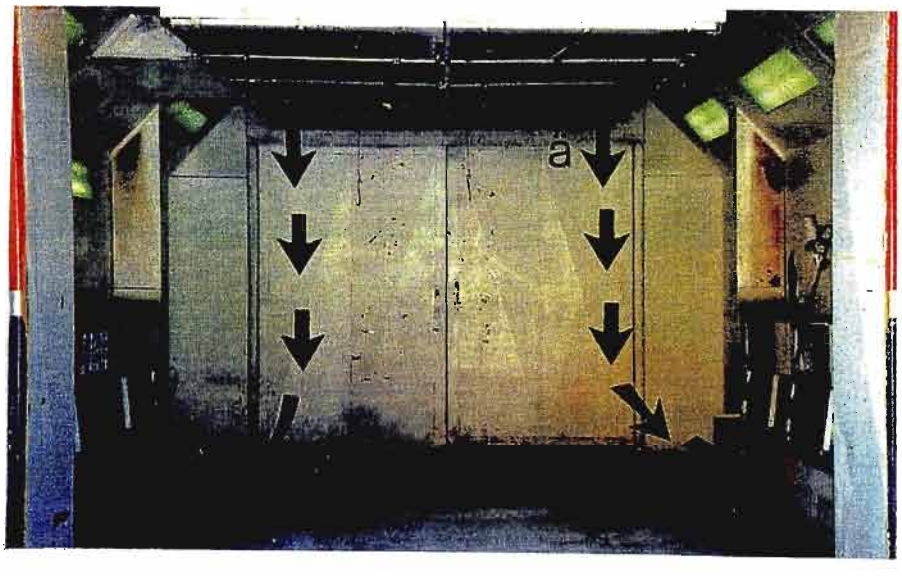


Plate 1.4: Inside view illustrating side draught booth where air is forced through the top filters (a) and extracted through the side outlets (b).

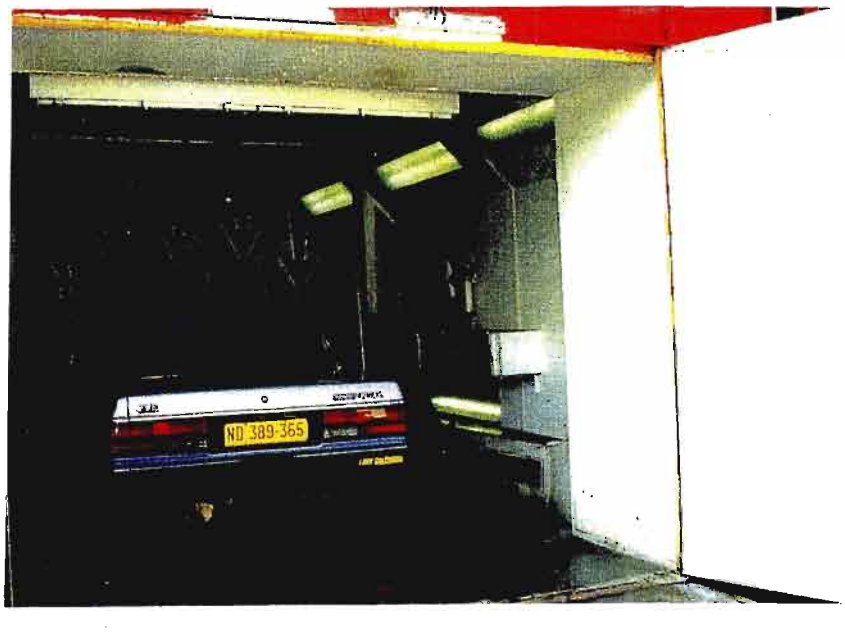


Plate 1.5: Illustrating vertical side draught booth. Note: Air flow direction moving downwards and around the sides of the vehicle before being extracted through the side outlets.

Plate 1.4 and 1.5: Vertical Side Draught Spray Booth

1.3.2.3 Vertical Down Draught Booth

Similar to the booth described above, in this booth the air is forced through the ceiling of the spray booth and directed downwards onto the object being sprayed. The spray mists are then discharged through grills at the bottom of the booth (plate 1.6 and 1.7). This design permits the greatest protection for the worker in comparison with the horizontal and vertical side draught booths.

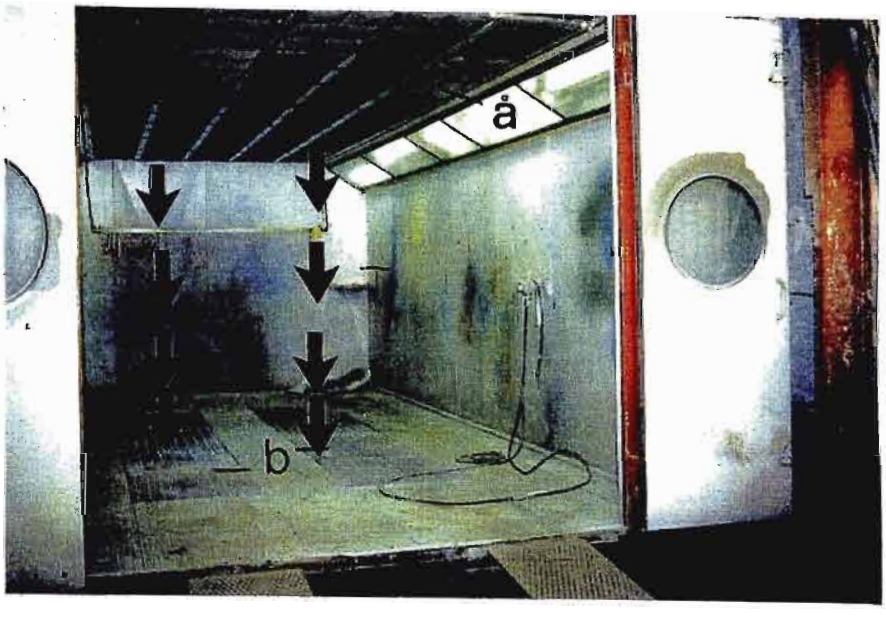


Plate 1.6: Inside view illustrating vertical down draught booth where air is forced in a downwards direction through the top filters (a) and extracted through the floor gratings (b).

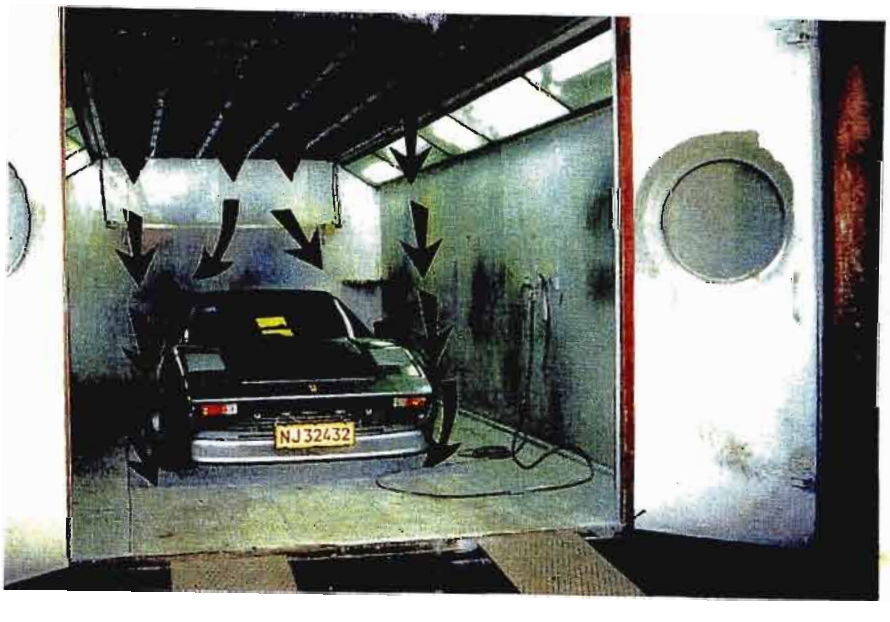


Plate 1.7: Illustrating vertical down draught booth. Air flow direction moving downwards and around the sides of the vehicle before being extracted through the floor grating.

Note: This is the most efficient system of all spray booths and recommended by leading paint manufacturers as the overspray is drawn away from the spray painters breathing zone at all times.

Plate 1.6 and 1.7: Vertical Down Draught Spray Booth.

1.3.3 Respiratory Protective Equipment (RPE)

There are various types of RPE available on the market. These include the simple dust mask, cartridge mask, half or full face airline respirators. Each type of respirator has both advantages and disadvantages and will be briefly described in this chapter. The effectiveness of a respirator in it's ability to protect the worker is assessed scientifically by means of being allocated a Nominal Protection Factor (npf). The npf is defined as:-

$$\text{npf} = \frac{\text{concentration of the contaminant in the atmosphere}}{\text{concentration of the contaminant in the facepiece}}$$

Nominal Protection Factors have been categorised according to table 1.2 below.

Table 1.2: Approximate nominal protection factors for respiratory protective equipment.

Type of respiratory protective equipment	Assigned nominal protection factor
RESPIRATORS:	
Single use filtering facepiece respirator	5
Half-mask cartridge respirator	10
Full-facepiece canister respirator	500-1000
Powered air purifying respirator	500
Powered visor respirator	10-20
BREATHING APPARATUS:	
Fresh air hose apparatus	50
Compressed air line apparatus	1000-2000
Self contained breathing apparatus	2000

(Source: Hansen DJ. Occupational Health Fundamentals, 1991)

1.3.3.1 Dust masks

Although these masks are frequently used in the surface coating industry they are only designed to remove small particles down to 6 microns. Particles of a smaller diameter than 6 microns would pass through the mask as would gases, fumes, vapours and spray mists. This type of mask is totally unsuitable for the motor vehicle refinishing trade. The protection factor is very low and may be regarded as 0 for gases, vapours and very small particles.

1.3.3.2 Cartridge masks

Cartridge masks are designed to remove specific contaminants from the working environment. This mask relies on the principle that the chemical in question must be detectable by smell as soon as breakthrough has occurred viz. when the gases or vapours saturate the activated charcoal filter and pass through the cartridge into the spray painter's respiratory system. In addition, the threshold of smell must be lower than the OEL-CL. However, because the threshold of smell for isocyanates is above the OEL- CL this type of mask is regarded as unsuitable. The protection factor for this mask is low and between 5 - 10.

1.3.3.3 Positive pressure airline masks

The positive pressure airline mask offers maximum protection to the wearer. Filtered air is obtained from a compressor and is forced across the wearer's breathing zone. Because of the fact that the air is above atmospheric pressure no contaminant would be able to enter the operators respirator. The protection factor is very high for this type of mask and in the region of between 1000-2000.

1.4 HEALTH HAZARDS OF ISOCYANATES

1.4.1 Summary of Health Effects

From a review of the related literature there is inadequate data documenting the health effects of HDI (Vandenplas et al ,1993). A summary of the health effects on TDI is listed in Table 1.3.

Table 1.3: Summary of the medical effects of exposure to toluene-2.4-diisocyanate. TDI

Routes of Entry	Symptoms
Ingestion	Corrosive. Sore throat. Abdominal pain. Diarrhoea.
Skin	Burning. Redness. moderate skin sensitiser. May be absorbed through the skin.
Eyes	Pain. Redness. Watering. Blurred vision.
Respiratory tract	Irritant. Sore throat. Cough. Shortness of breath. Possible systemic effects. Response: Asthma. Long term sensitisation effect.

Note: (i) Sensitisation may occur after exposure to levels below Time Weighted Average (TWA).
(ii) High toxicity.
(iii) Possible long term effects.
(iv) Severe irritant.

(Source: Croner's Handbook, 1993.)

Exposure to isocyanates are known to cause irritation of contact areas and, in more severe cases, breathing difficulties. The degree of irritation depends on the sensitivity of the contact areas (for example eyes), the isocyanate content in the materials and the duration of contact. The major hazard in the use of isocyanates arises from the inhalation of their vapours.

Breathing can be affected as a result of direct irritation of the respiratory tract or because of sensitivity reactions. Direct irritant or toxic responses are caused by the triggering of normal protective mechanisms of the upper respiratory tract.

The symptoms, depending on the total dose, appear 4 to 8 hours after exposure and they usually respond to supportive measures (medical treatment) after some time, following removal of the user from the source (New Brunswick Occupational Health and Safety Commission Report: 1986).

The clinical features of isocyanate-associated illness were summarised by Bruesch and Elkins, (1963). Eye, nose and throat irritation are usually the first clinical manifestations. Dry cough with chest pain or tightness of the chest often follow. Because the cough or wheeze is characteristically worse in the evening or at night, the patient or doctor may not recognise its occupational aetiology. Rhonchi or coarse rales are frequently present. In some workers the characteristic pattern of bronchial asthma is the initial manifestation; in others it develops late. Chest radiographs taken during the acute stage are usually interpreted as normal, although increased markings and patchy infiltration are occasionally seen. The clinical picture can then approximate to acute or chronic bronchitis, bronchial asthma or, rarely, pneumonitis (Wegman *et al*, 1977)

1.4.2 Cancer in the paint industry

Experimental tests carried out on animals now indicate that 2.4 TDI is a potential occupational carcinogen (OSHA 29 CFR, 1990). A survey of epidemiological studies of the paint manufacturing industry and painters conducted in the USA indicate that in manufacturing there was no significant increase in cancer risk, but in painters there was a significant increase, particularly in lung and bladder cancer (Wong and Morgan, 1988). Similar conclusions were reached by the "International Agency for Research on Cancer (IARC)", from a review of 300 papers. It was estimated that there is a consistent excess above the national average of all cancers of about 20% and cancer of the lung of about 40%. However, the agent responsible has not been identified (IARC, 1989).

A summary of Croner's table on the medical effects of exposure to TDI, is shown in table 1.3.

The oral toxicity for rats using LD criteria is 5800 mg/kg (Sax, 1984). This clearly indicates that toluene diisocyanate is classified as a "slightly hazardous" substance with regard to its ingestion properties. However, from its inhalation properties, it is regarded as extremely toxic and caution must be exercised against inhaling the vapours.

1.4.3 Sensitisation

The result of repeated exposure to isocyanate is the sensitisation of the exposed person, that is, development of an allergy. Sensitisation can occur, depending on the person, following a single exposure or several exposures. Once sensitised, the individual could contract asthmatic-like attacks on subsequent exposure however small the exposure is. Such sensitised persons may not be able to work in isocyanate contaminated environments for long periods of time or even indefinitely. The question on sensitisation has been addressed by many authors and their results have shown a varying response to a range of exposures. Zwi (1985) reports in his article "Isocyanates and Health - a review " that about 5% of people exposed to TDI become sensitised and suffer asthmatic reactions after subsequent exposure to extremely low concentrations.

Woolwich (1982) states that as many as 17% of those exposed may become sensitised and develop "allergic" symptoms. After exposure stops, recovery is usually rapid, but on re-exposure to even small concentrations of isocyanates, symptoms may recur with increasing severity. It has been observed in some individuals that they may even respond to a concentration as low as 0.0001 parts per million which is well below the OEL following sensitisation (O' Brien and Hurley, 1982). This fact has also been emphasised in an article "Isocyanates toxic hazards and precautions" (Health and Safety Executive, 1979). Other studies, which include cases of sensitisation to TDI ranging from 4% to 20%, are shown in Table 1.4 below.

Table 1.4: Percentage of subjects sensitised to TDI from 1964 -1981

Author	Year	% Subjects sensitised
Williamson	1964	5
Bruckner	1968	19
Carrol	1969	9
Adams	1970	20
Porter	1975	10
Weill	1981	4

(Source: Determination of the TLV 1984 Fourth Edition ACGIH)

The literature suggests that the dose and frequency of exposure are factors that affect the level of sensitivity. The importance of sensitisation of the individual must be stressed. Some chemicals like isocyanates have a sensitising action, and they are capable of setting up an allergic response. Initially this may have little or no effect after exposure the first time, but with each successive contact the response becomes more acute and even the slightest exposure can bring on an attack. This fact is also emphasised in an article under the title "Isocyanates: toxic hazards and precautions" by the Health and Safety Executive 1979 UK. Further evidence on the adverse effects of isocyanates on individuals resulting in cases of asthma and sensitisation was stressed by Falla and Glynn (1979), when they noted that the conclusions of the paint manufacturer, Bayer, did not follow their UK experience among spray-painters who had changed to twin-pack polyurethanes over a two-year period. Since 1976, when twin-pack polyurethane paints based on aliphatic prepolymers came into use in the UK for the spray painting of cars, many cases of respiratory impairment and sensitisation with symptoms characteristic of isocyanate causation have been reported by the Employment Medical Advisory Service (Tyrer, 1979).

The pulmonary function of individuals is also affected by excessive isocyanate exposure. In a study "Chronic pulmonary function loss from exposure to toluene diisocyanate", Wegman *et al,* (1977) reported that there was a significant association ($p < 0.005$) between acute and chronic decrement in FEV_1. He concluded that chronic occupational exposure to TDI at 0.003 ppm (0.0214 mg/m^3) or higher is unsafe. Therefore, to adequately protect workers' lungs, the paint industry recommends the use of an air-fed hood and an efficient down draught spray booth when isocyanate paints are being applied. The use of a cartridge respirator is not recommended, as a "breakthrough" would not necessarily be detected. Isocyanates have a detectable odour level, higher than the OEL. Therefore an operator would have been exposed to potentially harmful levels of isocyanates long before being able to detect them by smell through the vapour cartridge mask.

Due to the popularity of the twin-pack paints in the automotive trade, more and more operators are being exposed to this type of health risk through the application of base coat/clear coat paint. It is obvious that the problem will become more serious as time goes on.

A study of 150 spray painters who used paints containing hexamethylene diisocyanate (HDI) and trimeric hexamethylene diisocyanate (THDI) has been reported (Grammer *et al*, 1988). Measurements of ambient isocyanate levels, answers to respiratory questionnaire, and measurements of the amount of serum antibody to HDI bound to human serum albumin and also THDI bound to human serum albumin were evaluated. Since the spray painters wore respirators, isocyanate exposure was very low.

Although 8% reported respiratory tract symptoms only one worker was thought to have symptoms of work-related respiratory disease. Despite the apparently low exposures, 21% had antibodies to isocyanates. Approximately 12% had IgG and 5% had IgE antibodies (RAST) to one of the two isocyanates HDI or THDI (Grammer *et al*, 1988).

1.4.4 Health effects of solvents

In an earlier study Randolph *et al*, (1997) found that the solvent concentrations were very much lower than their respective recommended TLV-STEL ACGIH levels. The author therefore did not repeat the evaluation of solvents in the present study. Although in the literature it has been stated that solvents may cause skin problems with prolonged contact or burning or itching of the eyes. Solvents absorbed through the skin can lead to liver, kidney, and central nervous system toxicity. In the literature review, no evidence was found of significant adverse respiratory effects due to solvent exposure, in comparison to that of isocyanates.

1.5 MECHANISM OF ACTION CAUSING TOXICITY

A variety of mechanisms have been proposed to explain the toxicity of isocyanates. Immunologically, both humoral (IgE-mediated) and cellular mechanisms have been evaluated. Isocyanates are highly reactive with amino groups and can readily haptenize with plasma proteins producing neoantigens. IgE-mediated hypersensitivity mechanisms appear possible in the aetiology of isocyanate-induced asthma, especially when symptoms occur immediately after exposure. Investigators have demonstrated isocyanate-specific IgE antibodies in the sera of exposed workers.

The prevalence, however of these antibodies approximates 20% in some studies, suggesting that this may not be the major mechanism of isocyanate asthma. Furthermore, specific IgE antibodies have been detected in the sera of exposed, asymptomatic individuals (Butcher *et al,* 1983). Epidemiological studies have also failed to show a correlation between isocyanate asthma and atopy, further indicating that the disease is probably not entirely IgE-mediated. A possible role of cellular mechanisms has shown through the production of a leukocyte inhibitory factor by lymphocytes from sensitised individuals (Musk *et al*, 1988).

TDI has also been found to suppress the increase of intra-cellular cyclic adenosine monophosphate (CAMP) by the beta-agonist isoproterenol in peripheral blood lymphocytes indicative of a pharmacologic mechanism of action. Research data suggest that isocyanates may cause non-specific inhibition of a variety of membrane receptors and enzyme systems.

Both immunologic and non-immunologic mechanisms appear to be involved (Bernstein, 1982). Although much research has been directed toward the mechanism of isocyanate-induced disease, the complete pathophysiology remains unknown (Phillips and Peters, 1992).

1.5.1 Signs, symptoms and syndromes from toxic exposure

Isocyanates cause varied effects due to exposure. TDI can act as a direct irritant to mucous membranes, skin, and the respiratory system. It can also act as a sensitiser capable of causing such adverse effects as TDI-induced asthma and bronchial hyperactivity to nonspecific agents and can cause lung function decline in individuals not sensitive to the specific isocyanate.

1.5.2 Respiratory effects

The principal patterns of respiratory response to isocyanates are discussed below. Most of the available information is from studies on TDI although it has been stated that the responses to HDI are similar.

1. chemical bronchitis (following high doses):
2. isocyanate asthma and nonspecific bronchial hyperactivity (symptomatic variable airflow obstruction in sensitised subjects);
3. acute non-specific airway disease (acute asymptomatic deterioration in lung function during a workshift);

4. chronic nonspecific airway disease (chronic deterioration in lung function with prolonged low levels of exposure) ; and
5. hypersensitivity pneumonitis.

(Musk *et al*, 1988).

1.5.2.1 Chemical bronchitis

Acute exposure to isocyanates can cause irritation to the lining of the respiratory tract. Symptoms of bronchitis may occur upon inhalation. Cough with chest pain or tightness may also occur, frequently at night. Chronic bronchitis is reported to be more frequent in workers exposed to high concentrations or repeatedly to low concentrations of TDI (McKerrow *et al*, 1970). Most of the information is based on studies on TDI asthma as there is little data on the effects of HDI induced asthma's.

1.5.2.2 Isocyanate asthma

Occupational asthma is defined as a disease characterised by variable airflow limitations and/or bronchial hyperresponsiveness due to causes and conditions attributable to a particular working environment and not by stimuli encountered outside the workplace (Bernstein *et al*, 1993). Asthma occurring from exposure to isocyanates in a polyurethane manufacturing plant was first recorded in 1951 by Fuchs and Valade (1951). Possible predisposing factors for isocyanate asthma include, exposure to large or multiple isocyanate spills and upper respiratory tract infections, although usually there is no explanation (Banks *et al*, 1986). Depending on the criteria used to define sensitivity, it is estimated that between 5 and 30% of exposed workers develop asthma due to sensitisation (Musk *et al*, 1988).

Although varying periods of isocyanate exposure (one day to years) may exist before the development of asthma, isocyanate asthma more often develops within the first few months of exposure. The duration and connection of isocyanate exposure triggering sensitivity are unknown. Exposure to even low levels of isocyanates can cause asthma. Once sensitised, exposure to even smaller amounts can produce asthmatic episodes. Sudden death has occurred in sensitised subjects inadvertently exposed to relatively low concentrations of TDI (Musk *et al*, 1988). Workers who are found to be sensitised to isocyanates must be removed to jobs where no further isocyanate exposure will occur.

Many patients with occupational asthma due to TDI continue to have persistent asthma months or years after removal from exposure. In some subjects, the asthma may progress even if they are no longer exposed (Mapp *et al*, 1988).

Workers who develop isocyanate asthma may also have hypersensitivity to other environmental allergens. This nonspecific bronchial hyperactivity does not always accompany specific sensitivity to isocyanates. Nonspecific hyperactivity cannot be predicted from the presence of atopy or from the initial degree of airflow obstruction (Lam *et al*, 1979). Like isocyanate asthma, non-specific hyperactivity can be lost over time. It may persist, however, for prolonged periods following cessation of exposure to isocyanates. Decreases in isocyanate sensitivity and non specific hyperactivity have occurred after removal from exposure but appeared again upon re-exposure.

Asthma due to isocyanate sensitisation can be of immediate, late, or dual onset. Smooth muscle contraction is thought to be the mechanism for immediate asthmatic responses induced by isocyanates, since they quickly reverse after bronchodilators or spontaneously (Fabbri *et al*, 1987). By contrast, bronchodilators do not prevent late asthmatic responses induced by isocyanates.
Asthmatics without a history of exposure to isocyanates, even those with methacholine sensitivity, do not respond to TDI inhalation challenge, indicating an isocyanate-specific response. Prednisone has been shown to prevent both late asthmatic reactions and the associated increase in airway responsiveness. Prednisone has also been found to have no effect on the early component in those with dual responses. Elevated levels of inflammatory cells are found in TDI-sensitive individuals experiencing late or dual asthmatic episodes but not in those experiencing only immediate reactions. Late asthmatic reactions to TDI and the associated increase in airway responsiveness may be linked to an acute inflammatory process in the airways of sensitised subjects. Paggiaro and co-workers studied 114 subjects with asthma induced TDI (Paggiaro *et al*, 1986). Bronchial provocation with TDI elicited immediate responses in 24 subjects, late responses in 50, and dual responses in 40 subjects. Those with dual responses had a longer duration of symptoms and a greater prevalence of airway obstruction with a lower mean FEV_1. A methacholine challenge was performed on 27 subjects; those with dual responses showed greater nonspecific bronchial hyperresponsiveness than those with only late or early responses. Mapp and associates found bronchial hyperactivity diagnosed by positive methacholine inhalation challenge to occur in TDI asthmatics with dual or late but not immediate responses (Mapp *et al*, 1986).

In addition, six workers with a clinical history suggestive of TDI sensitivity had initial methacholine challenges which were negative but 8 hours after a TDI inhalation challenge developed positive methacholine responses (Mapp *et al*, 1986). Cross-reactivity to other diisocyanates by challenge testing has been seen in some people with TDI asthma who have no history of previous exposure to diisocyanates other than TDI.

In one study, 25% of the subjects with isocyanate asthma recovered completely within 10 months after exposure ended (Mapp *et al*, 1988). In those that recovered, methacholine responsiveness returned to normal, indicating that airway hyperresponsivness is not a predisposing factor for the occurrence of isocyanate-induced asthma. Some subjects with early or dual responses totally recovered, while some with dual responses lost only their immediate reactions becoming late responders. None with only late responses recovered.

MDI has also been reported to cause asthma and hypersensitivity pneumonitis (Zammit-Tabona *et al*, 1983). Only a small proportion of patients demonstrate IgE antibodies to MDI-protein conjugates. It is likely that most isocyanates react similarly and will eventually be shown to cause respiratory problems much like TDI.

1.5.2.3 Acute nonspecific airway disease

Several studies have shown that workers exposed to TDI experience asymptomatic airflow obstruction during the course of a workshift (Musk, Peters and Wegman, 1988). The degree of this acute change is correlated with long-term changes in pulmonary function and severity of exposure. Exposure to low levels of TDI has been shown to cause a dose-related acute loss of pulmonary function. At the same dose, chronic deterioration in FEV_1 has been seen. Therefore, it has been proposed that excessive long-term changes in lung function may be predicted in individuals from the daily change, which may provide a means of identifying susceptible subjects.

1.5.2.4 Chronic nonspecific airway disease

A dose-response relationship between prolonged low levels of exposure to isocyanates and chronic deterioration in lung function has been demonstrated.

Wegman *et al*, (1977) found that exposure to low levels of isocyanates in a polyurethane manufacturing plant produced a dose-response decrease in FEV_1 when exposed for more than 2 years to 0.002 ppm of TDI. Groups of workers exposed to higher concentrations had larger average annual decrements in FEV_1 than those exposed to lower concentrations. *Subjects showing the largest acute responses are likely to show the greatest chronic changes.* These effects were seen in subjects exposed to levels of TDI below the existing Occupational Exposure Limit - Control Limit (OEL-CL).

Diem *et al*, (1982) and associates prospectively studied a plant manufacturing TDI to evaluate the respiratory function of its workers. Personal air samples showed frequent excursions of TDI above 0.02 ppm. After 2 years there was no exposure-related decline in pulmonary function. Over 5½ years, those who spend 15% of their time working in an environment with 0.005 ppm TDI showed a greater decline in FEV_1 than other subjects. Non-smokers had an annual excess loss of 38 ml of FEV_1 equal to a total loss of 1.5 litres over a 50 year working lifetime. Smoking and the effects of TDI on lung function were not found to be additive. There was no additional effect in current or previous smokers. The potential therefore exists for long-term declines in pulmonary function in workers exposed to low levels of isocyanates (Diem *et al*, 1982)

1.5.2.5 Hypersensitivity pneumonitis

Hypersensitivity pneumonitis or extrinsic allergic alveolitis has been linked to isocyanate exposure. Generally, symptoms of hypersensitivity pneumonitis include fever, chills, malaise, dyspnea, and a non-productive cough. Chest radiographs may show diffuse patchy infiltrates or discrete nodules or may be normal even in symptomatic subjects. Pulmonary function testing may show a restrictive pattern and impaired diffusion capacity. Steroids have been shown to be effective in treating the illness, but further exposure must be avoided to prevent recurrence. Pulmonary opacities resulting from exposure to diisocyanates have also been reported accompanied by airflow obstruction (Musk *et al*, 1988). In one case, acute asthma followed hypersensitivity pneumonitis in a worker challenged with MDI in the laboratory. Exposure to toluene diisocyanate has also been reported to cause chronic restrictive pulmonary disease (IARC, 1986).

1.5.2.6 Other Effects

Direct exposure to solutions of isocyanates is irritating to the skin and mucous membranes and may cause contact dermatitis. Erythema, oedema, and blistering are possible. Exposure to aerosols may cause ocular irritation, rhinitis, and sore throat. Neurological symptoms including a feeling of drunkenness, numbness, and loss of balance have been described as occurring immediately after a single severe exposure to TDI by firemen in a burning polyurethane foam factory, with some symptoms persisting up to 4 years (US Dept. of Health, 1978). They also reported nausea, vomiting, and abdominal pain, which were transitory. Whether these complications resulted from the neurotoxic effects of isocyanates, hypoxia from respiratory reactions, or other simultaneous chemical exposure is not known.

1.5.2.7 Carcinogenesis

In animal studies, commercial grade TDI given by gavage has produced tumours in rats and mice in a dose-response relationship. After contact with water, TDI is converted to toluene diamine, which is carcinogenic to both mice and rats (Musk *et al*, 1988). This may explain the carcinogenicity by gavage. 2,4-Diaminotoluene, the hydrolysis product of 2,4 -TDI, caused similar tumours when tested in rats and mice (IARC, 1986). The International Agency for Research on Cancer (IARC) determined that there is sufficient evidence for the carcinogenicity of toluene diisocyanate to experimental animals but inadequate evidence to determine its carcinogenicity to humans (IARC, 1986). However, in the absence of adequate data in humans, it is reasonable to regard chemicals for which there is sufficient evidence of carcinogenicity in animals as if they represented a carcinogenic risk to humans. NIOSH recently released information classifying TDI and TDA as potential occupational carcinogens (NIOSH, 1990). Teratogenesis and reproductive effects have not been studied in animals or human populations. The present study was not designed to study the possible carcinogenic effects of HDI.

1.6 MANAGEMENT OF TOXICITY

1.6.1 Clinical examination

Medical history may reveal symptoms of cough, shortness of breath, nocturnal wheezing, and chest pain in workers with respiratory symptoms due to isocyanates. Symptoms may worsen with continued Isocyanate exposure. Depending on the type of respiratory response elicited, physical examination may reveal pulmonary wheezes, coarse rales, or a normal lung exam. Irritation of mucous membranes may be present, including redness and swelling. Dermal reactions consisting of mild irritation to erythematous blisters may be seen (Sullivan and Krieger, 1992).

1.6.2 Treatment

Immediate treatment of direct contact with eyes or mucous membranes should include irrigation with saline or water. Skin should be washed with soap and water and then with alcohol. Inhalation requires immediate removal to fresh air. Ingestion of TDI requires the administration of large quantities of water and inducing vomiting, unless the person is unconscious. Bronchodilators are used in ameliorating immediate asthmatic episodes. Theophylline partially inhibits both the immediate and late reactions of asthma induced by TDI, but does not affect the increase in airway responsiveness, apparently affecting a bronchoconstrictor component of the late asthmatic reaction rather than the inflammatory component (Mapp *et al*, 1987). Prednisone or high dose inhaled beclamethasone are useful in preventing both late asthmatic episodes and the increase in nonspecific bronchial hyperactivity induced by TDI.

1.6.3 Laboratory diagnosis

Specific IgE antibodies to monofunctional isocyanates have been reported in sensitised workers but specific IgE to diisocyanate conjugates have not been identified (Musk *et al*, 1988). In one study, *p*-tolyl monoisocyanate (TMI) conjugated to human serum albumin was used to identify specific IgE antibodies in three of four subjects sensitised to TDI but was not found in exposed but non-sensitised subjects (Chan-Yeung and Lam, 1986). There appeared to be a dose-response relationship between exposure concentration and number with a positive titre. Others have found only 0-16% of sensitised subjects with specific IgE antibodies to TMI. Specific IgE has also been shown to occur in exposed workers without asthma (Butcher *et al*, 1983).

1.6.4 Special diagnostic tests

Spirometry testing may reveal normal pulmonary function or airway obstruction in subjects with isocyanate asthma. Upon inhalation challenge, immediate, late, or dual asthmatic reactions may develop, defined as a 20% decrease in FEV_1. Challenge testing may be indicated in carefully selected cases although the risk of this is apparent. A diagnosis of isocyanate asthma can usually be made without the need to do an inhalation challenge. Isocyanate asthma may be diagnosed if the worker has reversible airflow obstruction associated with exposure to low levels of isocyanates. The doses of TDI used for inhalation challenges do not cause immediate or late bronchconstriction in normal subjects or in asthmatic subjects not sensitised to TDI, even if they have hyperresponsive airways (Paggiaro *et al,* 1986).

1.6.5 Health Surveillance Programme

Medical surveillance should be provided to all workers exposed to diisocyanates in the workplace. Preplacement examinations including a comprehensive medical and work history, with special emphasis on pre-existing respiratory conditions and smoking history should be performed (US Dept. of Health, 1978). A physical exam with emphasis on the respiratory system, chest x-ray, and baseline spirometry should be included. The worker must also be judged fit to use a respirator. Annual periodic exams consisting of interim medical and work histories, a physical exam, and pre- and post-shift or workweek spirometry should be performed.

If medical conditions are found that could be directly or indirectly aggravated by exposure to diisocyanates, for example, respiratory allergy, chronic upper or lower respiratory irritation, or chronic obstructive pulmonary disease, the worker should be counselled on the increased risk from working with these substances. If evidence of sensitisation is found, provisions must be made to remove the workers from further exposure.

It has not been shown that preplacement assessment is useful in the prediction of employees who will develop TDI-induced lung disease. Atopy and asthma unrelated to isocyanates do not predispose to isocyanate asthma. Not all subjects who have specific sensitivity to TDI have increased non-specific bronchial hyperactivity. Isocyanates in low concentrations have no effect on hyperactive airways. Therefore, methacholine testing is not likely to identify those who will develop TDI asthma.

Baseline methacholine testing is similar in subjects who develop immediate, dual, or late responses. The available evidence indicates that serial measurement of the FEV_1 is a useful means of identifying acute and long-term effects of isocyanates in a workforce. Wegman *et al,* (1997) demonstrated a correlation between acute and chronic effects of TDI, which may provide a way of identifying subjects who are at risk of developing long-term declines in FEV_1. An annual decrement in FEV_1 of 0.02 litres in an adult non-smoker would be anticipated from ageing alone. It has been suggested that all subjects should have pre-employment measurements and subsequent measurements at least annually or more often if symptoms arise. Workshift decrements of 300 ml or greater and annual decrements of 5% or 200 ml should be cause for evaluation and more frequent testing since these decrements may be associated with eventual chronic airflow obstruction or representative of asthma, which may become intractable (Phillips and Peters 1992).

1.6.6 Environmental monitoring methods

The NIOSH criteria document defines occupational exposure to diisocyanates as exposure to airborne levels above one-half the recommended time-weighted average (TWA) occupational exposure limit or above the recommended ceiling limit (US Dept. of Health, 1978). Adherence to all provisions of the standard is required at this level including periodic medical exams, respiratory protection, and personal monitoring.

Environmental monitoring of the workplace where diisocyanates are present should be conducted annually or after any process changes to determine whether there is exposure. If exposure is found to be present, personal monitoring is to be used in calculating the exposure of each employee occupationally exposed to diisocyanates. Area and source monitoring may be utilised to supplement personal monitoring.

Samples from each operation in each work area and each shift should be taken at least once every 6 months. Records of environmental exposures applicable to an employee must be included in the employee's medical record. Air levels of TDI can be measured by a variety of methods (Musk *et al,* 1988). The Marcali method and its derivatives, also called wet colorimetric methods, are the oldest and have been the reference for newer methods. They involve collecting air samples in a midget impinger by bubbling workplace air through an acid absorption medium. The intensity of the coloured derivative is measured spectrophotometrically.

Dry colorimetric methods are based on colour-forming reactions that occur when chemically impregnated paper tape is exposed to air containing isocyanates. After monitoring, the tape is passed through a reflectance meter for quantification. Chromatographic methods (gas chromatography, thin layer chromatography, and high performance liquid chromatography (HPLC) are the most sensitive for measuring and distinguishing between isocyanates but are technically difficult and expensive. The current NIOSH approved analytical method forms urea derivatives that can be measured quantitatively by HPLC with ultraviolet spectrometric detection (IARC, 1986).

1.7 LEGAL REQUIREMENTS

1.7.1 International exposure limits for isocyanates

The recommended and legal standards for airborne substances are laid down by a number of international agencies. These agencies include OSHA (USA); NIOSH (USA); ACGIH (USA); HSE (UK) and Ontario Regulations (Canada) [(OSHA, 1976; ACGIH, 1988; HSE, 1979)].

For prescribed levels for 2,4 toluene-diisocyanate, hexamethylene diisocyanate and isophorone diisocyanates, it can be observed that both OSHA and ACGIH and the Ontario Regulations prescribe the same level for an 8-hr TWA, that is, 0.005 ppm (0.04 mg/m^3) and a STEL of 0.02 ppm (0.15 mg/m^3). Since the exposures in the panel shops under investigation proximates to the STEL value (4 times 15 minute exposures) this criterion was used throughout the study.

NIOSH and Ontario Regulations state that a ceiling level of 0.02 ppm should not be exceeded at any time. The IDLH or the Immediate Danger to Life or Health level for isocyanates is 10 ppm (71.23 mg/m^3) and has been listed in the NIOSH 1985 "Pocket guide to chemical hazards" (NIOSH 1985: 226). Table 1.5 shows international exposure limit levels for isocyanates.

Table 1.5: International exposure limit levels for isocyanates.

	OSHA (USA)				NIOSH (USA)				ACGIH (USA)				ONTARIO REGULATIONS (CANADA)				HEALTH & SAFETY EXECUTIVE (U.K)			
	TWA 8hr.		STEL 15 min		TWA	10 min	C	IDHL	TWA 8hr.		STEL 15 min		TWA 8hr.		C	STEL 15 min	TWA 8hr.		STEL 10 min	
	ppm	mg/m^3	ppm	mg/m^3	mg/m^3	mg/m^3	ppm	ppm	ppm	mg/m^3	ppm	mg/m^3	ppm	mg/m^3	ppm	mg/m^3	ppm	mg/m^3	ppm	mg/m^3
TDI	0.005	0.04	0.02	0.15	0.035	0.14	0.02	10	0.005	0.045	0.02	0.15	0.005		0.02	0.15		0.02		0.07
HDI									0.005	0.035										
IDI									0.005	0.045										
ISOCY. GROUP NCO														0.02		0.07				

TDI - Toluene 2-4 di-isocyanate
HDI - Hexamethylene di-isocyanate
IDI - Isophorone di-isocyanate
IDHL - Immediate danger to life and health

As from August 1995, the South African exposure limits for all isocyanates have been set at 0.02 mg/m^3 TWA 8hr OEL-CL and 0.07 mg/m^3 STEL(sen).

1.7.1.1 STEL versus TLV (TWA) 8 hours exposure limit

For the purpose of the present investigation into the hazards to which spray painters using isocyanates are exposed, the most significant parameter to consider is the STEL or short term exposure limit level. This is equivalent to 4 exposures each of 15 minute duration with at least one hour interval between such successive exposures. Spray painters are often exposed to many small daily exposures varying from 5 to 15 minutes for spraying panels, doors, bonnets, boot lids and with up to 30 minutes for a complete car re-spray. The only time one would have to consider an 8-hour continuous exposure (excluding lunch and tea breaks) would be for personnel working at a factory, for example, at a motor assembly plant. Here the TLV-TWA (8 hour) exposure limit would be applicable. This study excluded the local motor vehicle assembly plant since it was situated outside the Durban Municipal area and thus outside the scope of the study.

In two similar United States studies on airborne exposure levels of HDI polyisocyanates, Janko *et al,* (1992) in the Oregon study 1980 - 1992, used the Oregon permissible exposure limited (PEL) of 1.0 mg/m^3 Similarly Myer *et al,* (1993), in the Miles Inc. study 1979-1987 used the established Miles Guideline Limit (MGL) of 1.0 mg/m^3 as a short term exposure limit for HDI polyisocyanates.

The author, in keeping with the abovementioned studies, based a recommended STEL value for HDI polyisocyanates (derived from the commercially known product Desmodur N) as a limit of 1.0 mg/ m^3.

1.7.2 South African exposure limits for isocyanates

In South Africa, the Occupational Health and Safety Act of 1993 (Act 85 of 1993) as read with the Environmental Regulations for Workplaces 1987, Notice No. R2281, for the first time, made provision for "prescribed limits" for hazardous or toxic substances to be laid down in law.

Prior to 1995 in the absence of any statutory standards, the ACGIH recommended standards were used by the South African Department of Labour as guidelines only, for the control of toxic airborne substances at the workplace. The new Regulations for Hazardous Chemical Substances, 1995, (Notice No R1179) set legal limits on the amount of chemical substance to which a person may be exposed. This regulation came into force on 25 August 1995 and is applicable throughout South Africa.

The standard for the isocyanates (all as NCO) is a time weighted average occupational exposure limit - control limit (TWA OEL-CL) has been established as 0.02 mg / m^3. The short term occupational exposure limit - control limit (short term OEL-CL) has been set at 0.07 mg / m^3. In addition, isocyanates have been listed as a chemical substance capable of causing respiratory sensitisation .

1.7.2.1 Reporting of isocyanate-induced asthma

Another important change in South African legislation is the inclusion of Section 25 of the Occupational Health and Safety Act, 1993. This section requires that any medical practitioner who examines or treats a person for a disease described in the third schedule of the Compensation for Occupation Injuries and Diseases Act, 1993, and which the practitioner believes arose out of a person's employment, then the matter is to be referred to the person's employer and the Chief Inspector. This provision applies to any isocyanate group induced asthma's. It follows that where such cases are reported then appropriate follow-up action would be taken by the Department of Labour's inspectorate.

References in the regulations to monitoring strategies include the EH 42 document which is a guidance note from the Health and Safety Executive (UK) on the "Monitoring Strategies for Toxic Substances, 1989" and also to the Occupational Safety and Health (NIOSH) Publication No. 77 - 173 of 1977 (USA). There are four basic steps in terms of the new legal requirements for evaluation exposure levels to HDI.

1.7.2.2 Peak flowmeters

Serial measurements of lung function at and away from work can be an important measurement in determining possible occupational asthma cases. However, many workers with occupational asthma are not in fact worse at work but are worse in the evening, after work, and in the night following work, and are often bad again the following morning (Burge, 1993). Their history is often of progressive deterioration throughout the working week with improvement which may take several days away from work to become obvious.

If lung function testing is to have a chance of documenting these changes, measurements have to be made away from work in the morning and the evening and on days when no work takes place at all.

The New Jersey Department of Health, a part of the SENSOR project (Sentinel Event Notification System for Occupational Risks) carried out a study on 70 cases of suspected occupational asthma, notified by physicians between May 1988 and January 1990. The purpose of this study was to identify the strengths and limitations of using portable peak flow meters to document suspected cases of occupational asthma that were reported on this state-wide surveillance project (Henneberger, 1991). Subjects who were still employed in suspect work sites were requested to test themselves for at least 30 days using a portable peak flow meter to generate serial measurements of their peak expiratory flow rates (PEFR). Of the 70 cases examined, 14 subjects were successfully tested and the PEFR data produced valuable information about their asthma-work association. The mean PEFRs l/min for work days and non-work days were 433 and 507 litres/min respectively with a difference of 74 l/min (standard error SE 17.8) for persons with an occupational pattern, in contrast to 454 and 455 litres/min with a difference of -1 l/min (standard error SE 6.6) for persons with a non-occupational pattern (Henneberger, 1991).

The study concludes that the proportion of subjects completing the tests would probably improve if it were conducted when their conditions were first diagnosed.

Furthermore, the collection of serial peak flow measurements to document occupational asthma would be best initiated by the treating physician when the patient first sought care, rather than waiting until the case was reported to the State Health Department.

1.7.3 Recommended - Monitoring strategies for the measurement of isocyanates

With the introduction of the new Regulations for Hazardous Chemical Substances, 1995, reference is made to two further comprehensive documents. These are the Health and Safety Executive (UK) publication EH 42, which is in the form of guidance notes on the "Monitoring Strategies for Toxic Substances, 1989" and also to the "OESSM" which is the Occupational Exposure Sampling Strategy Manual published by the National Institute for Occupational Safety and Health (NIOSH), publication number 77-173 of 1977 (USA).

The Regulations for Hazardous Chemical Substances refers to four basic steps for evaluation exposure levels to HDI. These steps are outlined below:

Step 1: Assessment

Firstly, an assessment to the risk of exposure to HDI in the workplace must be completed. If, after the risk assessment, it is found that a significant risk is present due to the various work procedures, the next step is the monitoring phase.

Step 2: Monitoring phase

This phase measures how much exposure to HDI the worker is receiving through occupational hygiene monitoring. If it is below the action level, viz. < 0.01 mg/m^3 for the TWA-OEL or < 0.035 mg/m^3 for the short term exposure level (STEL), then no further action is necessary. If, however, it is above the action level or exceeds the control level then certain steps have to be taken.

Step 3: Health surveillance

Health surveillance is important as it is used to protect both the short term and the long term health of the employee. Health surveillance includes:

(i) physical examination of the respiratory system and the skin
(ii) carrying out respiratory function tests
(iii) completion of a respiratory questionnaire.

Step 4: Control measures

To reduce the isocyanate exposure levels, control measures are implemented which examine such aspects as spray booth design, improved ventilation systems and the implementation of an effective personal protective equipment programme. This action should be sufficient to reduce the risk of exposure to HDI spray mists and vapours to a minimum. The author has drawn up a detailed strategy for the monitoring of hexamethylene diisocyanate as required by South African legislation and a copy of which has been included in Appendix A " A case study on Hexamethylene diisocyanates-Guidance Notes".

1.8 Overview of the problem

To summarise, it is clear from the related literature that the acute effects of exposure to isocyanates often lead to long term or chronic effects, especially in the case of TDI and that there is far less information on the health effect of HDI exposures. This study is therefore concerned with exposures to HDI, as fewer studies have been published in the literature. Furthermore since it has also been stated in the above review that in many cases the exact mechanisms involved in the production of asthma and subsequent sensitisation are often unknown, it is important not only to examine spirometric lung function parameters, but also to examine the possible immunological aspects of HDI induced asthma. Therefore in order determine the long term effects of exposure to HDI in the automotive spray painting industry, a comprehensive follow up study of a cohort of spray painters was undertaken.

CHAPTER TWO

THE PROBLEM AND ITS SETTING

2.1 THE STATEMENT OF THE PROBLEM

This study examined the respiratory health effects in a follow-up cohort of 40 spray painters (originally studied in 1989) who were exposed to paints containing hexamethylene diisocyanates (HDI), with particular reference to:

- the impact of cross-shift lung function changes in FEV_1;
- non-specific challenge test to identify bronchial hyperresponsiveness;
- the identification of the production of specific antibodies to HDI (RAST HDI);
- the effects of time on pre-FEV_1 baseline lung function from the 1992 to the 1996 study;
- and the evaluation of the environmental working conditions of the spray painters;

One of the principle objectives was therefore to demonstrate how these cumulative long-term exposures may have affected the spray painters' respiratory health status over the four year period. A number of objectives were formulated for this follow -up study and these are listed below.

2.2 THE OBJECTIVES

2.2.1 The first objective

The first objective was to analyse the respiratory effects of exposure to paints containing HDI with particular reference to their impact on cross-shift lung function changes experienced during the working day, in order to illustrate the contribution of HDI towards respiratory problems experienced by spray painters.

2.2.2 The second objective

The second objective was to analyse the respiratory effects of exposure to paints containing HDI with reference to production of antibodies to HDI in order to characterise IgE mediated hypersensitivity.

2.2.3 The third objective

The third objective was to analyse the respiratory effects of exposure to paints containing HDI with reference to the cumulative effects on base line lung function resulting from sustained isocyanate exposures in order to demonstrate the chronic effects resulting from such exposure.

2.2.4 The fourth objective

The fourth objective was to analyse the respiratory effects of exposure to paints containing HDI with particular reference to the environmental conditions of spray painters in order to explain how circumstances at working environment contribute to respiratory disorders.

2.2.5 The fifth objective

The fifth objective was to integrate the knowledge on the contribution of HDI towards respiratory problems experienced by spray painters with reference to IgE mediated hypersensitivity, the chronic effects and the contribution of the working environment to respiratory disorders in order to demonstrate how these cumulative long-term exposures may have affected their respiratory health status.

2.3 THE HYPOTHESES

The central hypothesis in this thesis is that HDI exposure carries both acute and chronic respiratory health effects which are related to exposure levels, duration of exposure and lack of adequate respiratory protection. This hypothesis may be divided as follows:

2.3.1 The first hypothesis

The first hypothesis is that the acute cross-shift changes in lung function relate to the levels of exposure to HDI experienced during the work shift.

2.3.2 The second hypothesis

The second hypothesis is that with the exposure to HDI the resultant decrease in lung function is due to IgE mediated hyperresponsiveness.

2.3.3 The third hypothesis

The third hypothesis is that the cumulative effects of exposure to HDI over a period of time will decrease the baseline lung function levels.

2.3.4 The fourth hypothesis

The fourth hypothesis is that exposures to HDI and the resultant decrease in lung function is associated with increased non-specific bronchial hyperresponsiveness.

2.3.5 The fifth hypothesis

The fifth hypothesis is that the quality of the respirator used, combined with spray booth efficiency, will contribute significantly to the spray painter's respiratory health status.

2.4 THE ASSUMPTIONS

2.4.1 The first assumption

The first assumption is that the environmental conditions including isocyanate exposure levels found during the evaluation of the spray booths are typically representative of the conditions under which the spray painter works.

2.4.2 The second assumption

The second assumption is that the respiratory protective equipment worn by the spray painter is representative of that type of equipment used by him on a regular basis.

2.4.3 The third assumption

The third assumption is that in some instances the adverse health effects evaluated at the employer's spray booth do not reflect the additional exposures received from the undertaking of private work (moonlighting).

2.5 THE DELIMITATIONS OF THE STUDY.

This investigation was based on cohort study of 40 randomly selected automotive spray painters employed in the municipal area of the City of Durban. The original study was initiated in March 1989 and formed the basis of a thesis submitted by the author towards the Master's Diploma in Technology (Public Health). Consequently the following delimitations will apply:

i. The study will cover only those spray painters who were involved in the original study. Cognisance is taken of the fact that some spray painters will be unemployed whilst others may no longer be employed in the motor vehicle industry.

ii. It will be concerned with workers using paints containing organic solvents including the isocyanate group (HDI) in the form of the twin pack and single pack polyurethane paints.

iii. The largest spray application a company undertakes involving the application of isocyanates, is a complete re-spray of a vehicle. This process, on average, takes thirty minutes to accomplish. Therefore the sampling time of the exposure was taken on average over a period of thirty minutes.

2.6 THE IMPORTANCE OF THE STUDY

In the initial cross-sectional study of forty spray painting establishments situated in the Durban municipal area, many spray booths were found to be operating under unsatisfactory conditions and, furthermore, it was apparent that in many instances the incorrect respiratory protective equipment had been provided by the employer and used by the employee. The study further demonstrated that 25% of the spray painters had significant cross-shift FEV_1 declines in lung function measured over a work shift (Randolph *et al*, 1997).

The consequences of isocyanate exposures are considerable in terms of symptoms, decrement in lung function, occupational related lung diseases and financial costs. Chan -Yueng (1986) reports that approximately 5 - 10% of workers exposed to TDI develop asthma. The asthmatic symptoms develop in weeks or months after the start of exposure. In sensitised patients exposures as low as < 0.005 ppm, may induce an attack of asthma. Studies involving hexamethylene diisocyanate (HDI) have not been as systematically studied as toluene diisocyanate (TDI). Chan -Yueng (1986) reported that clinical studies with hexamethylene diisocyanate (HDI) are less common than those involving other isocyanates. Furthermore Banks (1986) in discussing the adverse respiratory effects due to the less common isocyanates (including hexamethylene diisocyanate), reports that the data necessary to make conclusions about the risk of respiratory impairment in association with exposure remains inadequate. He then concludes by suggesting that although it appears that exposure to these agents (HDI) can cause respiratory tract disease (primary asthma), the paucity of data regarding prevalence of respiratory illness in persons exposed, suggests that their ability to induce respiratory illness is probably weak.
This theory needs to be examined and hence the importance of this study.

If diagnosis is delayed it is possible that the symptoms will not completely be resolved and that the abnormalities of lung will remain, even when the patient is removed from exposure.

It has been reported that sensitivity to TDI can persist for many years even in the absence of further occupational exposures and suggests that some patients with TDI induced asthma do not recover from their disease after being removed from isocyanate exposure. Moreover, continuous exposures to TDI in sensitised patients led to further deterioration in lung function and increase in non-specific bronchial reactivity, thus making it very important that patients with occupational asthma should be diagnosed early and removed from exposure as soon as possible (Chan-Yueng, 1986).

Overseas research has clearly indicated the extent of the isocyanate problem. Isocyanates are now the principle cause of occupational asthma in industrialised countries due to their high chemical reactivity and wide-spread industrial use. Every isocyanate regardless of its molecular form or volatility, should be considered hazardous (Vandenplas *et al*, 1993).

In a preliminary report of a surveillance scheme of occupational asthma in the West Midlands in the United Kingdom, the top four agents causing incidents of occupational asthma were **isocyanates**, colophony, flour and oil mist. These exposures closely matched the top four occupations **spray painters**, solderers, machine tool operators and bakers (Gannon *et al,* 1991) (Plate 2.1).

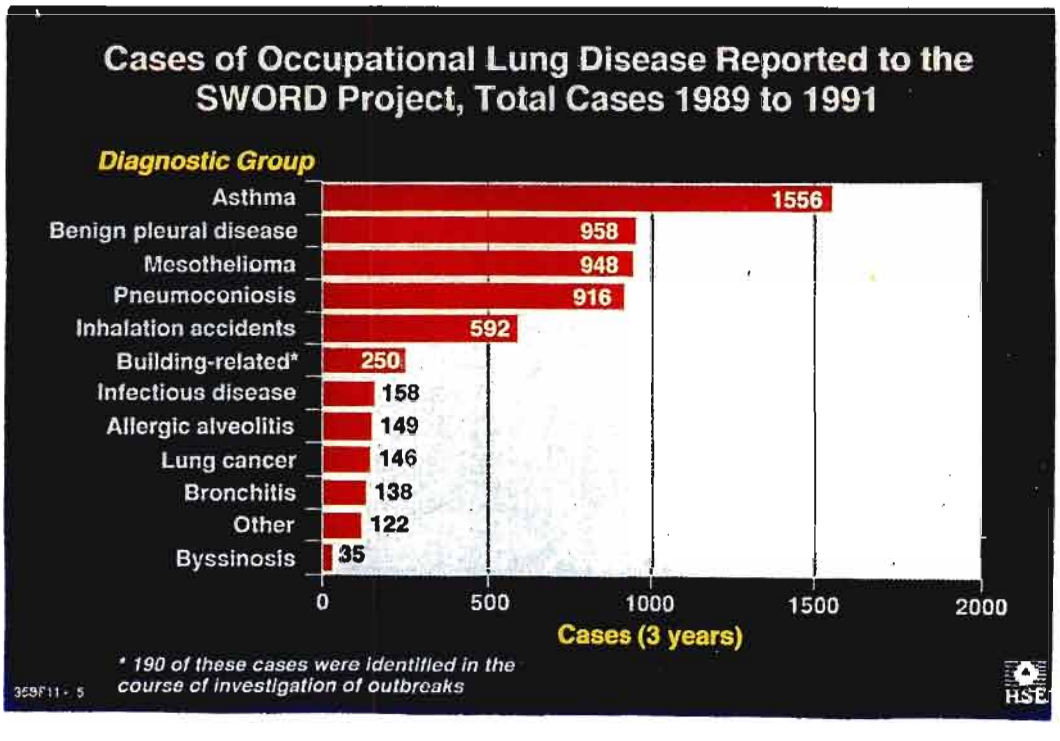


Plate 2.1: Cases of occupational lung disease reported to the SWORD project.

In June 1992 in South Africa the Compensation Commissioner acknowledged the importance of isocyanate induced asthma by placing it on the second schedule of listed compensatable diseases (Government Notice 576 of 1992). The solution to the problem would necessitate a comprehensive investigation as proposed by this study including spray booth evaluations, and the completion of a health questionnaire followed by lung function testing. From such a study appropriate recommendations could be drawn, including an action plan.

This study proposes to examine the working conditions, past and present, including respiratory health status, respiratory protective equipment and employees' attitudes towards safety. This prospective study is of particular importance as cross-sectional surveys are likely to underestimate the actual prevalence of isocyanate induced asthma, as workers with work-related respiratory symptoms tend to leave their place of employment (Vandenplas *et al*, 1993). Little is known of what happens to the workers afterwards since no evidence of this can be found in the literature, hence the need for this follow-up study.

Prior to the initial study, the indications were that none of the spray booths examined had been previously evaluated at any time or that isocyanate concentration levels were measured.

Finally, under the present health care system in South Africa, the cost of treating a patient suffering from occupational asthma is considerable, the costs being borne by the Compensation Commissioner, the employer, and in some instances the employee. Lost time due to absence from work resulting from ill-health would also be included in such costs. This study will also provide a valid database on the adverse effects of exposure to isocyanates in the automotive industry in South Africa. The data could be used to motivate for a more cost effective, healthier and safer working environment for spray painters. This could be achieved in the production and distribution of an "employers guideline" on the safety precautions in the handling of spray paint containing hexamethylene diisocyanate. The document will be based on actual South African working conditions and current legislation (Annexure A).

CHAPTER THREE
METHODS

3.1 INTRODUCTION

In this chapter a number of methods on how to capture the data were described and in order to make an evaluation of the spray-painter's health in relation to his environmental working conditions. The respiratory health status of the spray painters was determined by data obtained from: -

(a) a standardised respiratory questionnaire
(b) cross-shift lung function testing
(c) baseline lung function testing

Attitudes of the employee to safety in the spray booth were assessed by means of a safety questionnaire. Spray booth efficiency was determined by measuring concentrations of the main chemical pollutant, isocyanate and simultaneously the measurement of air flow and air flow patterns designed to remove these contaminants.

3.2 DESCRIPTIONS OF THE DATA NEEDED

The data were made up of two kinds, primary and secondary data.

3.2.1 The primary data

Two main categories of primary data were obtained:-

a) Questionnaires:

i) The responses of the spray-painters to a health questionnaire to assess their present state of health.

ii) The responses of the employee to questions on safety and the availability and usage of safety equipment.

b) Evaluation by Direct Measurement:

To obtain data for the study , tests and measurements were carried out under the following headings : -

i) Lung function testing.
ii) Peak flow measurements for both occupational (exposed) and non- occupational (non-exposed) subjects.
iii) Blood samples were taken from each spray painter to assess RAST to HDI and house dust mite tests.
iv) Air velocity and air currents movements within the spray booths were determined.
v) Samples of air were obtained and analysed to assess the HDI concentration levels within the spray booth under normal working conditions.

3.2.2 The secondary data

The secondary data required for this investigation can be divided into two broad categories. These are:-

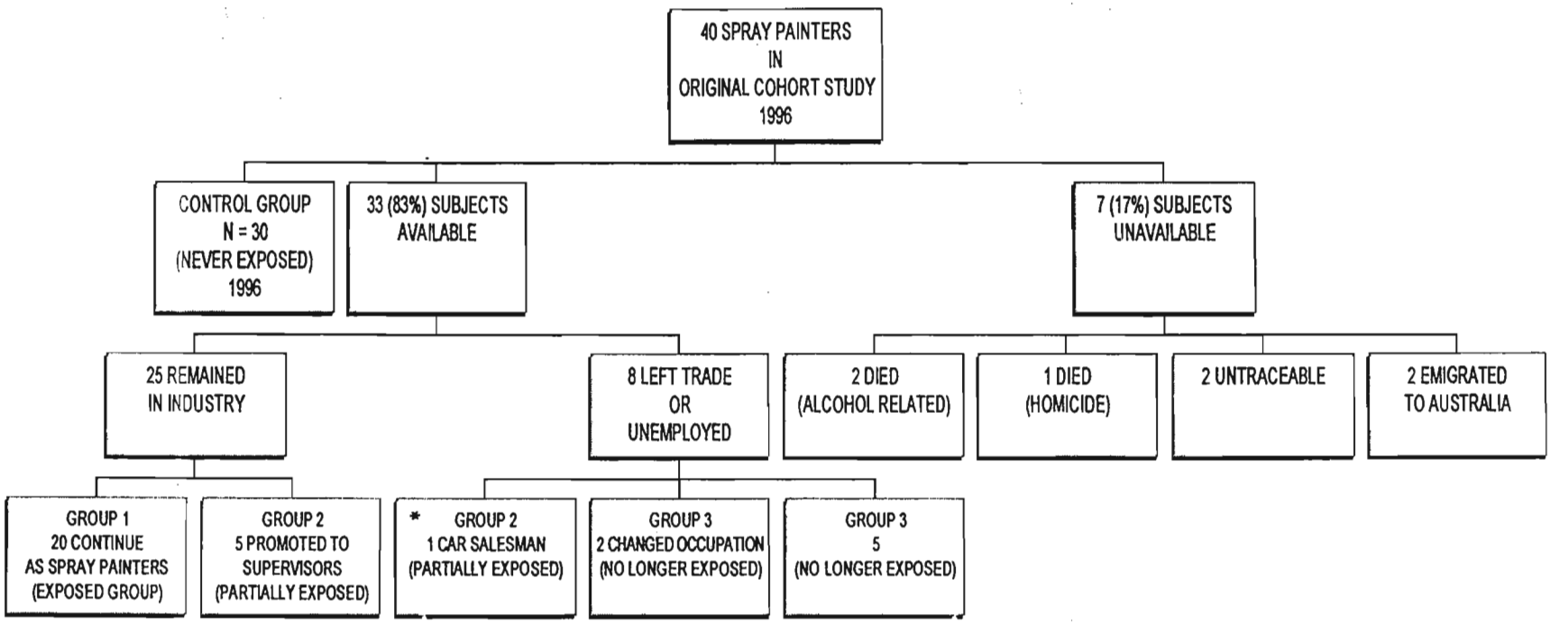
i) Research data taken from the initial research completed in 1992.
ii) Overseas and local literature on isocyanates from journals and books including publications of statutory and recommended standards such as OSHA, NIOSH and ACGIH agencies in the United States and the HSE publications from the United Kingdom on exposure levels were of relevance. Furthermore, local publications in the government gazettes, SABS specifications on " approved respiratory safety equipment " and also the minimum air flow requirements for spray booths as prescribed in the General Safety Regulations made under the Occupational Health and Safety Act 1993.

3.2.3 The criteria governing the admissibility of the data

Apart from the randomly selected control group, only information obtained from the 33 subjects who were either still involved in the spray painting industry or from those who had left the trade including the unemployed was evaluated. All subjects were personally contacted by the author and the relevant data was collected in terms of the objectives of the study as outlined in Chapter 2.

3.3 STUDY POPULATION

This study is a follow-up investigation of 33 spray painters and ex-spray painters selected from an original cohort of 40 workers who were first examined four years earlier (Fig. 3.1). From a table of random numbers, 40 spray painters were randomly selected from a list of 163 registered automotive spray painting establishments situated within the greater Durban area (Randolph *et al*, 1997). The lists were obtained from City Health Department and the Department of Labour Offices, Durban. Only 1 spray painter at each establishment was selected for study. The majority of the spray painting establishments had only one spray painter, however in 2 establishments where more than 1 worker was employed to undertake the spraying of motor vehicles, the longest serving worker was investigated.



* The car salesman was excluded from the tables because his exposure could not be classified as being similar to any of the other groups

Figure 3.1: Breakdown from the initial 40 spray painters to the remaining 33 subjects in the cohort study.

As indicated in Figure 3.1, seven workers were lost to the follow-up study for the following reasons:- 3 died, 2 emigrated and 2 were untraceable. Two of the deaths were attributed to excessive alcohol consumption and the third as a result of a homicide. In order to investigate the respiratory health status of the workers in relation to his working environment, several evaluations were conducted.

Information regarding the addresses of the two spray painters who had emigrated to Australia was obtained from relatives but despite letters being sent, no replies were received. The remaining 33 (83% of original cohort) spray painters and ex-spray painters, were arbitrarily categorised into three groups according to their exposures viz. exposed, intermittently exposed and no longer exposed. These groups have been defined as shown below.

i) Group 1 (exposed group)

Twenty spray painters who continued spray painting as in the first study, either in spray booths or in open workshops and who were therefore still "exposed " to the effects of HDI.

ii) Group 2 (partially or exposed group)

There was a total of 6 in this category. Of these, 5 were spray painters who had been promoted to the position of supervisors and who were therefore only intermittently exposed to isocyanates. Since the functions of supervisors are to examine the car at various stages of completion they may from time to time be exposed to low concentrations of HDI within the workshop when compared to levels of HDI in the actual spray booth. This group also includes one automotive paints salesman who was also exposed to intermittent isocyanate vapours, whilst demonstrating to customers on how to apply the automotive spray paint in the spray booth. Since the paint salesman exposure was unpredictable, he was difficult to classify according to these three group classifications.

iii) Group 3 (no longer exposed group)

There are 7 in this category, 5 who became unemployed and 2 who changed occupations. This group was therefore no longer exposed to the effects of HDI after leaving the trade.

iv) Group 4 (Control group-never exposed group)

This group comprised of a total of 30 subjects of which 12 (40%) Coloured and 18 (60%) Indian males (of similar ethnic origin to the first study), were randomly selected to serve as a control. According to the questionnaire, this group had never been exposed to dust or fumes in their work environment. They were classified as the "never exposed group".

3.4 DATA COLLECTION

3.4.1 Spirometry

3.4.1.1 Introduction

A Vitalograph Alpha® spirometer was used to test each spray painter's lung function. Prior to this study, no routine spirometric evaluation of spray painters had, according to the author's information, been undertaken in South Africa. A lung function test was performed on each spray painter using a Vitalograph Alpha ® to measure spirometric lung function variables. Each spray painter was pre-tested before commencing work in the spray booth, that is, during the early morning prior to that day's isocyanate exposure. Similarly, a post- test was carried out (after a complete spray job) in the late afternoon, allowing some 6 to 8 hours to elapse and thus time for the isocyanates to react within the subjects' lungs (Zwi, 1985).

In addition to the lung function test, a health questionnaire was completed stating the subjects' medical history, such as previous chest illnesses like TB, bronchitis, asthma and information on smoking habits. Rosenberg *et al,* (1986) described a similar technique of using a questionnaire followed by a lung function test in a follow-up study of isocyanate induced asthma cases.

A detailed interviewer - administered respiratory health questionnaire based on the standardised American Thoracic Society's (ATS) questionnaire, was completed for each subject. Questions included details about anthropometric data, smoking status, work related symptoms such as cough, wheeze, dyspnea, asthma and bronchitis. A copy of the health questionnaire is included in Appendix B.

3.4.1.2 The Instrument - the Vitalograph Alpha® spirometer.

The Vitalograph Alpha® is a portable spirometer manufactured by Vitalograph Ltd, Buckingham, England. It is designed for measuring expiratory parameters of forced vital capacity (FVC) and slow vital capacity (VC). The progress of each test is demonstrated via a liquid crystal display on the front panel of the instrument. The test results are based on a software cartridge, according to the predicted lung function regression equations for the European Community Coal and Steel. (ECCS) (Quanjer, 1983). A copy of the ECCS regression equations are included in Appendix C. These results are automatically produced on a print-out. This spirometer is fitted with a pneumotachograph type flowhead of large diameter capable of giving linear results throughout the entire physiological range of expiratory manoeuvres.

Flow through the flowhead and into the resistive element produces a positive pressure in respect of the surrounding air pressure at the pitot tube situated at the rear of the flowhead. The pressure is transferred to the transducer via a length of silicone rubber tubing. The pressure transducer output is converted into an electric signal and the microprocessor manages the data and displays the results on the screen. The Vitalograph Alpha conforms to the specifications of the ATS (Vitalograph Alpha Handbook).

Note: The European Community Coal and Steel (ECCS) predicted values were used, which discounted the predicted values by 15% for non-caucasians (Quanjer, 1983).

3.4.1.3 Spirometric Test procedures

In order to eliminate bias, the same spirometer was used as well as the same person (author) performed the tests in both the initial and follow-up studies. The procedure used for spirometric testing is set out below :-

1. The Vitalograph Alpha® was calibrated both before and after each survey using a 1 litre precision syringe. Where there was an error >3%, the calibration figure was discarded and the procedure for re-calibration followed. The ambient temperature was noted and the personal data including height, age and race group entered.

2. The subject's height was measured barefoot using a calibrated ruler. Measurements were to the nearest centimetre.

3. Each subject was clearly instructed on the procedure to be followed prior to the commencement of the lung function tests. It was important for the subject to conduct several practice attempts, so that the maximum effort was obtained and recorded (Vitalograph Alpha Handbook).

4. Where three acceptable readings of the VC and FVC showed a variation of <5%, the higher reading was automatically placed in the Vitalograph 'memory' system. Readings showing a variation in the lung function parameters >5% were discarded (Vitalograph Alpha Handbook).

5. Tests were performed with the subject in the standing position. Nose clips were not used since they are not very practical (White, 1989). As an alternative subjects were required to occlude their nasal passages using their thumb and forefinger prior to exhaling into the spirometer. Disposable mouthpieces which fitted easily into the mouth were used.

6. The Vitalograph Alpha® was designed to automatically calculate the VC, FVC, FEV_1, FEV_1/VC and FEV_1/FVC, FEF, and PEF values and give a print out of the results of the measured as well as the predicted values based on the "European Community Coal and Steel" values (ECCS, 1983).

3.4.1.4 Training instructions for performing spirometric testing

In order to ensure operator proficiency, prior to spirometric lung function testing, the author was instructed on the correct procedures to follow by the staff of the Thoracic Unit, Wentworth Hospital and Prof. U. G. Lalloo of the Respiratory Unit of the King Edward VIII Hospital, Durban. Furthermore, to verify the author's competency in the field of spirometric testing an experienced medical practitioner, accompanied the author and witnessed a lung function evaluation being performed on a spray painter at one of the spray booths.

3.4.1.5 Subject instruction for performing spirometric testing

It was essential that the subject performing the test was clearly instructed in the two spirometric manoeuvres, the VC and the FVC tests. The following protocol was carefully followed by the author and subject to ensure the accuracy of the test results.

Each subject was carefully instructed on the procedure to follow prior to the commencement of the test. The test required a very enthusiastic performance by the operator so that maximum effort was made when carrying out the forced expiratory test. Although all the spray painters had previously performed spirometric tests in the initial study it was still felt that two to three practice attempts were still necessary to remind the subjects of the correct procedures to follow. Before commencement it was important that subjects be reminded to keep their fingers clear of the flowhead mesh to ensure unimpeded air flow during exhalation. The detailed step by step instructions given by the operator to each subject are listed below.

i) SLOW VC TEST INSTRUCTIONS TO SUBJECT:

Let the subject hold the flowhead in one hand, then say " *I am measuring how much air you can get out of your lungs". "This is what you' ll do.* " Take a mouthpiece in your hand to demonstrate.

Step 1.

"*Breath in and out normally. Take in a deep breath and fill your lungs completely through your nose like this*" (and you do it).

Step 2.

"Now, put the mouthpiece into your mouth ... close lips around it.... like this ... so that there is no leakage there, not like a trumpet, with pursed lips".

Step 3.

"Next you breathe out into the instrument.... as much and as completely as you can.... like this". Pinching your nose tightly, you breathe through the mouthpiece. "That is all you'll have to do ".

Step 4.

After the subject has had three practice attempts and is ready to perform the test - select VC test from the menu. It is important that the flowhead is not moved excessively after the selection has been made. *"Now let's do the test.... anytime you're ready.... deep breath.... fill your lungs completely*". As soon as the subject has his lips sealed on the mouthpiece, encourage him. "*Slowly....go on.... breathe out.... as much as you can*". When you are satisfied that the subject has expired his total air volume.

"*Thank you that was very good*". Repeat test three times as required.

ii) FORCED VITAL CAPACITY TEST/ FLOW VOLUME CURVE INSTRUCTIONS TO SUBJECTS

Step 1

"I want to measure now how fast you can blow". "This is what you do ....breathe in and *out normally. Then take in a deep breath much deeper than before* ".

Step 2.

"*Put the mouthpiece into your mouth ... close your lips around it*"..... "*But this time, blow as hard and fast as you possibly can.... like this*".

Step 3

"Now let's do this test.... any time you're ready". As the subject is getting ready to do the test, you quickly reiterate the main points.

Step 4

Select FVC test from the menu. It is important that the flowhead is not move excessively after the selection has been made. After the first half second of the FVC test, urge in a raised voice. "Go on fast.... faster.... much faster.... go on.... go..on .... go *on*".

3.4.2 Measurement of Peak Expiratory Flow Rate

For many applications, the results of tests of lung ventilation are interpreted on the basis of serial measurements. Material changes such as occur in clinical medicine are easily detected; small annual changes due to smoking or to occupational air pollution are detected with more difficulty. Serial measurements can also be done using only one spirometric parameter, such as the peak expiratory flow rate (PEF). An inexpensive Peak Flow Meter is available to continuously monitor ventilatory function. on an ambulatory basis to detect the pattern of acute changes in relation to workplace exposures. Portable peak flow meters were used to measure each spray painter's peak expiratory flow rate (PEFR) according to the protocol used by Henneberger *et al,* (1991). After discussing the procedures to be adopted, the subject's consent was first obtained and the peak flow meter and a record sheet was delivered together with written instructions on how to follow the protocol. The subject was requested to conduct four trials a day before each meal and again at bedtime, thus making a total of 12 entries into the log sheet. For each trial, the subject had to blow with maximum effort into the peak flow meter and then record each measurement on the sheet provided. Instructions also included notification of any medication being taken and on how the use the peak flow meter. Practice attempts by each subject were made to ensure familiarity with the required procedures. Tests were to be conducted over a continuous period of 30 days and, when testing was completed, the author collected the flow meter and record sheet at the person's workplace.

Plate 3.1: Demonstration of the Mini-Wright peak flow meter

This study used the Mini-Wright peak flow meter manufactured by Clement Clarke International Limited catalogue number 920122910 to measure the peak flows in the subjects (Plate 3.1). The design of the peak flow meter was based on that drawn up by the Medical Research Council, UK. The scale used was from 60-800 litres per minute. Each spray painter was supplied with a disposable mouth piece.

3.4.3 Bronchial hyperresponsive tests/(PC_{20})

3.4.3.1 Introduction

Methacholine or histamine inhalation tests are useful means of confirming the diagnosis of asthma as well as helping to document that the asthma is caused by sensitisation to materials at work (Chan-Yeung, 1986). Measurement of non-specific bronchial hyper-reactivity is usually carried out by histamine or methacholine inhalation tests. There are two methods widely in use, the one described in detail by Cockcroft and co-workers was applied (Cockcroft, 1977).

Bronchial hyperresponsiveness tests using histamine were carried out at the Respiratory Unit, King Edward Hospital, Durban under the supervision of Prof. U. G. Lalloo. Details of the protocol are stated below and the procedure for applying the tests was strictly followed at all times, under the supervision of a medical doctor.

3.4.3.2 Aerosol generation

The most important factor to standardise when conducting the tests is the amount of aerosol delivered to the mouth. This is determined by the output of the nebuliser and the apparatus between the nebuliser and the mouth. The output is determined by the flow rate of air or oxygen through the nebuliser and the driving pressure. The output will vary not only between different models but also between different nebulisers of the same model.

A Wright nebuliser with a 3ml of solution in the container was used operating under a pressure of 50 p.s.i. (Cockcroft *et al*, 1977). Each nebuliser was calibrated to operate at a flow rate which gave an output of 0.13 - 0.15 μm particle size (aerodynamic mass median diameter). It does not appear important to measure this variation as particle size between 1.0 - 3.6 μm does not seem to influence the response (Ryan *et al*, 1981). Aerosol is delivered directly from the nebuliser into a face mask without intervening tubing or re-breathing bag.

3.4.3.3 Aerosol inhalation

The subject was seated, wearing a nose clip and breathing from the face mask held loosely to the face. The aerosol was inhaled during tidal breathing for two minutes. The subject was told to breathe normally. It was not necessary to monitor the frequency of breathing, minute ventilation or inspiratory flow rate. At higher doses of histamine the subjects were advised to close their eyes to avoid conjunctival irritation.

3.4.3.4 Solutions

Histamine acid phosphate in concentrations of 0.015, 0.03, 0.06, 0.125, 0.25, 0.50, 1, 2, 4, 8 and 16 mg/ml were used in the investigation. Higher concentrations of 64 mg/ml were not used in this research since the side effects may have been troublesome.

Sterile phosphate buffered saline (PBS) was used as a control and to prepare the solutions of histamine. Solutions have a pH of about 7.4 and were stored in a refrigerator at 4 °C.

Unbuffered solutions of histamine have a lower pH and this would increase bronchial responsiveness. The temperature of the solution in the vial alters the nebuliser output slightly and may alter the response, and therefore the starting temperature should be regulated. The histamine solution was renewed every 6 weeks.

3.4.3.5 Procedure

The following procedure was followed for each subject:

1. Record drug therapy including time of last dose. Beta receptor agonists were withheld for 8 hours, theophylline for 24 hours and slow release theophylline preparations and antihistamines for 48 hours before the test.

2. Each subject was informed about the purpose of the test and how it would be conducted. Emphasis was placed on the importance of performing the FEV_1 correctly each time.

3. The baseline FEV_1 was measured at least three times or until reproducible within 5%. The subjects were told not to blow right out to residual volume (RV) on FEV_1 manoeuvres as this may cause broncho-constriction. Baseline FVC was measured. These values were at body temperature (37^0) and pressure and fully saturated with water (BTPS) so that they could be compared to other measurements on separate days. The subjects FEV_1 was measured to ensure that baseline FEV_1 was > 60% predicted.

4. The subject was first required to inhale the control solution of sterile phosphate buffered saline (PBS). The nose clip was applied and the face mask held loosely over the nose and mouth and the subjects were required to breathe in a relaxed way by tidal breathing for two minutes. The container of the nebuliser was held vertically. The subjects were requested to hold the mask not the nebuliser.

5. The FEV_1 was measured at 30 and 90 seconds using the Vitalograph®. If the FEV_1 at 90 seconds was the same or lower than that at 30 seconds, the measurement was repeated at three minutes, and if needed, at two minute intervals until the FEV_1 started to rise. An example of the measurement data and the form used for consent and recording the information data is presented in Appendix D.

The FEV_1 was only measured once on each occasion unless it was not technically satisfactory when it was measured again straight away. If the FEV_1 fell by 20% or more or below one litre, the test was discontinued.

6. The subjects were advised that subsequent aerosol inhalation may produce mild cough, chest tightness or dyspnoea and should symptoms become uncomfortable to take off the mask.

7. Each subject was given inhalations of histamine for two minutes at intervals of five minutes. All starting concentrations were at 0.03 mg/ml.

8. After each inhalation of histamine the FEV_1 were repeated as in step 5 above. If the FEV_1 fell by 20% or more no further inhalations were given.

9. Upon the completion of the tests and after the FEV_1 had started to rise the subject was given two puffs of salbutamol. Subjects were then asked to wait and again the FEV_1 and the VC was checked to ensure return to baseline values before the subject was discharged from the Respiratory Unit, King Edward V111 Hospital.

3.4.4 RAST HDI / IgE Tests

Radioallergosorbent Test (RAST) is a specialised form of radioimmunoassay (RIA) for detecting antigen specific IgE, in which antigen is covalently coupled to cellulose discs. Antigen specific IgE binding to the disc is detected using radiolabelled anti-IgE. Samples of blood were obtained from 17 subjects at the work place in accordance with the approved protocol and sent directly to the laboratory for analysis. The reason only 17 blood samples were obtained from the 25 subjects was that 4 subjects had refused consent and 4 subjects were not available for testing. Total immunoglobulin E (IgE) was measured using the Kabi Pharmacia IgE Radio Immunoassay ACT kit. HDI specific IgE was assayed by radioallergosorbent test (RAST - HDI) using the Pharmacia CAP System (RAST kit lot No. K77 98863, expiry June 1995) in accordance with the manufacturer's instructions. (Pharmacia Cap System RAST Units (kUA/1)). WHO - IgE standard based calibrators are used for determination of total IgE and values are expressed in kUA/l. In Pharmacia CAP System RAST these standards are also used for determination of specific IgE antibodies and values are expressed in kUA/l where A represents Allergen specific antibodies. Values of 0.35 kUA/l and above represent a progressive increase in the relative concentration of allergen specific antibodies.

Values of less than 0.35 kUA/1 represent absent or undetected levels of allergen specific antibodies. In addition, the house dust mite and RAST was carried out to investigate a possible allergy from this source.

3.4.5 Spray booth evaluation

3.4.5.1 Introduction

In determining the concentration of isocyanates cognisance had to be taken of the following factors:

(i) The possible large range of very high and very low isocyanate levels to be found in the spray booths.

(ii) The limited sampling period of 30 minutes available at each booth.

(iii) The fact that certain chemical compounds, other than isocyanates, present in the spray booth atmospheres could interfere and influence the collection of and the analytical methods used, to accurately determine the concentrations of isocyanates present.

To overcome this problem a study of the related literature was made and a suitable method selected. The Health and Safety Executive (HSE) in their internal report reference IR/L/AO/83/201983 state that a number of acceptable methods can be used to determine concentration levels of the isocyanate group. The choice of using NIOSH method 5505 over other available methods was based on the reliability and accuracy of detecting low levels of the isocyanate group over a relatively small sampling period. The International Isocyanate Institute publication on the "Analysis of Isocyanates in Air" describes various recognised methods available to evaluate isocyanate levels. Details of the form used to evaluate each booth is shown in Appendix E.

The method using I - (2-methoxyphenyl) piperazine as a derivatising agent was selected for its applicability, range, precision and reliability, coupled with minimum amount of interferences. The literature further reports that in the lower range in a 10 litre sample, the following detection limits were obtained for TDI MDI and HDI.

TDI 0.2 $\mu g/m^3$ and greater
MDI 0.5 $\mu g/m^3$
HDI 0.2 $\mu g/m^3$

Precision was estimated at ±5% or better for the HPLC evaluation method. Warwick *et al*, (1981) in their evaluation of isocyanates in the foam industry used the electrochemical detection method utilising 1 - (2- methoxyphenyl) piperazine. They reported that this method was significantly more sensitive than other detection methods. Similarly, the Health and Safety Executive in their official report on the methods for the determination of hazardous substances (MDHS No 25-1983) recommend 1 - (2-methoxyphenyl) piperazine as an absorbing solution and high performance liquid chromatography as an analytical method for determining the concentration of the isocyanate group in the workplace atmosphere.

The NIOSH method 5505 issued 2/15/84 determines the total concentration of the isocyanate group regardless of the molecule to which the isocyanate is attached. A copy of this method is shown in Appendix F.

3.4.5.2 Sampling Method (NIOSH 5505)

The principle for this method of sampling is based on drawing a known volume of air through a glass impinger containing a "trapping" solution. To achieve this an SKC constant flow pump was connected to an impinger and run at a sampling rate of 1 litre per minute for 30 minutes. Each sample therefore contained a fixed volume of 30 litres and took the equivalent time for a spray painter to complete a re-spray of a vehicle. After each sampling period, the impinger (figure 3.2) was carefully removed to avoid spillage and the level of the solution, allowing for evaporation, was brought back to the 15 ml mark using pure toluene.

This procedure standardised each sample taken. The samples were then prepared for analysis (NIOSH Method 5505).

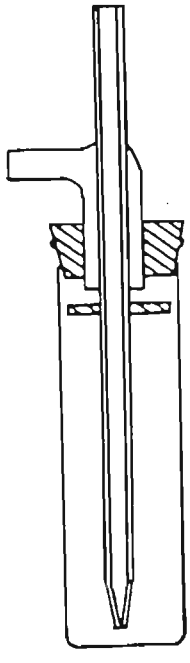


Figure 3.2: Impinger used for collecting the isocyanates (Health and Safety Executive MDHS 25, 1987: para 21)

3.4.5.3 Analytical Procedure

The NIOSH 5505 analytical method used high precision liquid chromatography. The organic isocyanates react to form urea derivatives. The resultant solution was concentrated and analysed with a high performance liquid chromatograph (HPLC). The Varian 5000 - LC5060 equipped with an ultra violet and electrochemical detector was used. Isocyanate derived peaks were identified on the basis of their electrochemical and ultra violet response.

A solution of 1-(2-Methoxyphenyl) Piperazine (MPP) is prepared in Merck Analar Toluene at a concentration of 43mg/l. This is refrigerator stored and is supplied to the author in 150ml medical flat glass botties.

(I) *Sampling*

- The author supplied the analyst with the sample topped up to 15 mls using Merck Analar Toluene.

(ii) *Preparation*

- aliquots of returned sample or retained control liquid are pipetted into #1 vials and 10 µl of Riedel de Haen Reagent Grade Acetic Anhydride is added using an SGE 10µl syringe.
- The vial is mounted in a gas purge rig mounted on a 50^0 C hot air bath.
- When the vial has evaporated to dryness 200µl of Merck Analar Methanol is added to the vial and it is left to stand for 20 minutes with frequent shaking.
- This solution is now ready for evaluation.

(iii) *Calibration*

- Working standards between 25 and 450 µg/l are prepared in METHANOL.
- Prepare a calibration graph of area versus amount in µg per 15ml of original solution. The calibration graph can be seen in Appendix G. Note: The amount present in the original 15ml sample is 1.5 times the concentration of the analysed solution (0.2ml aliquot 7.5 aliquots sample).

(iv) *Chromatography*

- Mobile Phase. 1.2g sodium acetate dissolved in 1 litre of distilled water. Dilute to 2 litres with acetonitrile and adjust pH to 6 with distilled water.
- Column Techsil10C8 25cm*4.6mm ex HPLC Technology.
- Detector 254 nm Varian fixed frequency.
- Pump Varian 2010 isocratic flow 1ml/min.
- Data System. Delta Chromatography System Version 4.1.
- Sample loop approximately 4µl.

(v) *Calculations*

- Read (Ms)µg of MPP per 15ml sample from the calibration graph for each sample.
- Calculate the initial amount (M1)µg of each reagent in µg by averaging the three samples prepared from the virgin sampling medium.
- Calculate the concentration of isocyanate groups (C µmol/m^3) in the air volume samples Vl.
- ((M1-Ms)*1000)/(192.26*V) µmol/m^3 of MPP

(vi) *Range*

- to 3.5 µmol MPP per sample.

(vii) *Applicability*

- This method is used to measure the total amount of MPP consumed, this then relates to the total amount of materials capable of reacting with MPP.
- This is then taken as the µmol/l of free isocyanates both monomeric and polymeric, liquid and vapour.
- The molecular mass of the commercial isocyanates are published by the manufacturers.

(viii) *Interferences*

- Phosgene. Acid Halides. Esters are capable of reacting with MPP and causing a positive bias.

(ix) *Cross Checks*

- The organic vapours associated with spray paints are readily measured. It is possible to get an independent estimate of the situation from this.

(x) *Comments*

- The sampling method does not differentiate between different forms of isocyanate. Aerosols, coarse particles and vapours are treated alike.

- The method relies on the integrity of the spray operator/paint manufacturer because the specific material is not identified. We only measure the MPP consumed.
- The MPP is competing with the paint polyols and water in the atmosphere for the isocyanate groups.
- The resulting MPP peak is not in general clear, at least one negative peak co-elutes. this making quantification difficult.

3.4.5.4 Air Velocity Measurement

The practical difficulties in measuring air velocities are the fluctuating air speeds and turbulence. These variables may be a result of poor spray booth design factors, varying motor outputs, blocked or partially blocked filters, the incorrect positioning of baffles and/or filters. Air velocities found in the spray booth vary from zero to a maximum of 1 m/sec. On average, velocities varied in the range of 0.1 to 0.5 m/sec.

The instrument selected must be capable of operating accurately within this range of application. To meet with these requirements, Bradley and Bodsworth (1983) in their evaluation of a large spray booth advocated the use of a hot wire anemometer. A thermistor may also be used to measure air velocity inside spray booths. Both instruments use the principle of the cooling effect of air passing over a heat-sensitive device. In the case of the thermistor it is a solid bead, whereas in the hot wire anemometer a very fine platinum wire is utilised. However, it was decided to select a thermistor bead anemometer for the survey, as it is more rugged and would be less likely to be damaged whilst in transit and whilst being used in the field.

(i) Airflow Thermistor

The thermistor used to evaluate air velocities in the spray booths was an "Airflow" thermal anemometer model TA-2-2 manufactured by Airflow Developments Ltd, High Wycombe, Buckinghamshire, England. This precision instrument gives direct readings of air velocity. The sensing element is a thermistor bead electrically maintained at a temperature of 120^{0}C.

Regarding the manufacturer's specifications for this instrument, velocity accuracy at 20 ^{0}C and 1013 m.bar is ± 3% full scale deflection (FSD). The velocity range for Model TA-2-2 is between 0 - 2 m/sec and the working temperature range is from 0 - 80^{0}C.

(ii) Evaluation method

A set of twelve readings of the air flows were taken for each evaluation which consisted of three readings taken from the front, rear and sides of the vehicle (figure 3.3). These air flow values were then recorded on a diagram and an average air flow was calculated.

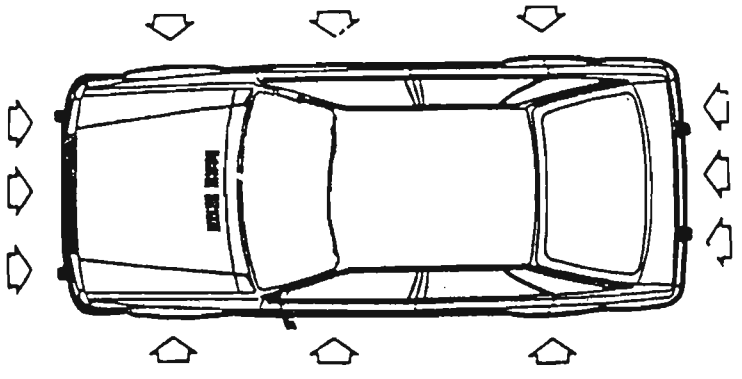


Figure 3.3: Position of the air velocity measuring points

The readings were taken at a height of 1.5 metres above the spray booth floor level in accordance with the General Safety Regulations (1986: No R1031) under the Occupational Health and Safety Act 1993. Where readings were found to fluctuate because of turbulence or intermittent air flows, the maximum deflection was recorded. This was decided in order to indicate the most favourable conditions under which spray booths were being operated. Before each set of readings was taken a battery check was made and the instrument was mechanically zeroed where necessary.

3.4.5.5 Air Flow Pattern Determination

It is necessary as part of the survey to estimate the air flow patterns in a spray booth to determine in which direction the contaminants are being removed. In order to accomplish this, air current tubes were used. These tubes emit a dense white smoke which is carried by the air stream in the spray booths. The use of air current tubes was advocated by Bradley and Bodsworth (1983) in their survey carried out in the United Kingdom. The inspectorate at the Department of Labour also makes use of Dräger air current tubes to determine air flow patterns in spray booths, and since these imported tubes are available locally it was decided to make use of this method of evaluation in the study.

(i) Evaluation Method

The Dräger operating instruction No. 4351, 4 th edition dated June 1986 as prescribed, was followed.

- Each tip of the air flow tube was broken;
- The air current tube was then inserted into the mouthpiece of the rubber bulb;
- Air was pumped through the rubber bulb, occluding the hole with the thumb.

Air flow direction was clearly visible by the emission of dense white smoke. Smoke patterns indicating turbulence forming around the vehicle were carefully sketched and noted in the records.

3.4.6 Employees' Health And Safety Questionnaire

A second questionnaire was completed regarding health and safety at the workplace including questions on respiratory protective equipment, health and safety training, the provision and availability of hazard data sheets on the application of HDI and finally the spray painter's perceptions of the risks involved (if any) in spraying with paint containing HDI. The format of the questionnaire is shown in Appendix H.

3.4.7 Statistical Analysis Of The Data

Data from the study on lung function of all 33 subjects which includes 20 spray painters still using paints containing isocyanates was analysed using a SAS statistical software package (SAS/STAT Users' Guide, Release 6.12 Fourth Edition). In particular, the following statistical analysis was performed, to indicate any trends or associations between the different variables under consideration. Descriptive statistics were calculated for all the variables of interest.

Means and standard deviations were calculated for continuous data and frequencies and percentages for categorical data. In the univariate analysis, the chi-square test was used to determine the significance of the association of the dependent variable, drop in FEV_1 < - 250 ml vs > - 250 ml with the independent categorical variables.

Students' paired t-test / Wilcoxon's test was used to test the significance of the mean change in FEV_1 levels (pre- and post-test values). Pearson's Correlation coefficients were used to determine whether there were any strong linear relationships between FEV_1 with age, length of service, air movement, percentage efficiency of the spray booth and exposure index levels. The Kruskal Wallis test was performed on the data .

A second independent statistical analysis was carried out between the exposed group (n=20) and the control group (n=30). The analysis included the two sample paired and unpaired t-tests, Pearson's Chi - square tests for the strength of association , ANOVA, and Logistic Regression Analysis. Pearson's Correlation Coefficient was calculated to determine whether there was a strong linear relationship between the outcome variable changes in FEV_1 and FEF_{25-75} with the independent variables viz, age, symptoms, length of service, booth efficiency and isocyanate concentrations. A multiple regression analysis was performed for each outcome variable and independent variables controlling for smoking.

3.4.7.1 Exposed groups vs Control Group

Paired t-tests, Chi-square and Logistic Regression Analysis.
Since a later control group was introduced into the study, a second independent analysis was performed on the data between the exposed, partially exposed , no longer exposed and the never exposed control group (n=30). Statistical tests performed included the two-sample paired and unpaired paired t -tests, Pearson's Chi-square test , ANOVA (analysis of variance) and finally Logistic Regression Analysis.

Exposed (E=1) and the non -exposed control (E =0) group were compared .

Confounding variables C_1... C_7 such as age, smoking status, height, race, length of service (exposure), mask usage and type and the outcome variables Y_1 ... Y_8 viz such as change in FEV_1, dermatitis, shortness of breath, wheeze, bronchitis, asthma and cough and were examined in a chi-square test and a logistic regression analysis.

3.4.7.2 Logistic regression analysis

The logistic regression of Y_1 on $E, C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8$

Y_2 on $E, C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8$

Y_3 on $E, C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8$

Y_4 on $E, C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8$

Y_5 on $E, C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8$

Y_6 on $E, C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8$

Y_7 on $E, C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8$

Y_8 on $E, C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8$

or simply Yi on $E, C_1, C_2, C_3 \ldots C_8$ where $i = 1, 2, 3 \ldots 8$ was used to obtain the optimistic regression model.

Where Yi is ΔFEV_1, dermatitis, eye irritation, shortness of breath, wheeze, bronchitis, asthma and cough. Ci is age, smoking status, height, race, length of exposure, mask usage, and mask type.

The logistic regression model was used to perform the regression of a dichotomous dependent variable Y_1 on a set of 8 explanatory (independent) variables $E, C_1, C_2, C_3 C_4 C_5 C_6 C_7$ and C_8 that affected Y_1. The explanatory variables are a combination of 3 continuous (C_1, C_3 and C_5) and 5 discrete ($C_2 C_4 C_6 C_7 C_8$) variables. Y_1 is the change in FEV_1 value.

The stepwise backward elimination procedure is to be used to identify factors that strongly affect the change in the FEV_1 value. At each of the analysis, the backward elimination procedure discards the least important effect from the logistic regression model. The process of elimination stops when no more "useless" effects can be removed from the model . The model that is obtained ultimately is called the "optimum" logistic regression model and will be used as an interpretation of the results.

CHAPTER FOUR

RESULTS

4.1 INTRODUCTION

The 4 year follow-up study of the cohort of spray painters was conducted between February 1992 and January 1995. This included the completion of a personal respiratory health questionnaire, measurements of cross-shift and baseline spirometric lung function, non-specific bronchial provocation testing (histamine) PC_{20}, RAST to (HDI), 30-day ambulatory peak flow measurements and environmental monitoring of spray booths. The environmental monitoring included measurements of HDI concentrations, air flow velocities and air flow patterns. Of the original cohort of 40 spray painters, 33 were available for the follow-up study. Figure 3.1 shows details of the breakdown from the initial 40 spray painters to the remaining 33 subjects in the follow-up study. In addition a non-exposed control group made up of 30 randomly selected male workers were from a Durban based warehouse and studied. In these subjects, a respiratory health questionnaire and pre and post shift spirometric lung function testing was performed using the same protocol as for the study population.

4.2 RESULTS OF THE FOLLOW-UP STUDY OF THE ORIGINAL COHORT

4.2.1 Health status questionnaire

4.2.1.1 Summary of demographic data, smoking status, symptoms and personal history

The columns in Table 4.1 below, show the demographic data, smoking status, race distribution, personal history and symptoms for the groups of subjects who were exposed, partially exposed, no longer exposed and never exposed (control group).

There was no significant difference between the mean age and height of all groups. The exposed and no longer exposed groups showed the highest mean pack years which was 13.9 and 16.9 respectively. Since there were small numbers in the different race groups, racial comparisons were not possible.

Ten (50%) of the exposed spray painters (n=20), had eye irritation and 8 (40%) had dermatitis of the hand [Figure 4.2(a)(b)]. There were no cases of TB and 2 (10%) cases of asthma in the exposed group. These asthma cases had been diagnosed from childhood. One (5%) of the spray painters from the exposed group suffered from bronchitis, which is defined as a productive cough for most days or three or more consecutive months over a period of two or more years (American Thoracic Society, 1982).

Table 4.1: Demographic data, smoking status, personal history and symptoms of exposed, partially exposed, no longer exposed, all subjects and control groups. Data expressed as nominal values.

		Exposed Group (n=20)	Partially Exposed Group (n=5)*	No Longer Exposed Group (n=7)	All Subjects Group (excl, control) (n=32)	Control Group (n=30)
		Mean	Mean	Mean	Mean	Mean
Age(yrs)		34.7 (±8.0)	41.2 (±11.4)	38.7 (±6.4)	36.4 (±8.3)	32.2 (±9.7)
Height(cm)		171.6 (±7.0)	172.2 (±10.1)	164.4 (±13.6)	169.4 (±10.2)	171.9 (±9.3)
Pack years		13.9	5.6	16.9	9.5	9.3
Smoking Status	Never	9(45%)	2(40%)	1(14%)	12(38%)	10 (33%)
	Current	8(40%)	2(40%)	5(72%)	16(50%)	16(53%)
	Ex.	3(15%)	1(20%)	1(14%)	4(12%)	4 (14%)
Race:		No of Subjects	No of Subjects	No of Subjects	No of Subjects	No of Subjects
	Coloured	10(50%)	1(20%)	4 (57%)	15(47%)	12(40%)
	Indian	9(45%)	2(40%)	3 (43%)	14(44%)	18(60%)
	White	1(5%)	2(40%)	0	3(9%)	0
	Black	0	0	0	0	0
Personal History:						
	TB	0	0	0	0	0
	Asthma	1(5%)	1(20%)	0	2 (7%)	0
	Bronchitis	1(5%)	0	0	1(3%)	1(3%)
Symptoms:		No of cases	No of cases	No of cases	No of cases	No of cases
	Cough	3 (15%)	1(20%)	0	4(13%)	2(7%)
	Sputum	6 (30%)	0	0	6(19%)	2(7%)
	Wheeze	7 (35%)	0	0	7(22%)	0
	Dyspnea	4 (20%)	0	1(14%)	5(16%)	2(7%)
	Eye Irritation	10 (50%)	0	0	10(31%)	1(3%)
	Dermatitis	8 (40%)	0	0	8(25%)	2(7%)

* The parially exposed paint salesman was excluded from the above table as his exposure levels were difficult to predict.

Table 4.2 shows a statistical comparison between the exposed and control groups. There was no significant statistical difference between the mean age, height, smoking status and race for these two groups.

Table 4.2: A statistical comparison of the demographic data, smoking status, personal history and symptoms of the exposed and control groups.

		Exposed Group (n=20)	Control Group (n=30)	p Values
		Mean	Mean	
Age(yrs)		34.7 (±8.0)	32.2 (±9.7)	0.35
Height(cm)		171.6 (±7.0)	171.9 (±9.3)	0.94
Pack years		13.9	9.3	0.19
Race:		No of Subjects	No of Subjects	0.31
	Coloured	10(50%)	12(40%)	
	Indian	9(45%)	18(60%)	
	White	1(5%)	0	
	Black	0	0	
Personal History:				
	TB	0	0	
	Asthma	1 (5%)	0	0.17
	Bronchitis	1 (5%)	1 (3%)	0.77
Symptoms:		No of cases	No of cases	
	Cough	3 (15%)	2 (7%)	0.34
	Sputum	6 (30%)	2 (7%)	0.29
	Wheeze	7 (35%)	0	0.15
	Dyspnea	4 (20%)	2 (7%)	0.30
	Eye Irritation	10 (50%)	1 (3%)	0.001
	Dermatitis	8 (40%)	2 (7%)	0.004

The two sample unpaired t- test was carried out on the above variables and the two groups exposed and never exposed groups.

From Table 4.2 it can be concluded that with respect to the variables age, height, smoking status and symptoms of wheeze and cough that these two groups are similar. However the two groups are significantly different as regards dermatitis ($p = 0.004$) (@ $\alpha = 5$ % level) and eye irritation ($p = 0.001$) (@ $\alpha = 5$ % level)

4.2.1.2 Age distribution

Figure 4.1 shows the age distribution of 20 spray painting employees. The largest group or 9 (45%) of the spray painters are between the ages of 30 - 34 years. There were no spray painters under 24 years of age and only 2 (10%) were found in each of the 35 - 39 and 40 - 44 year age groups respectively. There were no spray painters over the age of 54 years.

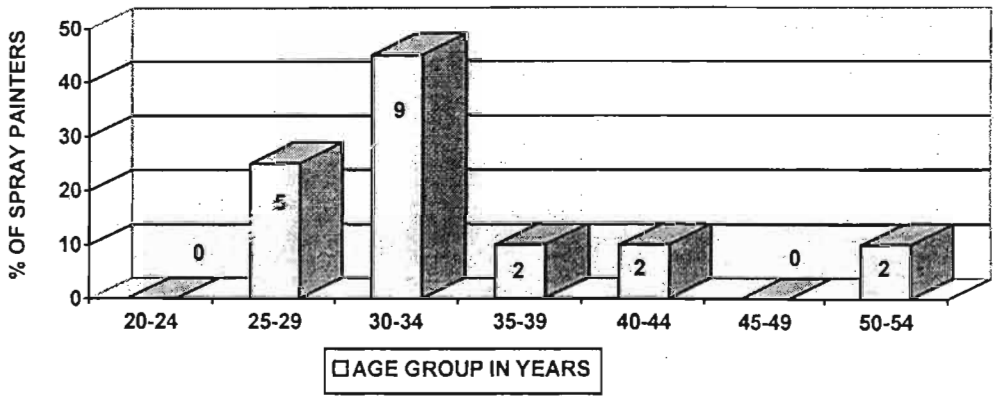
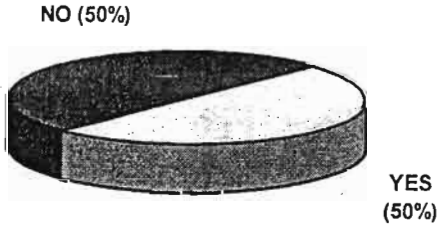


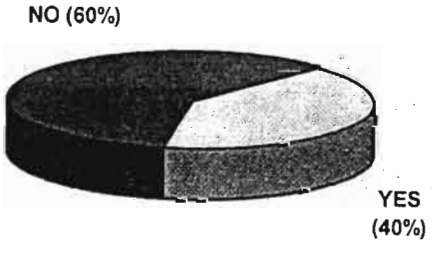
Figure 4.1: Age distribution of 20 spray painting employees

4.2.1.3 Incidence of eye irritation and dermatitis of the hand

Figure 4.2(a)(b) show of the 20 exposed spray painters, 50% had eye irritation and 40% had dermatitis of the hand as shown in Table 4.1 above.



4.2(a) EYE IRRITATION



4.2(b) DERMATITIS OF THE HAND

Figure 4.2(a) Percentage number of spray painters indicating symptoms of eye irritation.
Figure 4.2(b) Percentage number of spray painters indicating symptoms of dermatitis of the hand.

4.2.1.4 Race distribution

The racial composition of the study subjects is shown in Figure 4.3 (a) exposed subjects (n=20) and (b) all subjects (n=32).

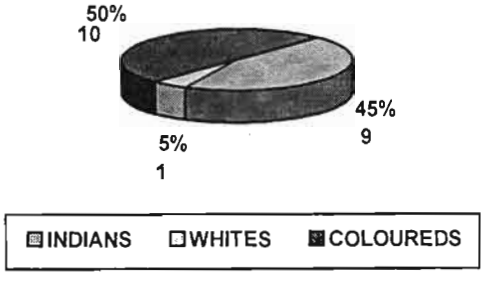


Figure 4.3(a): Exposed Subjects Group

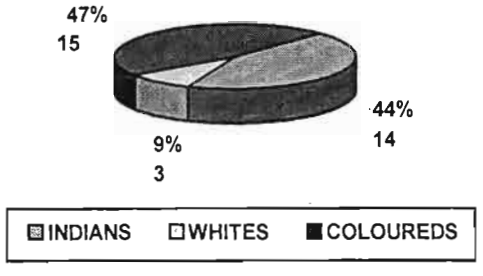


Figure 4.3(b): All Subjects Group

Figure 4.3(a)(b): Race distribution of the study subjects (a): exposed subjects (spray painters) and (b): all subjects.

4.2.1.5 Length of service distribution

Figure 4.4 demonstrates the percentage number of spray painters (n=20) in relation to the length of service. Forty five percent of the spray painters were in the 6 - 10 year service group, 25% in the 11 - 15 group and no spray painters with more than 35 years service.

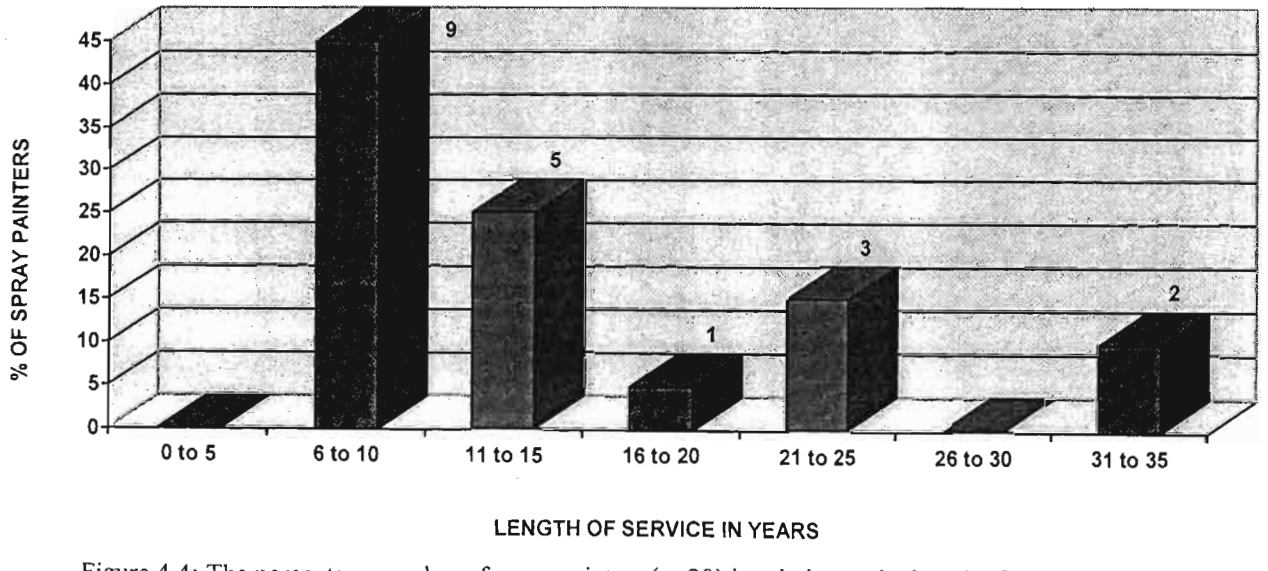


Figure 4.4: The percentage number of spray painters (n=20) in relation to the length of service.

4.2.2 Objective one: Lung function test results

The results of the pre-tests and the post-tests are shown in tables 4.3, 4.4 and 4.5 respectively.

4.2.2.1 Pre/Post-test pulmonary function of the predicted and measured values of 20 spray painters

The mean pre- FEV_1 and post- FEV_1 measured values were 3.7 and 3.4 litres respectively. The FEV_1 decrease = 297ml(8%).

Table 4.3: Demographic data, Pre and Post test lung function results of exposed subjects (spray painters) exposed to paints containing HDI. (n = 20)

	PRE	POST
	Mean (±SD)	Mean (±SD)
Age (yrs)	34.7 (± 8.0)	
Height (cm)	171.6 (± 7.0)	
Length of service (yrs)	14.7 (± 8.4)	
Lung function Pre and Post test results (litres)		
VC (meas)	4.37 (± 1.0)	4.19 (± 0.9)
VC (pred)	4.16 (± 0.5)	4.16 (± 0.5)
VC (% pred)	104.49 (± 16.4)	100.72
FVC (meas)	4.61 (± 1.0)	4.40 (± 1.0)
FVC (pred)	4.00 (± 0.5)	4.00 (± 0.5)
FVC (% pred)	114.71 (± 17.7)	110.00
FEV_1 (meas)	3.71 (± 0.8)	3.41 (± 0.9)
FEV_1 (pred)	3.36 (± 0.4)	3.36 (± 0.4)
FEV_1 (% pred)	110.07 (± 19.2)	101.44
FEV_1 / VC (meas)	85 (± 5.0)	82 (± 15.0)
FEV_1 / VC (pred)	70 (± 4.0)	70 (± 4.0)
FEV_1 / VC (Diff in % pred)	15	12
FEV_1 / FVC (meas)	81 (± 7.0)	78 (± 12.0)
FEV_1 / FVC (pred)	84 (± 1.0)	84 (± 1.0)
FEV_1 / FVC (Diff in % pred)	-3	-6
$FEF_{(25-75)}$ (meas)	4.07 (± 1.1)	3.75 (± 1.2)
$FEF_{(25-75)}$ (pred)	3.92 (± 0.4)	3.92 (± 0.4)
$FEF_{(25-75)}$ (% pred)	104.00	95.66

ΔFEV_1 = - 297ml (8%)
ΔFEF_{25-75} = - 320ml/sec. (7.9%)

4.2.2.2 *Pre/Post-test pulmonary function of the predicted and measured values of 5 partially exposed subjects*

The mean pre- FEV_1 and post- FEV_1 measured values were 3.7 and 3.4 litres respectively.

The FEV_1 decrease = -282ml (7.8%).

Table 4.4: Demographic data, Pre and Post test lung function results of partially exposed subjects (supervisors) exposed to paints containing HDI. (n = 5)

	PRE	POST
	Mean (±SD)	Mean (±SD)
Age (yrs)	41.2 (± 11.4)	
Height (cm)	172.2 (± 10.1)	
Length of service (yrs)	23.2 (± 9.3)	
Lung function Pre and Post test results (litres)		
VC (meas)	4.44 (± 1.0)	4.36 (± 1.0)
VC (pred)	4.25 (± 0.4)	4.26 (± 0.4)
VC (% pred)	104.59 (± 18.0)	102.42 (± 19.2)
FVC (meas)	4.62 (± 1.3)	4.46 (± 1.2)
FVC (pred)	4.05 (± 0.4)	4.05 (± 0.4)
FVC (% pred)	113.20 (± 24.0)	109.30 (± 21.3)
FEV_1 (meas)	3.66 (± 1.0)	3.38 (± 0.9)
FEV_1 (pred)	3.36 (± 0.4)	3.36 (± 0.4)
FEV_1 (% pred)	108.15 (± 24.7)	99.61 (± 20.4)
FEV_1 / VC (meas)	82 (± 9.6)	78 (± 12.9)
FEV_1 / VC (pred)	73 (± 6.6)	73 (± 6.6)
FEV_1 / VC (Diff in % pred)	+9	5
FEV_1 / FVC (meas)	79 (± 4.2)	76 (± 9.4)
FEV_1 / FVC (pred)	83 (± 2.3)	83 (± 2.3)
FEV_1 / FVC (Diff in % pred)	-4	-7
$FEF_{(25-75)}$ (meas)	3.81 (± 1.5)	3.56 (± 1.6)
$FEF_{(25-75)}$ (pred)	3.87 (± 0.5)	3.87 (± 0.5)
$FEF_{(25-75)}$ (% pred)	99 (± 40.0)	92.35 (± 42.7)

ΔFEV_1 = - 282ml.(7.7%)
ΔFEF_{25-75} = - 256ml./sec (6.7%)

4.2.2.3 *Pre/Post-test pulmonary function of the predicted and measured values of 7 no longer exposed subjects*

The mean pre- FEV_1 and post- FEV_1 measured values were 3.2 and 3.1 litres respectively.

The cross shift FEV_1 decrease = -54 ml) (1.7%).

Table 4.5: Demographic data, Pre and Post test lung function results of no longer exposed subjects to paints containing HDI. (n = 7)

	PRE	POST
	Mean (±SD)	Mean (±SD)
Age (yrs)	38.7 (± 6.4)	
Height (cm)	164.4 (± 13.6)	
Length of service (yrs)	- -	
Lung function Pre and Post test results (litres)		
VC (meas)	3.43 (± 1.2)	3.37 (± 1.3)
VC (pred)	3.65 (± 0.8)	3.65 (± 0.8)
VC (% pred)	90.40 (± 22.6)	88.46 (± 23.5)
FVC (meas)	3.67 (± 1.4)	3.63 (± 1.4)
FVC (pred)	3.49 (± 0.7)	3.59 (± 0.8)
FVC (% pred)	100.61 (± 28.9)	97.11 (± 28.7)
FEV_1 (meas)	3.14 (± 1.4)	3.09 (± 1.3)
FEV_1 (pred)	2.94 (± 0.5)	3.02 (± 0.6)
FEV_1 (% pred)	102.05 (± 35.3)	98.3 (± 32.0)
FEV_1 / VC (meas)	90 (± 11.0)	88 (± 9.0)
FEV_1 / VC (pred)	68 (± 1.0)	70 (± 5.0)
FEV_1 / VC (Diff % pred)	+21 (± 11.0)	+21 (± 7.0)
FEV_1 / FVC (meas)	85 (± 9.0)	85 (± 8.0)
FEV_1 / FVC (pred)	84 (± 3.0)	84 (± 3.0)
FEV_1 / FVC (Diff % pred)	+1 -	+1 -
$FEF_{(25-75)}$ (meas)	3.99 (± 2.4)	3.84 (± 2.0)
$FEF_{(25-75)}$ (pred)	3.60 (± 0.3)	3.69 (± 0.4)
$FEF_{(25-75)}$ (% pred)	108.0 (± 61.9)	101.7 (± 52.1)

ΔFEV_1 = - 54ml. (1.7%)
ΔFEF_{25-75} = - 160ml./sec (4%)

Table 4.6: Comparison of mean demographic data, Pre and Post test lung function results of all groups: exposed, partially exposed, no longer exposed and control groups.

	Group 1 (n = 20) exposed		Group 2 (n = 5) partially exposed		Group 3 (n=7) no longer exposed		Group 4 (n=30) control never exposed	
Age(yrs)	34.7		41.2		38.7		32.2	
Height(cm)	171.6		172.2		164.4		171.9	
Length of service exposed to HDI(yrs).	14.7		23.2		20.2		N/A	
Lung function Pre and post tests (litres)	Pre	Post	Pre	Post	Pre	Post	Pre	Post
VC(m)	4.37	4.19	4.43	4.36	3.43	3.37	3.90	4.04
VC(p)	4.16	4.16	4.25	4.25	3.65	3.65	4.43	4.45
VC(%p)	105.05	100.72	104.24	102.59	93.97	92.39	88.04	90.79
FVC (m)	4.61	4.40	4.62	4.46	3.67	3.63	3.99	4.04
FVC (p)	4.00	4.00	4.05	4.05	3.49	3.49	4.43	4.45
FVC (% p)	115.25	110.00	114.07	110.12	105.16	104.01	90.07	90.79
FEV_1 (m)	3.71	3.41	3.66	3.38	3.14	3.09	3.23	3.25
FEV_1 (p)	3.36	3.36	3.36	3.36	2.94	2.94	3.88	3.89
FEV_1 (%p)	110.42	101.49	108.93	100.60	106.80	105.10	83.25	83.55
FEV_1/VC(m)	85	82	82	78	92	92	83	80
FEV_1/VC(p)	70	70	73	73	68	68	87	87
FEV_1/VC(d) (%diff)	+15	+12	+9	+5	+24	+24	-4	-7
FEV_1/FVC(m)	80	78	79	76	86	85	81	80
FEV_1/FVC(p)	84	84	83	83	84	84	87	87
FEV_1/FVC (%diff)	-4	-6	-4	-7	+2	+1	-6	-7
$FEF_{(25-75)}$(m)	4.07	3.75	3.81	3.56	3.99	3.84	3.34	3.41
$FEF_{(25-75)}$(p)	3.92	3.92	3.87	3.87	3.60	3.60	4.62	4.62
$FEF_{(25-75)}$(%p)	103.83	95.67	98.45	91.99	110.83	106.67	72.29	73.81
Δ FEV_1 ml.	- 300		- 280		-50		+20	
Δ $FEF_{(25-75)}$ ml./ sec	- 320		- 250		-150		+70	

Note: control group mean Δ FEV_1 = + 20 ml. (corrected to 2 decimal places)
= + 17 ml (corrected to 3 decimal places)

m = measured

p = predicted

4.2.2.4 *Comparison of pulmonary function decrease between non-smokers and smokers*

There were 11 smokers and 9 non-smokers in the exposed group (n=20) .

The comparison of spirometric lung function between the two groups is shown in table 4.7

Table 4.7: Mean lung function values and standard deviations for smokers and non-smokers.

NON-SMOKERS (n = 9)					SMOKERS (n = 11)				
	MEAN		SD			MEAN		SD	
Age (yrs)	34	±	9.43		Age (yrs)	35	±	7.09	
Height(cms)	172.11	±	9.55		Height(cms)	171.18	±	4.47	
	Pre		SD	Post	SD	Pre	SD	Post	SD
VC	4.35		1.03	4.21	0.96	4.39	0.98	4.17	0.93
FVC	4.77		1.04	4.54	1.03	4.49	1.02	4.27	1.03
FEV_1	3.76		0.76	3.41	0.85	3.66	0.93	3.42	0.93
FEV_1 / VC	88.22		11.61	82.44	18.07	82.82	6.59	81.64	11.76
FEV_1 / FVC	79.78		9.30	76.67	15.71	81.00	4.17	79.64	7.72
PEF	521.11		116.63	508.67	140.66	499.09	91.98	509.10	145.68
FEF_{25-75}	4.12		0.86	3.79	0.87	4.03	1.28	3.71	1.45
ΔFEV_1	= - 350ml (9.3%)			ΔFEV_1		= - 240ml (6.6%)			
ΔFEF_{25-75}	= - 330ml/ sec (8.01%)			ΔFEF_{25-75}		= - 320ml/ sec (7.9%)			

Although the values for PEF and FEF_{25-75} were lower in the smokers, the differences were not significant between smokers and non-smokers. However, there was a significantly lower cross-shift change in FEV_1 in the smokers. It was also observed that smokers tended to use the appropriate respiratory equipment more frequently than the non-smokers.

4.2.2.5 *Comparison of pulmonary function of asthmatic and bronchitis cases*

In order to investigate the effect of co-morbid respiratory disease on lung function the cross- shift lung function values for the 2 asthmatic cases and 1 bronchitis case was examined individually. The results are shown in Table 4.8, 4.9, 4.10 respectively. The striking findings is that the asthmatic who used a positive airline mask showed a positive cross -shift change in FEV_1 +210 ml (Table 4.9). The asthmatic who used the sub-optimal cartridge mask showed a marked decrease in the difference in FEV_1 - 640 ml (Table 4.8). Statistical comparison was obviously not possible because of the small numbers.

Table 4.8: Pulmonary function results of asthmatic case (Ref. No. 7).

	Pre-test	Post-test
Age (yrs)	31	n/a
Height (cms)		
VC	5.22	4.75
FVC	5.51	4.82
FEV_1	4.88	4.24
FEV_1 / VC	94%	89%
FEV_1 / FVC	89%	88%
PEF	614	666
FEF_{25-75}	5.99	5.88

Δ FEV_1 = -640ml (13.11%). Ref. No. 7 wore a cartridge mask.

Table 4.9: Pulmonary function results of asthmatic case (Ref. No. 12).

	Pre-test	Post-test
Age (yrs)	50	
Height (cms)	171	
VC	3.25	3.28
FVC	3.17	3.36
FEV_1	2.55	2.76
FEV_1 / VC	78%	84%
FEV_1 / FVC	80%	82%
PEF	648	624
FEF_{25-75}	3.23	3.23

Δ FEV_1 = 210ml (8.24%). Ref. No. 12 wore a positive pressure airline mask.

Table 4.10 Pulmonary function results of bronchitis case (Ref. No. 29).

	Pre-test	Post-test
Age (yrs)	25	
Height (cms)	188	
VC	5.79	5.92
FVC	6.47	6.31
FEV_1	5.05	4.65
FEV_1 / VC	87%	79%
FEV_1 / FVC	78%	74%
PEF	668	668
FEF_{25-75}	4.69	3.76

Δ FEV_1 = -400ml (7.92%). Ref. No. 29 wore a cartridge mask.

4.2.2.6 *Summary of the lung function values for the exposed or all group (n==20) .These include the following categories,- smokers(n=11), non-smokers(n=9), asthmatics (n=2) and bronchitis (n=1).*

In Figure 4.5 below, are the FEV_1 (pre), FEV_1 (post) and summarises all of the lung function values for all cases, smokers, non-smokers, asthmatics and bronchitis cases.

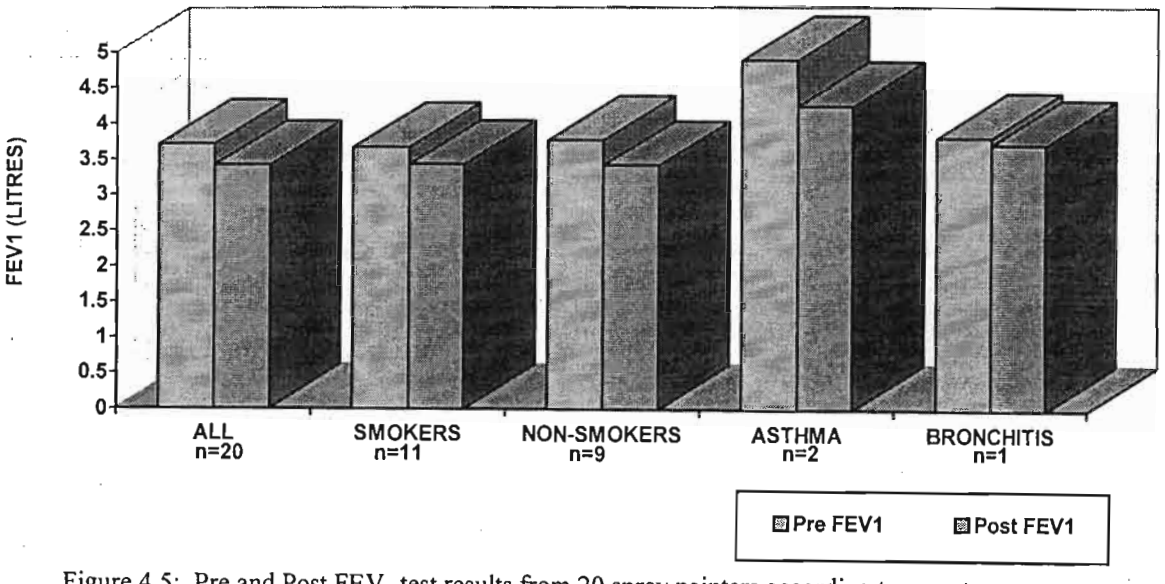


Figure 4.5: Pre and Post FEV_1 test results from 20 spray painters according to symptoms.

Figure 4.6 (a) below shows the cross-shift changes in FEV_1 of all categories as listed in Figure 4.5 above

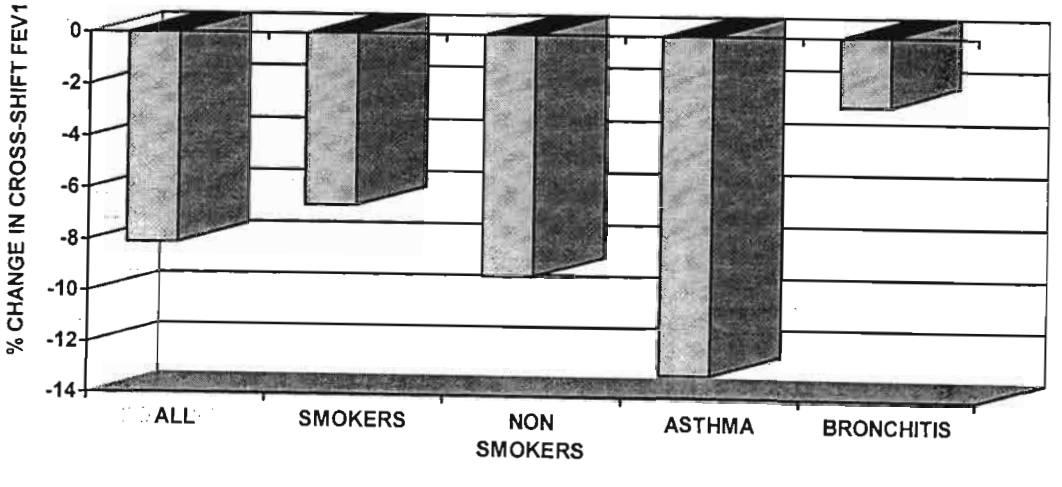


Figure 4.6 (a): Percentage decrease in cross-shift FEV_1 in spray painters (n = 20).

Figure 4.6 (b): below shows the percentage cross-shift ΔFEV_1 in the 2 asthma cases, one using an airline mask (increase in FEV_1), the other using a cartridge mask (decrease in FEV_1).

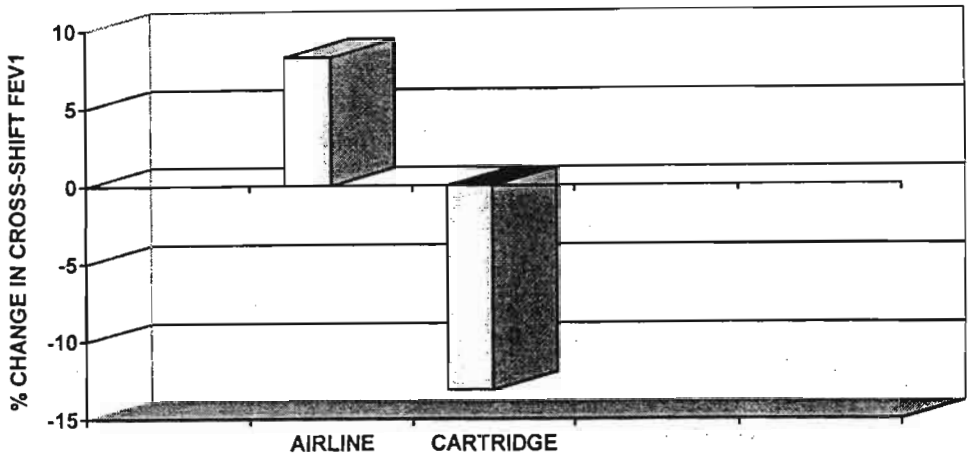


Figure 4.6 (b): Percentage cross-shift ΔFEV_1 in the 2 asthma cases (ref. No's 7 and 12).

4.2.2.7 Clinically significant cross-shift declines in study B

In Table 4.11, there were 9 (45%) of the spray painters (n=20), showing clinically significant cross- shift changes in FEV_1. Table 4.12 shows 3 (60%) of the partially exposed supervisors (n=5) with significant declines in FEV_1. There were no cases of large FEV_1 declines in the no longer exposed group.

* Clinically significant means cross-shift FEV_1 < - 250ml (HSE MS8 1983).

Table 4.11: Spray Painters exhibiting significant* cross- shift decreases in FEV_1 requiring further medical assessment (n = 20).

Case No.	Smoking Status	Δ FEV_1 ml	% Decr.
04	C	460	- 14.2
06	N	1230	- 38.6
07	E	640	- 13.1
09	N	380	- 9.3
11	C	950	- 31.5
17	N	500	- 11.9
18	N	250	- 5.7
29	N	400	- 7.9
31	E	460	- 9.1

C=Current
N=Never
E=Ever

Mean Δ FEV_1 585.56 ml (-15.68%)
*As defined in HSE Guidance Note MS. 8 "Isocyanates - Medical Surveillance" 1983.

Table 4.12: Partially exposed supervisors exhibiting significant* cross- shift decreases in FEV_1, requiring further medical assessment (n=5).

Case No.	Smoking Status	Δ FEV_1 ml	% Decr.
14	E	410	- 8.1
21	C	310	- 11.7
36	C	560	- 13.0

Mean Δ FEV_1 -426.66 ml (10.92%)

*As defined in HSE Guidance Note MS. 8 "Isocyanates - Medical Surveillance" 1983.

The mean decrease in FEV_1 for group 1 (exposed), group 2 (partially exposed) and group three (non-exposed) were 297ml, 282ml and 54 ml respectively. Figures 4.7, 4.8, 4.9 and 4.10 list each case with the corresponding decline in FEV_1. Figure 4.10 shows the control group with a cross-shift increase of 17.4 ml.

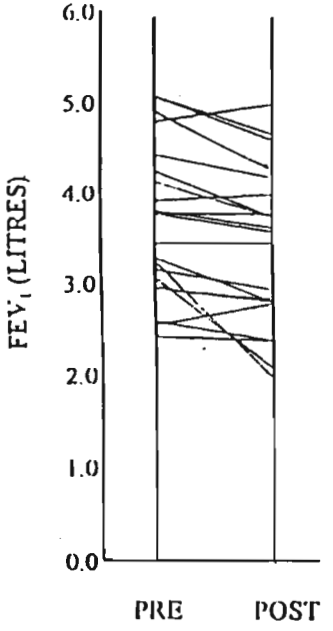


Figure 4.7: ΔFEV_1 in exposed spray painters (n=20) Mean ΔFEV_1 = - 297ml.

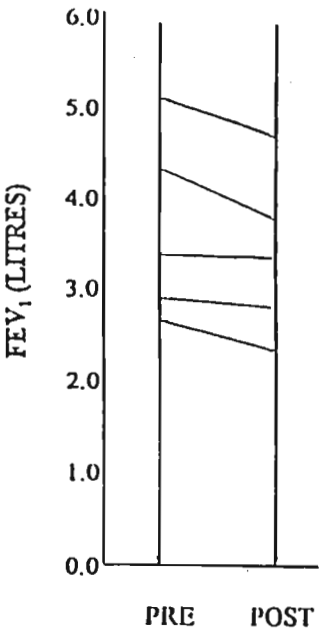


Figure 4.8: ΔFEV_1 in partially exposed group (n=5) Mean ΔFEV_1 = - 282ml.

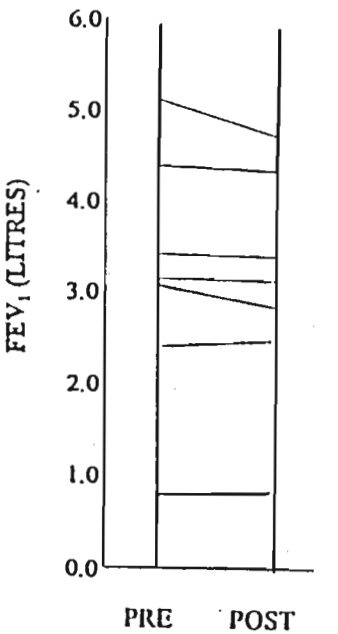


Figure 4.9: ΔFEV_1 in no longer exposed group (n=7) Mean ΔFEV_1 = - 54ml.

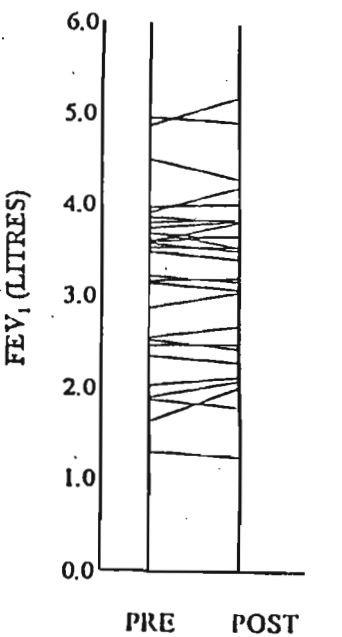


Figure 4.10: ΔFEV_1 in never exposed control group (n=30) Mean ΔFEV_1 = + 17ml.

Figures 4.7, 4.8, 4.9, 4.10: Measured pre and post cross - shift changes in Δ FEV_1 study B in the exposed, partially exposed, no longer exposed and the never exposed control group.

4.2.3 Objective two: IgE, RAST for House Dust Mite, HDI and tests for BHR

4.2.3.1 Immunoglobulin E (IgE) to House Dust Mite

Five subjects (ref. 4, 11, 13, 17 and 36) showed raised IgE levels, viz. IgE >100 and 6 subjects showed levels > 0.35 for the house dust mite test (ref. 4, 11, 12, 13, 14 and 36) (Table 4.13).

4.2.3.2 Radioallergosorbent test for HDI (Rast HDI)

There was only one subject (ref 13) who had a positive RAST (HDI) (Table 4.13). This was a weak positive value of 1 and the drop in his lung function (FEV_1) was not different from those spray painters who were not positive.

4.2.3.3 Bronchialhyperresponsiveness test (BHR)

Thirteen subjects had no bronchoconstriction on the histamine challenge ie. no bronchial hyperactivity. Three subjects (ref. 6, 7 and 28) had a PC_{20} at concentrations of 14.4, 6.8, 3.0 mg/ml histamine respectively (Table 4.13). Subject ref. 7 had been previously diagnosed as asthmatic from childhood and subject ref. 28 had been a few years earlier diagnosed as having obstructive lung disease by his physician One subject (ref 26) was unable to perform the histamine challenge test as his baseline FEV_1 was < 0.78 litres, i.e. less than 60% of his predicted value (Table 4.13). The subject suffered from kyphoscoliosis and was observed in the initial study spraying in a poorly ventilated workshop without adequate respiratory protective equipment.

Table 4.13: Immunological responses, IgE, BHR , RAST for House Dust Mite and HDI for 17 subjects, who were either spray painters or ex-spray painters.

Subj.	Sympt	Cross-shift ΔFEV_1 (ml)	Cross-shift ΔFEV_1 (%)	IgE (KU/l)	RAST HDI (Grade)	RAST House Dust Mite	* PC20 Hist. (mg/ml)	Remarks
+ 4	W	- 460	- 14.15	316	< 0.35	3.30	>32	Uses triple dust mask
+ 6	-	- 1230	- 38.56	87	< 0.35	<0.35	14.4	Sprays in workshop- no mask
+ 7	A	- 640	- 13.11	76	< 0.35	<0.35	6.8	Asthma sufferer from childhood
+ 11	-	- 950	- 31.46	387	< 0.35	2.60	>32	Sprays with handkerchief under mask
+ 12	B&W	+ 210	8.24	98	< 0.35	12.30	>32	nil
+ 13	-	- 210	- 6.71	586	1.00	1.50	>32	Sprays with fan off due to dust problem
- 14	-	- 410	- 8.06	48	< 0.35	0.40	>32	Supervisor
+ 17	D	- 500	- 11.85	524	< 0.35	<0.35	>32	nil
* 19	-	- 30	- 0.96	97	< 0.35	<0.35	>32	Changed employ.- no further exposure
- 21	-	- 310	- 11.74	53	< 0.35	<0.35	>32	Diagnosed obstructive lung disease
+ 24	-	+ 70	+ 1.79	69	< 0.35	<0.35	>32	nil
* 26	D	+ 20	+ 2.56	7	< 0.35	<0.35	**n/a	No exposure - unemployed
+ 28	-	- 200	- 7.78	83	< 0.35	<0.35	3.0	Diagnosed obstructive lung disease
30	-	- 480	- 11.37	85	< 0.35	<0.35	>32	Intermit.exposure -car paint salesman
+ 35	-	- 20	- 0.53	93	< 0.35	<0.35	>32	nil
- 36	D	- 560	- 12.96	668	< 0.35	1.30	>32	supervisor
+ 38	D	- 180	- 4.76	40	< 0.35	<0.35	>32	nil

Key to Reference in Table 4.15	
+	spray painters exposed to paints containing HDI in spray booth
-	supervisors with possible marginal exposure to HDI
*	no exposure due to change in occupation or unemployed
**	test not performed FEV_1 < 60% predicted

Symptoms:
A= Asthma
B= Bronchitis
D= Dyspnoea
W = Wheeze

4.2.4 Objective three: Baseline changes in lung function from 1992 to 1996

4.2.4.1 Baseline changes in pre FEV_1 from study A to B

The mean changes in baseline FEV_1 from study A to study B for the whole study group (n=33), was 75 ml (Table 4.14). This was over a 4 year period and represents an annual decline of 18.5 ml which is an acceptable decline for non-smokers. However, there were 9 (27%) cases taken from all of the 33 subjects where the individual changes in baseline FEV_1 was >90ml per annum or equivalent to >360 ml over the 4 year follow-up period (Table 4.14)(ref. 6, 10, 15, 21, 22, 29, 35, 37, 38). From Figures 4.11, 4.12 and 4.13, of the 20 exposed spray painters, the mean baseline decrease over the 4 year period was -165ml, whereas for the partially exposed supervisors a pre FEV_1 increase of +106ml was noted. The paint salesman showed a baseline increase of 520ml whilst the seven non-exposed group showed a decrease of -31ml over the 4 years which is within the normal decline for non-smokers.

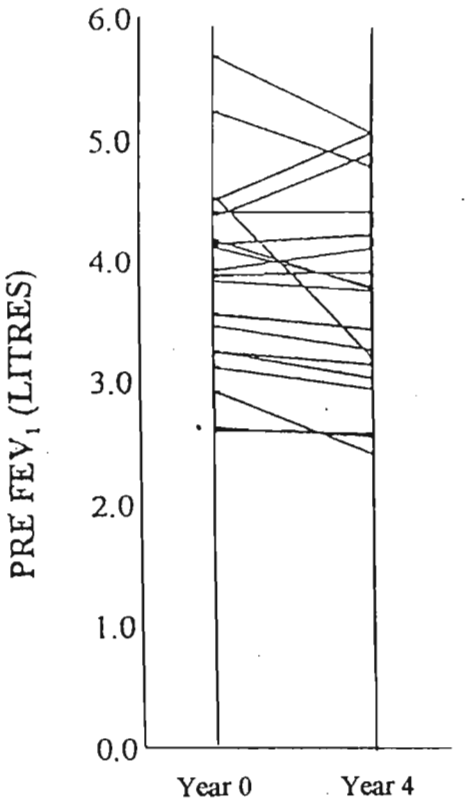


Figure 4.11: Exposed spray painters (n=20)
Mean Δ FEV_1 (meas) = - 165 ml/4yrs
Mean Δ FEV_1 (meas) = - 41.25 ml/yr
Mean Δ FEV_1 (pred.) = - 20.25 ml/yr

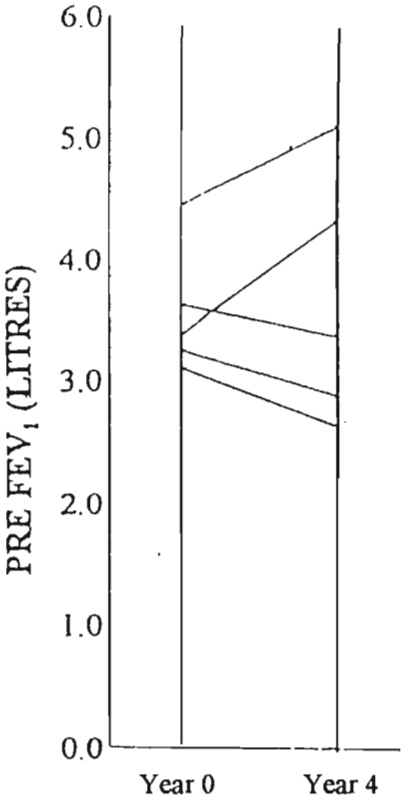


Figure 4.12: Partially exposed supervisors (n=5)
Mean Δ FEV_1 (meas) = +106 ml/4yrs
Mean Δ FEV_1 (meas) = + 26.5 ml/yr
Mean Δ FEV_1 (pred.) = - 21.5 ml/yr

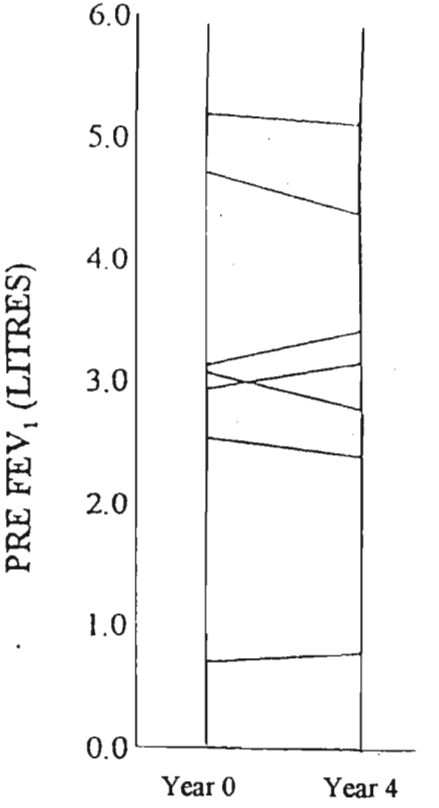


Figure 4.13: No longer exposed (n=7)
Mean Δ FEV_1 (meas) = - 31 ml/4yrs
Mean Δ FEV_1 (meas) = - 7.85 ml/yr
Mean Δ FEV_1 (pred.) = - 22.5 ml/yr

Figures 4.11, 4.12, 4.13: Measured and predicted baseline changes in Pre FEV_1 from study A to B.

4.2.4.2 Comparison of cross-shift declines in study A and B and baseline declines from study A to B

Spirometric results of the first study (n=40), compared with the results of the second study (n=33) showed a mean cross-shift declines in FEV_1 of 130.5ml (SD203)(P=0,0002) and 297ml (SD323) (P=0,0001) respectively. Therefore the differences in the pre- and post- FEV_1 lung function test results, were found to be statistically significant.

Table 4.14: All subjects by age, smoking status, **cross-shift** lung function in studies A and B, and **baseline** from Study A (1992) (n=40) to Study B (1996) (n=33).

Ref. (No.)	Study B Age (yrs)	Study B Smoke. Status (Pack/yr)	Study A Cross-Shift FEV_1 (ml)	Study A Cross-Shift FEV_1 (%)	Study B Cross-Shift FEV_1 (ml)	Study B Cross-Shift FEV_1 (%)	Study A Base-line Pre FEV_1 (l)	Study B Pre FEV_1 (l)	Δ FEV_1 (B-A) (l)	Δ FEV_1 (B-A) (%)
4	39	C 24	- 170	- 4.94	- 460	- 14.15	3.44	3.25	- 0.19	- 5.52
5	39	E 9	- 50	- 1.60	- 20	- 0.59	3.12	3.40	0.28	8.97
6	27	N -	- 20	- 0.44	- 1230	- 38.56	4.53	3.19	- 1.34	- 29.58
7	31	E 3	- 260	- 5.92	- 640	- 13.11	4.39	4.88	0.49	11.16
8	26	C 10	- 450	- 11.78	- 180	- 4.81	3.82	3.74	- 0.08	- 2.09
9	28	N -	- 210	- 5.36	- 380	- 9.27	3.92	4.10	0.18	4.59
10	33	N -	- 180	- 5.57	- 90	- 3.13	3.23	2.88	- 0.35	- 10.84
11	30	C 10	- 140	- 4.33	- 950	- 31.46	3.23	3.02	- 0.21	- 6.50
12	50	C 36	30	1.15	210	8.24	2.62	2.55	- 0.07	- 2.67
13	32	N -	- 30	- 0.93	- 210	- 6.71	3.23	3.13	- 0.10	- 3.10
14	47	E 12	- 60	- 1.35	- 410	- 8.06	4.46	5.09	0.63	14.13
15	33	C 20	- 130	- 2.49	120	2.51	5.22	4.78	- 0.44	- 8.43
16	39	C 12	- 220	- 7.21	20	0.72	3.05	2.78	- 0.27	- 8.85
17	30	N -	- 700	- 16.91	- 500	- 11.85	4.14	4.22	0.08	1.93
18	32	N -	- 240	- 5.44	- 250	- 5.67	4.41	4.41	0.00	0.00
19	30	C 10	110	3.75	- 30	- 0.96	2.93	3.14	0.21	7.17
21	58	C 41	- 90	- 2.92	- 310	- 11.74	3.08	2.64	- 0.44	- 14.29
22	42	C 12	- 310	- 10.69	- 50	- 2.07	2.90	2.41	- 0.49	- 16.90
23	30	N -	- 220	- 6.09	- 40	- 1.19	3.61	3.36	- 0.25	- 6.93
24	32	C 7	- 30	- 0.78	70	1.79	3.87	3.90	0.03	0.78
25	46	C 38	- 120	- 2.32	- 380	- 7.44	5.18	5.11	- 0.07	- 1.35
26*	40	N -	- 60	- 0.70	20	2.56	0.70	0.78	0.08	11.43
28	55	N -	0	0.00	- 200	- 7.78	2.60	2.57	- 0.03	- 1.15
29	25	N -	- 360	- 6.35	- 400	- 7.92	5.67	5.05	- 0.62	- 10.93
30	29	C 9	- 80	- 2.16	- 480	- 11.37	3.70	4.22	0.52	14.05
31	28	E 7	240	5.31	- 460	- 9.13	4.52	5.04	0.52	11.50
32	34	N -	160	4.52	10	0.29	3.54	3.42	- 0.12	- 3.39
34	40	C 10	- 180	- 5.81	- 140	- 4.78	3.10	2.93	- 0.17	- 5.48
35	43	N -	- 410	- 9.83	- 20	- 0.53	4.17	3.76	- 0.41	- 9.83
36	38	C 7	330	9.76	- 560	- 12.96	3.38	4.32	0.94	27.81
37	31	C 7	50	1.06	- 60	- 1.37	4.71	4.39	- 0.32	- 6.79
38	37	E 14	- 320	- 7.79	- 180	- 4.76	4.11	3.78	- 0.33	- 8.03
40	46	C 17	150	5.93	70	2.92	2.53	2.40	- 0.13	- 5.14

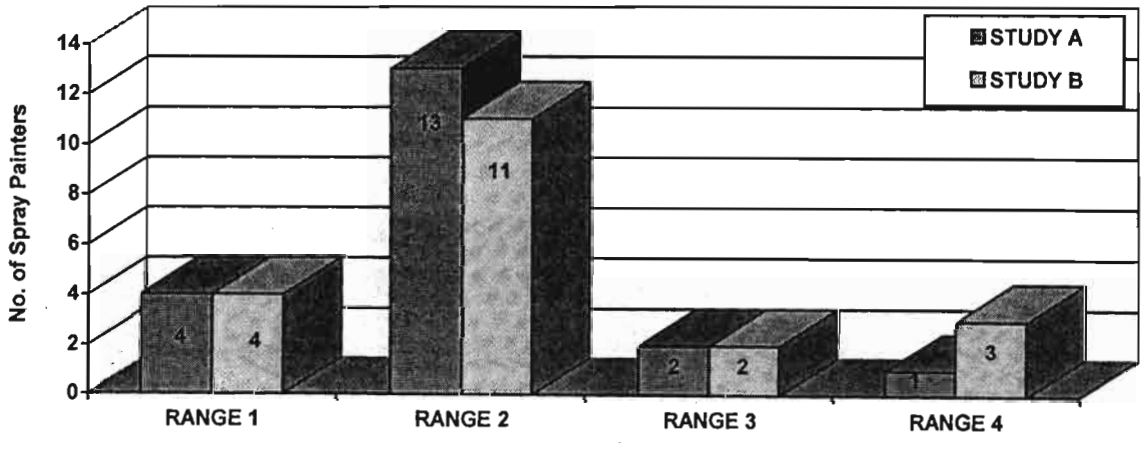
*This subject suffers from kyphoscoliosis.

Table 4.14 of computed statistics (continued)

Stat.	Study B Age (yrs)	Study A Cross-Shift FEV_1 (ml)	Study A Cross-Shift FEV_1 (%)	Study B Cross-Shift FEV_1 (ml)	Study B Cross-Shift FEV_1 (%)	Study A Base-line Pre FEV_1 (l)	Study B (l)	Δ FEV_1 (B-A) (l)	Δ FEV_1 (B-A) (%)
Mean	36.364	-120.303	- 2.977	-245.758	- 6.435	3.670	3.595	- 0.075	- 0.016
SD	8.257	04.369	5.398	305.495	9.093	0.942	0.976	0.414	0.107
Varian.	68.171	41766.5	29.136	93327.4	82.684	0.888	0.952	0.171	0.012

C = Current Smoker
E = Ever Smoker (has smoked before but no longer smoking)
N = Never Smoked

Figure 4.14 below shows the percentage distribution of cross-shift FEV_1 in study A and B of the 20 spray painters who continued spray painting. In range 1 and 3 there has been no changes . However the decrease in range 2, is reflected by an equal increase in range 4 which is the largest % decrease in cross- shift FEV_1 . (< -14%)



Key to Range Distribution	
RANGE 1	Δ FEV_1 > 0%
RANGE 2	- 10% < Δ FEV_1 < 0%
RANGE 3	- 14% < Δ FEV_1 < -10%
RANGE 4	Δ FEV_1 < -14%

Figure 4.14: Percentage distribution of cross-shift FEV_1 in study A and B of the 20 spray painters who continued spray painting. The four categories range from Δ FEV_1 < - 14% to Δ FEV_1 > 0%.

Table 4.15: ECCS **baseline changes** in predicted Δ FEV_1 over 4 year period for all subjects n =33

Ref . No.	Predicted FEV_1 study A litres	Predicted FEV_1 study B litres	Difference between study A -B litres
4	3.27	3.17	0.10
5	3.31	3.23	0.08
6	3.96	3.91	0.05
7	3.70	3.63	0.07
8	3.63	3.60	0.03
9	3.30	3.22	0.08
10	3.31	3.21	0.10
11	3.25	3.13	0.12
12	2.98	2.90	0.08
13	2.94	2.87	0.07
14	3.67	3.60	0.07
15	3.42	3.32	0.10
16	3.05	2.95	0.10
17	3.46	3.36	0.10
18	3.70	3.60	0.10
19	3.14	3.07	0.07
21	2.92	2.84	0.08
22	2.81	2.73	0.08
23	3.89	3.78	0.11
24	3.61	3.49	0.12
25	3.39	3.29	0.10
26	1.98	1.90	0.08
28	2.63	2.56	0.07
29	4.07	3.98	0.09
30	3.49	3.42	0.07
31	3.59	3.52	0.07
32	3.28	3.19	0.09
34	3.14	3.04	0.10
35	3.86	3.75	0.11
36	3.45	3.38	0.07
37	3.54	3.44	0.10
38	3.37	3.29	0.08
40	2.81	2.71	0.10
mean (litres)	3.3309	3.2448	0.086
sd	0.42351	0.42325	0.0195

ECCS Predicted baseline ΔFEV_1
Δ FEV_1 = 86ml/4year
Δ FEV_1 = 21.5 / year

As there was no control group (never exposed) in the first study the actual baseline decline in lung function was compared with that predicted from the regression equation of the ECCS (Table 4.15).

These regression equations to predict FEV_1 values based on age and were derived from cross-sectional data in healthy subjects. The predicted **baseline** decline in FEV_1 over 4 years for each of the 33 subjects taken from the original study is shown in Table 4.15. The actual decline in baseline FEV_1 in the 20 exposed subjects from study A to study B is shown in Table 4.16. The spray painters had twice the predicted decline in FEV_1 during this period (41.25 ml/year vs 20.25 ml/year).

The partial exposed workers had an increase of 26.5 ml /year, while the no longer exposed group had a decline of 7.85ml/ year. Statistical comparisons between each group were not possible because of the small numbers involved (Tables 4.17 and 4.18) .

Table 4.16: Measured and predicted **baseline changes** in Δ FEV_1 over 4 year period for 20 exposed spray painters still continuing spray painting .

Ref. No	Measured FEV_1 Study A (litres)	Measured FEV_1 Study B (litres)	Diff. in Measured FEV_1 Study A-B (litres)	Pred. FEV_1 Study A (litres)	Pred. FEV_1 Study B (litres)	Diff. in Pred. FEV_1 Study A-B (litres)
4	3.44	3.25	- 0.19	3.27	3.17	0.10
6	4.53	3.19	- 1.34	3.96	3.91	0.05
7	4.39	4.88	+0.49	3.70	3.63	0.07
8	3.82	3.74	- 0.08	3.63	3.60	0.03
9	3.92	4.10	+ 0.18	3.30	3.22	0.08
11	3.23	3.02	-0.21	3.25	3.13	0.12
12	2.62	2.55	-0.07	2.98	2.90	0.08
13	3.23	3.13	-0.10	2.94	2.87	0.07
15	5.22	4.78	-0.44	3.42	3.32	0.10
17	4.14	4.22	+0.08	3.46	3.36	0.10
18	4.41	4.41	0.00	3.70	3.60	0.10
22	2.90	2.41	- 0.49	2.81	2.73	0.08
24	3.87	3.90	+0.03	3.61	3.49	0.12
28	2.60	2.57	-0.03	2.63	2.56	0.07
29	5.67	5.05	-0.62	4.07	3.98	0.09
31	4.52	5.04	+0.52	3.59	3.52	0.07
32	3.54	3.42	-0.12	3.28	3.19	0.09
34	3.10	2.93	-0.17	3.14	3.04	0.10
35	4.17	3.76	-0.41	3.86	3.75	0.11
38	4.11	3.78	-0.33	3.37	3.29	0.08
Mean	x=3.872	x=3.707	x= 0.1650	x=3.402	3.321	x =0.0855
Sd	0.81	0.84		0.39	0.40	0.02

Difference in Measured FEV_1 Study A-B

Δ FEV_1 = -165 ml /4years
= - 41.25 ml / year

Difference in Predicted FEV_1 Study A-B

Δ FEV_1 = -81 ml / 4years
= -20.25 ml / year

Table 4.17: Measured and predicted **baseline changes** in Δ FEV_1 over 4 year follow up period for 5 partially exposed supervisors still continuing in the spray painting trade.

Ref. No	Measured FEV_1 Study A (litres)	Measured FEV_1 Study B (litres)	Diff. in Measured FEV_1 Study A-B (litres)	Pred. FEV_1 Study A (litres)	Pred. FEV_1 Study B (litres)	Diff. in Pred. FEV_1 Study A-B (litres)
10	3.23	2.88	- 0.35	3.31	3.21	0.10
14	4.46	5.09	+0.63	3.67	3.60	0.07
21	3.08	2.64	- 0.44	2.92	2.84	0.08
23	3.61	3.36	- 0.25	3.89	3.78	0.11
36	3.38	4.32	+0.94	3.45	3.38	0.07
mean	x= 3.552	x= 3.658	Δ FEV_1 = 0.106	x= 3.448	x= 3.362	Δ FEV_1 =0.086
sd	0.54	1.03		0.37	0.36	

Difference in Measured FEV_1 Study A-B

Δ FEV_1 = + 106 ml /4years
= + 26.5 ml / year

Difference in Predicted FEV_1 Study A-B

Δ FEV_1 = -86 ml / 4years
= -21.5 ml / year

Table 4.18: Measured and predicted **baseline changes** in Δ FEV_1 over 4 year follow-up period for 7 no longer exposed subjects.

Ref. No	Measured FEV_1 Study A (litres)	Measured FEV_1 Study B (litres)	Diff. in Measured FEV_1 Study A-B (litres)	Pred. FEV_1 Study A (litres)	Pred. FEV_1 Study B (litres)	Diff. in Pred. FEV_1 Study A-B (litres)
5	3.12	3.40	+ 0.28	3.31	3.23	0.08
16	3.05	2.78	- 0.27	3.05	2.95	0.10
19	2.93	3.14	+ 0.21	3.14	3.07	0.07
25	5.18	5.11	- 0.07	3.39	3.29	0.10
26	0.70	0.78	+ 0.08	1.98	1.90	0.08
37	4.71	4.39	- 0.32	3.54	3.44	0.10
40	2.53	2.40	- 0.13	2.81	2.71	0.10
mean	x= 3.1743	x= 3.1429	x= 0.0314	x=3.0314	x=2.9414	0.09
sd	1.47	1.40		0.52	0.52	

Difference in Measured FEV_1 Study A-B

Δ FEV_1 = - 31.4 ml /4years
= - 7.85 ml / year

Difference in Predicted FEV_1 Study A-B

Δ FEV_1 = -90 ml / 4years
= -22.5 ml / year

Table 4.19 below, shows that those spray painters who were least exposed to HDI from the date of the first study A to that of the second study B displayed an improvement in baseline FEV_1. Ref. nos. 5, 19, 26 had baseline increases in FEV_1 as opposed to Ref. 16, 25 , 37 and 40 who demonstrated baseline decreases in FEV_1. Clearly the workers who were the longest away from HDI exposure showed an improved Δ FEV_1 (E,G,F).

Table 4.19: Changes in **baseline** lung function in Group 3 (No longer exposed group) from study A to B.

Ref No.	Date of baseline Study A	Date of termination of occupation	Date of follow - up Study B	No. of months away from work since last exposure to HDI	Incr/Decr Baseline ΔFEV_1(ml) over 4 years
25 (D)	JUNE 1989	FEB1993	MAR 1993	1	- 70
37 (A)	AUG 1989	JAN 1993	FEB 1993	1	- 320
16 (B)	MAY 1989	SEPT1992	FEB 1993	6	- 270
40 (C)	AUG 1989	SEPT 1992	MAR 1993	6	- 130
26 (E)	JUNE 1989	AUG 1991	SEPT 1992	13	+ 80
5 (G)	APR 1989	JAN 1991	APR 1993	28	+ 280
19 (F)	JUNE 1989	AUG 1990	MAR 1993	30	+ 210

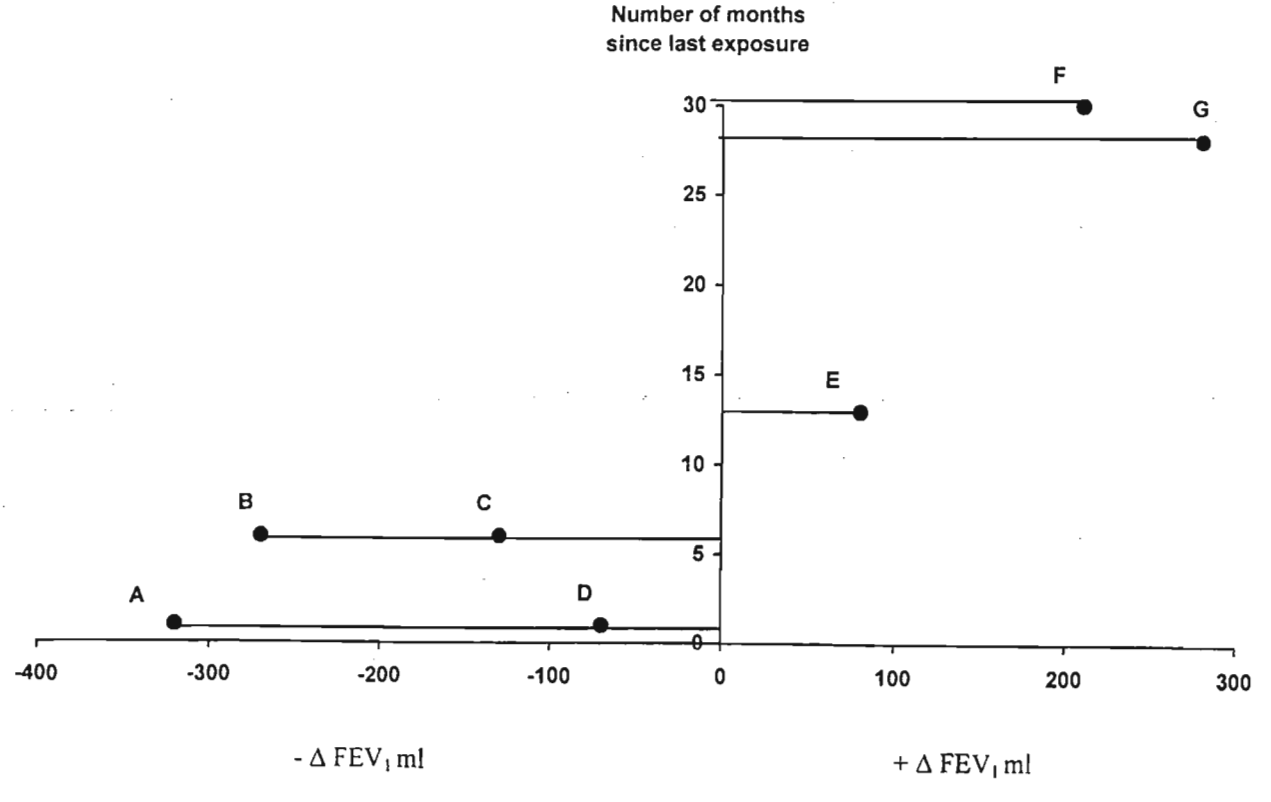


Figure 4.15: Baseline changes in pre FEV_1 lung function in the no longer exposed group (n=7) in relation to the number of months away from work (lapse in number of months since last exposure to HDI).

The graph in figure 4.15 shows baseline changes in those spray painters who had either ceased to be exposed to HDI through change in occupation, or who had become unemployed. The total period in months of non-exposure to HDI, up to the second baseline study was plotted against their respective change in baseline FEV_1 values. The results show that those subjects who had a non-exposure period < 6 months had a negative baseline Δ FEV_1 (points A,B,C,D), whereas those subjects with a non-exposure period > 6 months had a positive baseline Δ FEV_1 (points E,F,G).

4.2.4.3 Peak expiratory flow rate measurement (PEFR)

The peak expiratory flow rate in study B was measured in 21 subjects. The subjects were categorised into 2 groups comprising, those who were still exposed to HDI, the occupational group and those no longer exposed to HDI, the non occupational group (Table 4.20).

Table 4.20: Peak flow data by individual subjects:- Difference in PEFR between work and non-work days.

mean PEFR L/min				
PEFR Pattern	Type of day			Difference
	Ref. No.	W	NW	W - NW
Occupational	4	487	487	0
	7	658	667	-9
	8	584	574	+10
	13	646	645	+1
	14	605	630	-25
	15	602	636	-34
	17	599	522	+7
	21	492	507	-15
	23	564	539	+25
	24	450	498	-48
	28	493	432	+61
	29	602	595	-7
	30	507	504	+3
	31	625	627	-2
	35	566	569	-3
	36	600	654	-54
Non Occupational	5	584	592	-8
	25	593	601	-8
	26	248	244	+4
	37	588	574	+14
	40	399	360	+39

W = Work days;
NW = Non work days;

From Table 4.20, the values shown in the "difference" column, indicated that there was no difference in the mean PEFR for both the working and non-working days. These results applied to both the exposed (occupational) and no longer exposed (non- occupational) groups. From this it can be stated that serial measurements taken during working and non-working days of the mean PEFR, do not appear to be good indicators of potential cases of isocyanate-induced asthma. Ref. No. 7 was the only asthma case (diagnosed at childhood) which appeared in the table. The results of the PEFR showed a small increase in the non-working day compared to the working day viz. 9 L/min.

4.2.5 Objective four: Environmental Working Conditions

4.2.5.1 Booth type (general)

The design and the effectiveness of the ventilation system of the spray booth will often determine its efficiency. Eighteen spray booths were examined and classified into the three basic design types:

(i) Horizontal flow (plates 1.1, 1.2 and 1.3);
(ii) Vertical side draught (plates 1.4 and 1.5);
(iii) Vertical down draught (plates 1.6 and 1.7).

The distribution of these designs types viz. horizontal, vertical side and vertical down draught among the 18 establishments was 33%, 11% and 56% respectively (Figure 4.16). Since each of the three designs has a different legal minimum air flow as prescribed by the General Safety Regulations, No. R1031 of 1986), the criteria used to judge the efficiency was based on the prescribed legal minima (Figure 4.17). This is 0.5, 0.4, and 0.3 metres per second for the horizontal, vertical side and vertical down draught booths respectively.

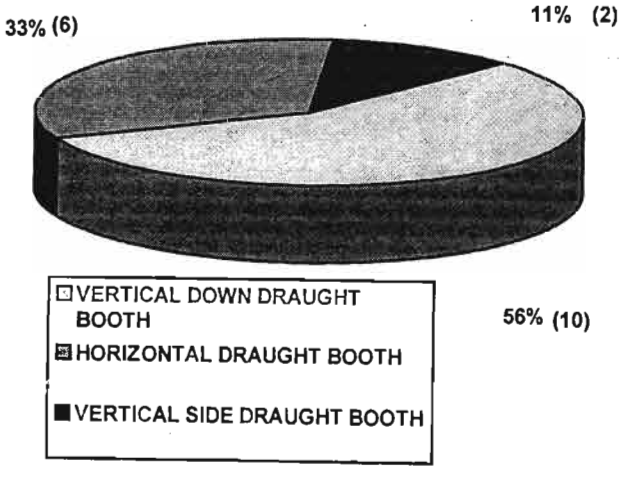


Figure 4.16: Distribution of spray booth designs among the 18 establishments

4.2.5.2 Spray booth efficiency

Standards to judge efficiency, for example, 'good', 'fair', 'poor' and 'very poor' were shown in Figure 4.17. Thus, for each spray booth, the following criteria were applied, based on the legal minimum air flow standard prescribed for each booth type and the definitions of good, fair, poor and very poor. A total of 18 spray booths were examined and divided up into the following booth types.

(i) Horizontal flow type booth

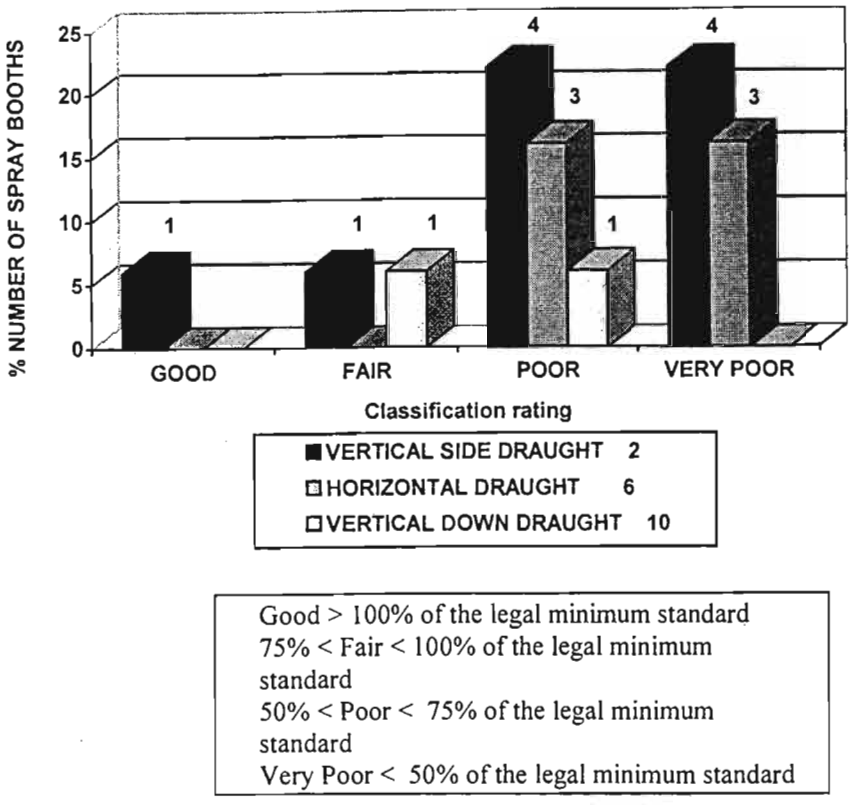
Six booths (33%) were tested, none were in the 'good' and 'fair' categories, 3 were 'poor' and 3 were 'very poor'. This type of booth is regarded as the least efficient of the three basic designs since the spray mists are frequently found in the operator's breathing zone (Figure 4.17).

(ii) Vertical side draught booth

Two booths (11%) were vertical side draught booths. From Figure 4.17 it can be seen that none were in the 'good' category. One was found to be 'fair' and one was classified as 'poor'.

(iii) Vertical down draught booth

Ten booths (56%) were of the vertical down draught type. Figure 4.17 shows that 1 was 'good', 1 'fair', 4 'poor' and 4 'very poor'. The criteria for being 'good' is based on the principle that a minimum amount of spray mist should be in the operator's breathing zone. The minimum legal flow rate is 0.3 m/sec. Twenty percent (20%) of the vertical down draught booths met this requirement (good, fair category).



Good > 100% of the legal minimum standard
75% < Fair < 100% of the legal minimum standard
50% < Poor < 75% of the legal minimum standard
Very Poor < 50% of the legal minimum standard

Figure 4.17: Classification and criteria used to judge the efficiency of spray booths, based on prescribed legal minima air velocities.

4.2.5.3 Summary of air movement test results

In section 1.3.2 the related literature, spray booth design was discussed. The efficiency is related to the effective removal of contaminants from the "breathing zone". The results indicated that in all three design types there were spray booths with poor air flow capacities. Overall, the vertical down draught type was the commonest booth design in this study. Only 1 was classified as good and 1 fair, the rest being poor or very poor. The criteria used to judge spray booth efficiency was based on prescribed legal minima air velocities as indicated in Figure 4.17 above.

4.2.5.4 Smoke pattern evaluations

Air flow patterns as described in section 3.4.5.5 were established using Dräger smoke tubes to determine turbulence in the spray booth. The results are shown in Table 4.20. Patterns of turbulence were drawn onto a diagram where its position was noted. Moderate to severe turbulence was judged as being where turbulence occurred on two or more sides of the vehicle. The judgement of turbulence was subjective since turbulence was not measured using a specific instrument but its severity was judged by the observer. From Table 4.21, most of the horizontal and vertical side draught booths showed the presence of turbulence. The vertical down draught booth showed 30% turbulent air flows.

Table 4.21: Moderate to severe turbulence in the 3 different types of spray booths.

Booth Type	% Showing Moderate to Severe Turbulence	Number of Booths Examined
Horizontal	83%(5)	6
Vertical (side)	100%(2)	2
Vertical (down)	30%(3)	10

4.2.5.5 Spray booth HDI concentrations

The purpose of determining the concentrations of the isocyanate group in the booths, was to establish an index value which may be used as a comparison against the prescribed standard. The index is obtained by dividing the concentration by its Threshold Limit Value (TLV). For example, Table 4.22 lists the concentration values found in each spray booth and using sample number 1 as an example the calculation was as follows:

Example:

$$\text{Index} = \frac{\text{Concentration (mg/m}^3\text{)}}{\text{TLV (STEL) (mg/m}^3\text{)}}$$

$$= \frac{14.20}{1.00}$$

$$= 14.20$$

Where :- TLV = STEL short-term exposure limit value = 1,00 (Oregon Study)

Concentration = Concentration of the HDI group (mg/m^3)

By definition an index value >1 is regarded as being in excess of the acceptable level (ACGIH - Threshold Limit Values). NIOSH Method 5505 was used to determine concentration levels. Table 4.21 shows the levels of the HDI (N=C=O) group concentrations. Table 4.22 shows the index value against each spray booth sample. The ideal index should be <1 and there were only 2 (11%), out of the 18 booths and 3 garages, met the acceptable standard. Case number 11 showed an index value of 0.16 and in one other case, reference 34, isocyanates were not detected. This implies that the remainder, or 89% (16 booths) were found to be above the recommended levels. This is in agreement with the report of the H.S.E. (guidance note EH16) where a number of cases of environmental measurements have proved that isocyanate concentration levels in the working environment were considerably above the recorded TLV levels.

From Table 4.22 it can be seen that in study B the indices ranged from 0 - 59.68 mg/m^3. The mean concentration was 14.64 mg/m^3 with a standard deviation of 13.063 mg/m^3. In comparison study A shows a smaller range from 0 - 6.63 mg/ m^3 with a mean concentration of 1.622 mg/m^3 and a corresponding small standard deviation of 1.793 . There was therefore a significant difference between the two studies, study B having a much higher HDI concentration than found in study A. Since the TLV used had a value of unity, the concentration and index values were identical. The Short Term Exposure Level (STEL) of 1mg/m^3 (as in the Oregon study) was used since most spray painters were subjected to relatively small intervals of exposure, probably lasting up to a maximum of 30 minute duration. This would represent the time taken to complete a vehicle re-spray. Furthermore the Oregon study being an 8 year follow- up study on HDI would provide a suitable comparison model to the 4 year study on HDI exposure.

Table 4.22: HDI index for each spray booth (n=18) and workshops and domestic garages (n=3)

Ref. Number	N = C = O Concentration (mg/m^3)		*Index Value	
	Study A	Study B	Study A	Study B
4	6.63	14.21	6.63	14.21
6	1.50	6.37	1.50	6.37
7	0.86	20.70	0.86	20.70
8	1.25	14.45	1.25	14.45
9	2.70	19.90	2.70	19.90
11	1.44	0.16	1.44	0.16
13	2.63	13.68	2.63	13.68
16	5.75	11.23	5.75	11.23
17	0.13	8.95	0.13	8.95
18	0.0	59.68	0.0	59.68
21	0.19	4.41	0.19	4.41
22	0.63	8.44	0.63	8.44
24	2.88	11.33	2.88	11.33
28	ND	12.44	ND	12.44
29	0.3	6.63	0.3	6.63
31	1.3	37.80	1.3	37.80
32	2.5	15.71	2.5	15.71
34	1.63	ND	1.63	ND
35	0.25	10.61	0.25	10.61
36	ND	13.94	ND	13.94
38	1.50	16.91	1.50	16.91

*Index value = $\frac{\text{Concentration}}{\text{TLV}}$ (see paragraph 4.2.5.5 above)

KEY: H = horizontal booth (6), VS = vertical side draught (2), VD = vertical down draught (10), W = workshops/garages (3)

Study A
mean concentration = 1.622 mg/m^3
standard deviation = 1.793
range: 0 - 6.63 mg/m^3
ND = not detected

Study B
mean concentration = 14.645 mg/m^3
standard deviation = 13.063
range: 0 -59.68 mg/m^3
ND = not detected

4.2.5.6 Employees' Questionnaire (Employees Perspective of Health and Safety)

(i) Respiratory protective equipment

The General Safety Regulations 1986 specify that approved protective equipment shall be provided by the employer and worn by the employee. Respiratory equipment provided by employers and used by employees may be divided into the four classifications, no mask, dust mask, cartridge mask and airline mask (chapter 1 paragraph 1.3.3).

Although the Health and Safety Executive (UK) recommends that when spray painting with isocyanates, air line masks should be used, only 7 (35%) were actually worn by the spray painters. This mask is considered to be the most suitable as it offers the most efficient form of protection to the wearer. The dust mask, being the least suitable form of protection was made available to and worn by 2 (10%) of the spray painters. The group which is most severely exposed to the effects of isocyanates include the "no mask" and "dust mask" group comprising 5% and 10% respectively. This represents a total of 15% of those spray painters examined in the survey.

Figure 4.18 shows the distribution of no mask, dust mask, cartridge mask and airline mask as being 5%, 10%, 50% and 35% respectively. This study shows that the majority of spray painters used the cartridge type mask.

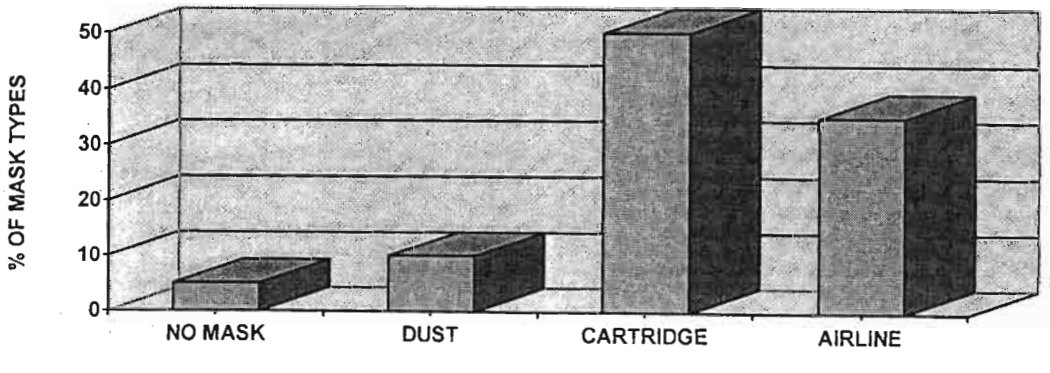


Figure 4.18: Distribution of no mask, dust mask, cartridge mask and airline mask amongst the 20 spray painters.

(ii) Information on health risks and the availability of hazard data sheets

To obtain information on health risks and the provision of data hazard sheets, each spray painter was asked specific questions in this regard. The following replies were obtained and are shown in Table 4.23. It is apparent from the replies received to questions 1, 5 and 12 that the large majority of spray painters are aware of the health risks involved in using paints containing isocyanates. It is also clear that the majority of spray painters, 82.4% had not been issued with hazard data sheets on isocyanates by their employers (Question 4).

Table 4.23: Information obtained from the employees health and safety questionnaire

	Questions and responses to employees health and safety questionnaire	% Response	
		YES	NO
1	Do you regard the use of a respirator necessary when applying paints containing isocyanates ?	94.7	5.3
2	Has your employer provided you with a respirator ?	100	Nil
3	Does the respirator provided have eye protection ?	10.5	89.5
4	Has your employer made a hazard data sheet available ?	17.6	82.4
5	Are there any risks involved in spray painting ?	100	Nil
6	Has your employer made your aware of the dangers of using HDI based paints ?	47.1	52.9
7	Has your employer arranged or any safety training whilst you were learning the trade ?	58.8	41.2
8	Does your employer/manager insist that you wear a respirator at all times while spray painting	76.5	23.5
9	Are you prepared to take the responsibility and the health risks by not wearing the respirator ?	35.3	64.7

10	How regularly, if ever, do you use a respirator ?	NEVER	RARELY	SOMETIMES	USUALLY	ALWAYS
		5.3	5.3	5.3	26.3	57.8

11	What type of respirator do you regard as suitable for use with twin pack paints ?	NONE	DUST/M	CART./M	AIR LINE/M
		Nil	Nil	22.2	77.8

12	To what degree in your opinion is there a risk of contracting isocyanate induced asthma from spray painting?	NONE	SLIGHT	MODERATE	SEVERE
		Nil	5.2	10.5	84.3

4.3 STATISTICAL RESULTS

4.3.1 Exposed vs Partially Exposed vs No Longer Exposed Groups.

Data was analysed using the SAS statistical package for all groups excluding the controls.
Since the sample size was small, data was stratified into three basic groups, all groups, exposed group, partially exposed and no longer exposed groups. The no longer exposed group comprised of those who became unemployed or had changed their occupations and who were therefore no longer exposed to the effects of HDI at the time of the second study.

Students paired t-test was used to test the significance of the mean cross-shift changes in FEV_1 levels from pre and post tests for subjects who were still exposed to isocyanates at the time of study B. The lung function results of the first study when compared with the second study showed a mean **cross-shift** decrease in FEV_1 of all the exposed groups in Study A to be 130ml. (sd 203) ($p=0.0002$) and of Study B to be 297ml. (sd 323) ($p=0.0001$) respectively. Therefore the difference in the mean cross - shift FEV_1 values from time 0 to time 4 years was therefore 167ml. The Kruscal Wallis test was performed on the data and a significant difference was found in the change between the pre shift predicted FEV_1 and the pre shift measured FEV_1 from study A to study B.

Pearsons Correlation Coefficient was calculated to determine whether there was a strong linear relationship between the outcome variable changes in FEV_1 and FEF_{25-75} with the independent variables viz, age, symptoms, length of service, booth efficiency and isocyanate concentrations. The correlations were found to be weak.

A multiple regression analysis was performed for each outcome variable and independent variables controlling for smoking. There was no significance amongst the groups examined (excluding the control group). These statistical findings were similar to those findings in study A.

4.3.2 Exposed groups vs Control Group

Since a later control group was introduced into the study, a second independent analysis was performed on the data between the exposed, partially exposed , no longer exposed and the never exposed control group (n=30). Statistical tests performed included the two-sample paired and unpaired paired t -tests, Pearson's Chi-square test, ANOVA (analysis of variance) and finally Logistic Regression Analysis.

Exposed and the non -exposed control (E=1and E=0) groups were compared .

Confounding variables C_1-C_7 age (C_1) , smoking status (C_2) , height (C_3) , race (C_4), length of service (exposure)(C_5), mask usage (C_6) and mask type (C_7) and the outcome variables Y_1 -Y_8 viz change in FEV_1 (Y_1), dermatitis (Y_2), eye irritation (Y_3) shortness of breath (Y_4), wheeze (Y_5), bronchitis (Y_6), asthma (Y_7) and cough (Y_8) and were examined in a chi-square test and a logistic regression analysis.

4.3.2.1 Results from independent t - test

Independent t- test for age, race , height, smoking status, shortness of breath, and wheeze was examined. The null hypothesis H_0 was **accepted** in that there was no statistical difference between the exposed and control groups with respect to age, race, height, smoking status, shortness of breath, and wheeze. In other words these two groups had similar characteristics with respect to these variables. However, the null hypothesis H_0 was **rejected** in that there was a statistical difference with regards to cross-shift change in FEV_1, in the number of incidents of dermatitis and the number of cases of eye irritation between the exposed spray painters (n=20) and the never exposed control group (n=30).

*4.3.2.2 Chi square test on the **baseline** changes in FEV_1 from study A to study B.*

The measured mean baseline decrease in pre FEV_1 from study A to study B was 41.25 ml per annum compared to the predicted mean baseline decrease in FEV_1 of 20.25ml per annum from study A to study B. (Figure 4.11). The results of the chi square test at the 5% level, showed no statistical significance between the difference in these two means. The reason for this was as result of the standard error (SE) of the differences of the measured baseline FEV_1 values, being too large.

4.3.2.3 Results from the logistic regression analysis

Yi on E, C_1, C_2 ..... C_7 , i = 1, 2, 3 ... 8 (ref chapter 3.4.7.1 (2))

The logistic regression model was used to perform the regression of a dichotomous dependent variable Y_1 on a set of 7 explanatory (independent) variables C_1, C_2, C_3 C_4 C_5 C_6 and C_7 that affected Y_1. The explanator variables are a combination of 3 continuous (C_1,C_3 and C_5) and 4 discreet (C_2 C_4 C_6 C_7) variables.

Y_1 is the change in FEV_1 value such that :-.

Δ FEV1 < - 250 ml = Y_1 and

Δ FEV1 > - 250 ml = Y_2

The optimum logistic regression model using the chi square test for goodness of fit indicated that change cross -shift change in Δ FEV_1 where Δ FEV_1 < -250 ml is best explained by the Logit optimum regression model given by the formula :-

$$\log \frac{\pi (G, C7)}{1 - \pi (G, C7)} = \alpha + \beta_1 G + \beta_2 C_7$$

The variables contained in the optimum logistic regression model as seen above are G, which is related to the group classification (viz. exposed , partially exposed , no longer exposed and never exposed groups) and C7 which refers to respirator type worn (viz. no mask, dust mask , cartridge and airline mask).

Table 4.24: The final logistic regression model .

Variable	Parameter Estimate	Standard Error	Wald Chi-square	Pr.> Chi-square
Intercept	6.1216 (α)	2.0915	8.5665	0.0034
G	- 2.7995 (β_1)	0.8545	10.7334	0.0011
C7	- 15124 (β_2)	0.5899	6.5719	0.0104

Table 4.24 shows the optimum logistic model and since the standard errors is very small, it is an indication that the adequacy of the model is satisfactory. The fact that the p-value associated with G and C7 is smaller than the level of significance ($\alpha = 0.05$) shows that exposure to HDI in combination with the mask type worn , explains the decrease in the dependent variable (cross-shift FEV_1) being < -250 ml, quite well.

i. Exposure effect:

From the statistical analysis, it was demonstrated that as the exposure changes from the most exposed group to the never exposed control group, the odds *against* a decrease in FEV1< 250ml, *increase* by a factor 16:1.

ii. Mask effect:

Similarly, as the mask type used , varies from the least effective to the most effective viz no mask, dust mask, cartridge mask, and airline mask , the odds *against* a decrease in FEV1< 250 ml, *increase* by a factor 5:1

CHAPTER FIVE

DISCUSSION

5.1 INTRODUCTION

This study examined some of the immunological and environmental factors which may have contributed to the respiratory health status of workers exposed to paint containing isocyanates and compared the results obtained between the various exposure groups. Rosenberg and Garnier (1986), described a technique of using a medical history questionnaire followed by the application of lung function tests in a follow-up study on isocyanate induced asthma cases. Although this study was multidimentional in nature, a similar approach was adopted by using a questionnaire followed by spirometric testing. As discussed in paragraph 3.3, the follow-up cohort was divided into 3 exposure groups, viz. "exposed", "partially exposed" or "no longer exposed" groups. In order to compare cross-shift changes ΔFEV_1 between each group based on HDI exposure, the partially exposed and the no longer exposed groups would have had to be exposed to HDI within the spray booth environment as in the case of the exposed group. This would be unethical, as some spray painters had left the trade for health reasons and may have reacted adversely to HDI upon subsequent re-exposure. Therefore in this study subjects exposed to HDI was as a result of their normal working conditions and not as a result of any external intervention. It also evaluated the effectiveness of control measures which may have been in force at the time of the investigation.

This study has shown:-

1. Respiratory symptoms were similar in the exposed group compared to subjects in community based studies, however there was an excessive number of cases of dematitis of the hand and eye irritation found in the exposed group (paragraph 4.2.1.3).

2. The difference between the mean pre and post test cross- shift values in FEV_1 in the follow-up study was 297 ml, which was statistically highly significant ($p= 0.0001$).

3. Cross-shift declines in lung function in the exposed group was more marked than those in the partially exposed, no longer exposed and the never exposed control group. This suggests that cross-shift declines in lung function are dependent on the exposure level (Table 4.6)

4. A comparison in the cross-shift declines between smokers and non smokers for both studies, showed greater declines in the non smokers (Table 4.7).

5. Immunological response (IgE), RAST (HDI) and BHR (histamine PC_{20}) testing were found to be unsuitable markers for the prediction of longitudinal decline in lung function of workers exposed group to HDI (Table 4.13).

6. Annual baseline declines in pre FEV_1 lung function in the exposed group was found to be in excess of the ECCS predicted values (Table 4.16).

7. Peak expiratory flow rate measurements (PEFR) were not helpful in identifying workers with excessive cross-shift decline in FEV_1 following exposure to HDI (Table 4.20).

8. Spray booth efficiency based on the prescribed legal minima air velocities, showed a large distribution of the spray booths in the "poor" and "very poor" classification (Figure 4.17).

9. HDI levels monitored in 16 of the 18 spray booths (89%) were found to be in excess of the legislated OEL-CL value for isocyanates (Table 4.22).

10. Approved respiratory protective equipment (positive pressure airline mask) a requirement of the Department of Labour and highly recommended by the paint manufacturers, was utilised by only 7 of the 20 (35%) spray painters in the exposed group (n=20) (Figure 4.18).

11. Removal from exposure to HDI for a period greater than 6 months has in some cases, shown a "recovery" in the spray painter's Baseline FEV_1 (Figure 4.15).

5.2 ACUTE RESPIRATORY EFFECTS AND HEALTH QUESTIONNAIRE

5.2.1 Medical history: (Respiratory symptoms from questionnaire)

5.2.1.1 Respiratory symptoms

Peters and Murphy (1970) describe four general patterns of respiratory response to TDI.

- Chemical bronchitis in response to high concentrations exposures
- An asthma like condition in response to low concentrations in sensitised workers.
- Acute falls in ventilatory capacity such as FEV_1 during one work shift
- Chronic decrement in pulmonary function with prolonged exposure

There was a decrease in the number of cases of cough and phlegm from the first to the second study . The number of cases of shortness of breath increased from 10% to 20%. The number of chronic bronchitis cases remained the same at 5% whereas the asthma cases decreased slightly from 7.5% to 5% in the second study (exposed group).

There were only 2 subjects in the study who had clinically diagnosed asthma. These subjects had asthma since childhood. The implication is that those spray painters who developed asthma may have left the industry resulting in the "healthy worker effect". However many workers had significant cross-shift declines in lung function. Musk (1988) has estimated that 5% of exposed workers develop clinically apparent asthma due to isocyanate sensitization, although values of up to 30 % have been reported. He further states that this would be dependent on exposure levels and the duration of exposure.

From the symptoms outlined above by Peters and Murphy (1970) in their study on TDI exposures, it appears from the present study that HDI shows similar effects in acute falls in ventilatory capacity during the work shift, followed by chronic decrement in pulmonary function over a prolonged period.

The prevalence of chronic respiratory health symptoms in this study were similar to that found in a South African community based study conducted by Lalloo in 1992 (Lalloo, 1992).

5.2.1.2 Eye irritation

From the employees questionnaire 10 (50%) of the exposed spray painters, none in the partially and no longer exposed groups and 1(3%) in the never exposed control group, were found to have eye irritation or burning sensation of the eyes. In the initial study 55% of the spray painters exposed to HDI spray mists suffered from some form of eye irritation. Filatova *et al,* studied 82 workers at a plant manufacturing HDI and all of the 82 workers had complained of eye irritation after being in contact with HDI (Filatova *et al,* 1968). NIOSH also reported that HDI liquid, vapour, mists or aerosols can cause severe eye irritation with pain and watering of eyes, redness, and swelling of the eyelids (NIOSH, 1978). Damage to the cornea can occur but normally the effects are reversible and do not result in permanent injury. Mobay, a leading manufacturer of HDI found that levels of 0.05 to 0.1 ppm can cause irritation and watering of the eyes (Mobay, 1984). Exposures to HDI were found to cause severe eye irritation in a Draize test on rabbits exposed to spray mists (NIOSH, 1978). In the follow-up study, none of the 20 workers wore full-face masks to protect their eyes against spray mists.

5.2.1.3 Dermatitis of the hand

The questionnaire also examined the number of spray painters with dermatitis of the hand. There were 8 (40%) cases of dematitis in the exposed group, none in partially exposed group and no longer exposed group with 2 (7 %) in the never exposed control group. Whilst the number of cases of eye irritation decreased from the initial study to the follow-up study, the number of cases of dermatitis amongst the spray painters increased from 32% to 40% (Table 4.1).

Hardy (1979) reported that the non respiratory health effects due to isocyanate exposure, included skin sensitisation following contact with isocyanates. In skin tests carried out on rabbits the application of undiluted HDI for 24 hours in a standard Draize test caused severe irritation (NIOSH, 1978). A piece of cotton saturated with 0.5 ml. HDI caused severe reddening and swelling with tissue death when placed on a rabbits ear for 30 minutes (HSDB, 1993). Testing the potency of HDI using the mouse ear swelling test, it was found that 50% of the animals were sensitised at a dose level of 0.73 mg/kg . Furthermore, it was found that HDI was the most potent of the isocyanates (HDI, MDI, TDI and SMDI) tested. Musk, Peters and Wegman, showed the possibilities of producing allergic skin sensitisation in guinea pigs and mice with solutions of TDI . Dermal contact with TDI may result in respiratory tract hypersensitivity as shown in guinea pigs (Musk, Peters and Wegman, 1988). This is important because Thorne demonstrated that cross-sensitivity was observed between HDI and MDI, SMDI and TDI (Thorne, 1987).

The combined effects of HDI on the hand together with the common practice amongst spray painters to either wash or wipe their hands in thinners to remove excess paint, may account for the high prevalence of dermatitis found amongst the spray painters. None of the spray painters in both studies used any form of hand protection ie. gloves.

5.2.1.4 Lung and bladder cancer

In the review of the related literature (1.4.2) on exposures to isocyanates, reference was made to Wong and Morgan's (1988) paper stating that there was a significant risk, in cases of skin and bladder cancer amongst spray painters. A similar finding was made by the International Agency for Research on Cancer (IARC) from a review of 300 papers (IARC, 1989). This study was not designed to diagnose lung and bladder cancer, however the questionnaire did ask if any other diseases were present. There were no reported cases of cancer, in any form, amongst the subjects exposed to HDI. However, this may be explained by the relatively short follow-up period of this study and the long latency period required before the development of cancer symptoms amongst exposed subjects.

5.2.2 Spirometry

5.2.2.1 Cross-shift declines (general)

In the initial study, the mean cross-shift decrease in forced expiratory volume in 1 second (FEV_1) was 130.5ml (SD 203.2) (Randolph *et al,* 1997). The difference between the mean pre and post test values of FEV_1 was statistically significant (p=0.0002). The lung function data of the 40 spray painters indicated that 10 (25%) showed clinically significant cross-shift declines viz. declines > 250 ml. (Health and Safety Executive, 1983).

In the follow-up study the mean cross-shift decline was 297 ml (SD 323) (95% confidence interval 172.8; 421.2). The difference between the mean pre and post test values in FEV_1 in the follow-up study was highly significant (p= 0.0001). Cross-shift spirometric lung function data of the follow-up study showed that 9 (45%) of the 20 spray painters who had continued to spray paint had clinically significant declines > 250ml (according to the above HSE executive criteria). Gandevia in a much earlier study showed a mean cross-shift decreases in FEV_1 of 180 ml. and Peters noted a mean cross-shift decline FEV_1 of 220ml. (Gandevia 1963; Peters *et al,* 1968).

The mean cross-shift ΔFEV_1 between the initial and follow-up studies was found to have further declined by 167ml. from 130.5 ml to 297ml. This further decrease in lung function reflects the possible cumulative effects of exposure to HDI combined with the effects of cross-shift exposures on the day of the follow-up evaluation.

5.2.2.2 *Cross-shift declines:- smokers vs non smokers*

Lung function data indicates that in both studies there was a larger decrease in the cross-shift values amongst non-smokers compared to smokers. The mean decrease in FEV_1 for non-smokers (n=11) was 9.3% compared to 6.6% for smokers (paragraph 4.2.2.4), (Table 4.7).

Examination of the follow-up data in this study showed two important points :-

(i) the unexpected larger decrease in FEV_1 found amongst non-smokers when compared to smokers.

(ii) that more smokers were wearing the appropriate respiratory protective equipment, when compared to the non-smokers.

This practice would ensure a higher protection factor and thus better protection against the effects of HDI spray mists. The alternative explanation for the group observed is that smokers lung's, due to the irritation effects caused by smoking may be more sensitive to the exposure of isocyanates than non-smokers, hence their greater inclination to wear the respiratory protective equipment provided. The most important observation is that the correct respiratory protective equipment protects the spray painters.

5.2.2.3 *Cross-shift declines:- exposed groups vs control group*

If one examines the subjects mean cross-shift declines in FEV_1 according to the potential degree of exposure, the results were as follows:-

(i) spray painters (exposed group), ... ΔFEV_1= -297ml
(ii) supervisors (partially exposed group), ... ΔFEV_1= -282ml
(iii) unemployed or changed occupation (no longer exposed group), ... ΔFEV_1= -54ml
(iv) never exposed to HDI (control group), ... ΔFEV_1= +17ml

These results clearly demonstrate that the decreases in FEV_1 are related to the potential HDI exposure levels at the work place. The control group although randomly selected, closely matched the exposed group in respect to age, height, ethnic background and smoking status. In the control group, the mean cross-shift change was +17ml. This may be explained by the circadian rhythm effect in which a persons pre and post lung function actually increases over the work- shift.

Examination of the individual data showed that the largest decrease in cross-shift decline FEV_1 was ref. no. 6 whose FEV_1 decrease was recorded at -1230 ml. (Tables 4.13 and 4.14). This decrease was probably due to the fact that the spray painter was observed by the author spraying in his work shop without any form of mechanical ventilation and also without wearing a respirator. The spray mists would have been inhaled directly into the spray painters lungs hence the large cross-shift decline or more likely the subject could have been sensitised to HDI. A further example of the value of wearing suitable protective equipment is shown in Table 4.8 and Table 4.9 in which the cross-shift FEV_1 in the 2 asthma cases (ref. 7 & 12) were -640ml and + 210 ml respectively. The former spray painter wore a cartridge mask with a low protection factor whilst the latter was found to be using a positive pressure airline mask with a high protection factor (paragraph 1.3.3.2 and 1.3.3.3).

In summary it appears that the amount of cross-shift decline in FEV_1 may be dependent upon the following inter-related hygiene factors:-

- the concentration level of HDI to which the subjects were exposed
- the duration of the exposure to HDI
- the type of respirator worn by the operator
- the spray booth design (horizontal, vertical side and vertical down draught)
- the existing form of engineering control (mechanical ventilation)
- the type of spray gun used (viz conventional high pressure atomised spray gun vs low pressure high volume spray gun)

5.3 IMMUNOLOGICAL RESPONSES IgE, RAST TO HDI, HDI AND HISTAMINE PC_{20}.

5.3.1 Immunological response

The objectives of the first study were to examine lung function parameters only, in particular FEV_1 and also to evaluate the environmental working conditions to which the spray painters were being exposed. However, no immunological or bronchial provocation testing was carried out. Furthermore with pre and post lung function testing each spray painter was used as his own control (ATS, 1987). The basic objectives of the study were therefore merely to conduct cross-shift lung function tests and examine any resultant changes in relation to the environmental working conditions.

In contrast. the second study, in addition, examined the question of an immunological response to HDI and therefore IgE levels and the response to RAST (HDI) were investigated. It was also resolved if possible to examine a closely matched control group and use this as a comparison with the exposed group (Table 4.1).

5.3.2 PC_{20}

This method was used and described under chapter 3 (methods). Reference no. 6, 7, and 28 had a PC_{20}, at concentrations of 14.4 , 6.8, and 3.0 mg/ml histamine respectively and one subject, ref. no. 26, was unable to perform the histamine challenge test as his baseline FEV_1 was only 0.78 litres. From the results of the provocation testing, airway hyperresponsiveness is considered to be present when the provocation concentration causes a fall in FEV_1 of 20% viz . PC_{20} < 8mg/ml. histamine. There were only 2 cases (ref. 7 and 28) in this study in this category (Table 4.13). Ref. 7 had been an asthma sufferer since childhood and ref. 28 had been spraying for many years in his own domestic garage under poor standards of industrial hygiene. He had also been medically examined by a physician and diagnosed as suffering from obstructive lung disease.

5.3.3 Immunoglobulin E, Rast to HDI and House Dust Mite

In the blood test reports only five subjects (ref. 4, 11, 13, 17 and 36) showed raised IgE ,viz IgE >100 kU/ litres (n=17) of which 4 had also showed raised House Dust Mite. With respect to the house dust mite test, 6 subjects reference (ref. 4, 11, 12, 13, 14, 36) indicated levels > 0.35 kU/l. (Table 4.13).

There was only one spray painter (6%) ref. no. 13 with a positive RAST (HDI) result of +1, however this subjects decrease in FEV_1 was no different from those spray painters who were not positive. It appears that this test is not suitable in this category of industry (Table 4.13). The subject who was positive had no distinguishing characteristics from the other subjects. A positive RAST to HDI test implies that the mechanism for sensitisation is IgE mediated. It could well be that the workers who developed isocyanate induced asthma by exposure to HDI, could have left the industry (healthy worker effect). From the literature Patterson *et al,* (1987) refers to the suggestion that isocyanate induced asthma is IgE mediated, but states that the presence of a specific diisocyanate IgE has been shown only in a few workers with symptoms. Musk, Peters and Wegman, (1988) refer to the fact that specific IgE antibodies to monofunctional isocyanates have been reported but specific IgE to diisocyanate conjugates have not been identified. At the same time Grammer (1988) reported on a study of 150 spray painters who used paints containing HDI and THDI. Measurements of ambient isocyanate levels, answers to questionnaires, and measurements of serum antibody to HDI and THDI bound to human serum albumin were evaluated. Since the spray painters wore respirators, isocyanate exposure was assumed to be very low and although 8% reported respiratory tract symptoms only one worker was thought to have work related respiratory disease. Approximately 12% had IgG antibodies to one of the two isocyanates (HDI and THDI) whilst 5% had IgE antibodies to one of the two isocyanates. In a similar follow up study in Stockholm Sweden, Tornling *et al,* examined car spray painters exposed to HDI over a six year period and found none of the workers had specific IgE antibodies against isocyanates and therefore concluded that the study did not support the concept that lung impairment was immunologically mediated (Tornling *et al,* 1990). It was also, found that there was no significant difference between the IgE levels of the spray painters and the control group.

Karol conjugated the antigen p-tolyl monoisocyanate to human serum albumin and demonstrated the presence of these antibodies in the serum of some TDI sensitive persons by RAST. However, the prevalence of these antibodies in persons with challenge test-proven isocyanate induced asthma approximated to just 20%. This fact suggests that it may not be a major allergen responsible for isocyanate induced asthma or that the antigen bound to human serum albumin was inadequately sensitive (Karol *et al,* 1978). In a study carried out by Soderlund on 20 TDI exposed workers in a South African chemical and processing factory, he reported that 2 (10%) had high levels of TDI specific IgE. The IgE test results combined with the low RAST (HDI) result suggests that that the obstructive effect on the airways is not IgE mediated (Soderlund, 1993).

5.4 BASELINE CHANGES IN LUNG FUNCTION

5.4.1 Chronic effects

The chronic mean decline in FEV_1 per annum over the 4 year exposure period was assessed by dividing the total decline in pre FEV_1 from year 0 to year 4 by the number of years of exposure (4). This was calculated from the data obtained initially from the first study and compared to that obtained in the follow-up study. As expected the decline was most marked in the workers who continued spray painting (exposed group). The results were as listed below as:-

Δ FEV_1 = - 41.25 ml per annum in the exposed group (Table 4.16).
Δ FEV_1 = + 26.5 ml per annum in the partially exposed group (Table 4.17) and
Δ FEV_1 = - 7.85 ml per annum in the no longer exposed group (Table 4.18).

The larger decrease was, as expected, found in the exposed spray painter group who continued in the trade as spray painters. This is the most important group from an exposure point of view, and showed a mean annual baseline decline in FEV_1 of 41.25 being more than double the predicted ECCS value of 20.25 ml (ECCS, 1983).

The positive increase in the base line values in FEV_1 for the supervisors could not be explained . The sample size (n=5) was too small to make any definite conclusion about this observation. The overall baseline measured decline in pre FEV_1 for the group as a whole (n=33) was 18.75 ml /annum. The predicted decline for the same group was 21.5 ml./annum. (± 0.0195). This result indicates the group as a whole showed FEV_1 declines which were slightly lower than normal decline. Since there was no control group in the original study, the predicted annual baseline declines were taken from the ECCS predicted values which were used as a standard. These predicted declines were obtained from the prediction equations contained in Appendix C

The American Thoracic Society (ATS) state in their review of lung function testing, that where a person is used as his own control as in the case of cross-shift lung function testing it is not necessary to have a control group (ATS, 1987). However, despite this fact the author used a closely matched "never exposed" control group as a comparison in cross-shift changes in lung function in study B.

In other studies on exposures to TDI, the following mean annual declines have been reported. Peters *et al*, -110 ml., Wegman showed that the lowest exposure group had a normal decline -20 ml., middle exposure group -42ml., and the highest exposure group -102ml. respectively. Diem, Jones and Hendrick (1982) reported -24ml. per annum., whilst Jones, reported annual declines of -67ml. in current smokers and -53 ml. in non-smokers.

From the literature the baseline decline of -4 1.25 ml/year in this study approximates to the middle exposure group of Wegman's study.

Reviewing the individual annual baseline declines in this study, the data showed ten (30%) spray painters were found to have decreases in FEV_1 >90 ml per annum. Based on longitudinal studies the normal expected yearly decrements in FEV_1 are small, 20 to 30 ml./yr. in non-smokers or 40 to 50 ml. for smokers (Burrows *et al,* 1986, Glendmeyer *et al,* 1982, Vollmer *et al,* 1990). It has been shown that to develop significant airflow obstruction the average rate of decline in FEV_1 during adult life probably needs to be > 90 ml. per annum or three times the normal decrement as seen in a non smoker. (Buist and Vollmer, 1988). The ten cases reported above are very important in that these **baseline declines** exceeded the predicted declines due to ageing alone and therefore possibly indicate chronic lung function changes in FEV_1 over the 4 year follow-up period. Furthermore, of these 10 cases, only 3 (ref. 6, 21, 29) had corresponding clinically significant **cross-shift declines** in FEV_1 > 250ml (Table 4.11 and 4.12), reflecting the possibility that the cross-shift declines are probably as a direct result of the HDI exposure carried out on the day of the evaluation, whereas longitudinal declines would be as a result of the cumulative effects of past chronic exposures to HDI. Wegman *et al,* (1977) reporting on the chronic effects of TDI stated that there was a significant association ($p < 0.005$) between acute and chronic decrement in FEV_1 and concluded by reporting that exposures to TDI at 0.003 ppm (0.0214 mg /m^3) or higher is unsafe. In contrast to these results, a 6 year follow-up study by Tornling found that compared to the smoking control subjects, the smoking spray painters had greater yearly reduction in FVC , FEV_1 and VC (Tornling, 1990).

Baseline changes in the FEV_1 in the no longer exposed group (Figure 4.15) shows the total period in months of non-exposure to HDI, up to the time of the follow-up baseline study. The number of months of non-exposure were plotted against baseline changes in FEV_1. The graph shows a trend that as the number of months exceed 6 since the last exposure, the baseline FEV_1 values will tend to improve. This finding needs to be investigated in further research on HDI in order to determine the rate of "recovery" following cessation from HDI exposures.

In some instances spray painters leave the trade due to ill health and the researcher is left with only so called "healthy workers" in the study , this is known as the "healthy worker effect". From the age distribution figures (figure 4.1), the largest age group was between the ages of 30-34 years. There were only 2 found in each of the 35-39 and 40-44 year age groups and there were no spray painters over the age of 54 years. This could be as a result of the healthy worker effect as people tend to leave the trade due to ill-health. In this follow- up study, the author is aware of three spray painters leaving the trade due to health reasons.

5.4.2 Longitudinal study versus cross-sectional study

This study examined both longitudinal and cross-shift changes in FEV_1 and whilst there are merits in both methodologies, it must be emphasised that longitudinal spirometry has a distinct advantage over cross-shift measurements. Longitudinal spirometry allows the identification of a worker experiencing an excessive pulmonary function loss, before the loss would become apparent through conventional cross- sectional testing and interpretation. This is particularly true for workers whose initial FEV_1's are above average (100% of predicted or higher) and are regarded as normal (Hankinson and Wagner, 1993). Therefore the data for longitudinal studies also becomes more reliable especially if it is carried out on a yearly basis as any unexpected or sudden variation from the norm would become immediately apparent and could be quickly detected and reassessed. This would not be the case of data from a cross-sectional study. Furthermore the results of this study supports the view of a number of authors who have found evidence that data from cross- sectional studies, cannot be used to draw inferences about individual patterns of longitudinal decline (Burrows *et al,* 1986, Dockery *et al,* 1985, Dontas *et al,* 1984, Flood *et al,* 1985).

In summary longitudinal studies are likely to provide the most accurate and reliable estimates of spirometric lung function decline for both individuals and populations. Cross - sectional studies on the other hand are cheaper and quicker to conduct Cross- sectional studies are a particular useful screening tool for identifying potentially affected or high risk subjects who require further medical follow- up. Both assessments have a role to play in occupational health monitoring (Eisen, 1993). Progressive annual declines suggest the need to take action to prevent chronic changes. It is most important to detect these declines in or to prevent sensitisation in the subject or occupational asthma.

5.4.3 Peak Expiratory Flow Rates (PEFR)

In this study 21 subjects performed the PEFR measurements over a period of 30 consecutive days according to the protocol outlined in chapter 3 (methods). Initially the data was examined to see if there was a difference in peak flow measurements between working and non working days. Serial measurements of the PEFR taken, showed an even distribution between increases and decreases from work days to non - work days and visa versa. In order to validate the data obtained from the self administered PEF measurements and that obtained by the author using the Vitalograph Alpha ®, the data was then examined and compared. The pre test measurements obtained using the two different methods showed no statistical difference between the data at the 95% confidence level.

Similarly the post test measurements also showed no significant difference between the data sets at the 95% confidence level. This indicates that there was a strong correlation between the measurements recorded by the author using the Vitalograph Alpha® and those obtained from the workers who carried out their own lung function using the peak flow meter. There was also no significant difference in the pre and post test cross - shift measurements in the peak expiratory flow rates using either the Vitalograph or peak flow meter to record the data. (see students t-test, statistical report, chapter 4).

Therefore the PEFR did not indicate large or significant declines in cross-shift measurements as was shown in both the FEV_1 and FEF_{25-75}. One may conclude from this study that PEFR measurements are insufficiently sensitive to be useful as an early warning indicator of possible occupational asthma. Berube *et al,* 1991 concurs with these results by showing that changes in peak flow are proportionally less than the FEV_1 in the same individual with asthma (Berube *et al,* 1991). Burge (1993) in his reference to peak flow meters discusses the urgent need to have linear calibration of peak flow meters which may remove some of the confounding factors in the calculation of diurnal changes.

He concludes that methods are needed to increase the sensitivity of serial peak flow measurements which should be achievable with the use of a computer diagnostic aid.

5.4.4 Lung function parameters PEFR versus FEF_{25-75}

In reviewing the lung function data, PEFR were measured both by the author in routine cross- shift monitoring and also by the subjects when carrying out the 30 day peak flow self -monitoring exercise. Although extensively used over work shifts it has been found that when assessing occupational asthma, PEFR demonstrates greater variability than measurements of FEV_1 and VC.

In addition PEFR is "effort dependent" and insensitive to early change in the peripheral airways. In contrast flow rates measured by the FEF_{25-75}, reflect the patency of the small airways and is therefore a more sensitive predictor of early changes in lung function.

This study suggests that the FEF_{25-75} values of the exposed group showed greater declines than their corresponding FEV_1 values, (-320ml. vs -297ml.) (Table 4.6). The technical performance of the procedure and the interpretation of the data obtained have been standardised making the measurement of small airways an ideal tool for epidemiological investigations (American Thoracic Society : 1987).

5.5 ENVIRONMENTAL CONDITIONS AND ASSOCIATED FACTORS

5.5.1 Spray booth evaluations

The negative effects on spray painters lung function has been described above, in particular cross- shift declines. Poor working environments will exert a detrimental effect on the workers health status. The potential factors which contributed to the workers health status were examined in the study were:-

1. HDI concentration levels.
2. Spray booth efficiency .
3. Type and usage of respiratory protective equipment

In general it was found that few spray booths complied with the legal provisions under the General Safety Regulations, 1986 and the Hazardous Chemical Substances Regulations, 1995 made under the Occupational Health and Safety Act 1993. Furthermore 65% of the spray painters were not using the airline respirator as recommended by the first study and the major paint manufacturers of automotive paints.

In the first study at least 50% of the spray painting establishments used the vertical down draft booth which is considered to be the most efficient type and therefore said to conform to good principles of spray booth design. Despite this fact, excessive concentrations of HDI were found in the operator's breathing zone. When the Oregon 1980-1990 study was compared with the follow -up study the percentage of samples exceeding the Oregon PEL of 1 mg/ m^3 for polyhexamethylene diisocyanate were 66% and 90% respectively (Janko *et al,* 1992).

The initial and follow-up studies, spray booths were found to exceed the Oregon PEL of 1mg /m^3, with a mean polyhexamethylene concentration of 1.62 mg/m^3 (± 1.793) and 14.645 mg /m^3 (± 13.063) respectively (Table 4.21). The booth concentration ranges varied from Not Detected (ND) to 18.4 mg/m^3 in the Oregon study compared to ND to 6.63 mg/m^3 in the initial study and ND to 59.68 mg/m^3 in the follow-up study (Table 4.22).

The discrepancy between the US study, the initial study and the follow -up study in the HDI concentration results may be explained by the possible stricter legal enforcement and control measures operating in the United States and the gradual deterioration in the maintenance of the local spray booths over the 4 year follow-up period. Tornling *et al*, (1990) reported that the mean exposure level in his study was twice as high for HDI and more than 10 times higher for HDI - BT compared with the results from an American factory spraying trucks cabs (Grammer *et al,* 1988). Tornling explains that the high exposure levels might be due to different working routines and different respiratory protective equipment. The American spray painters used respirators with a protection factor of 100, and total compliance was assumed whereas Tornling (1990), in his study protection factors of 2, 5 or 100 was assumed. In the follow –up study as in the first study only personal airborne sample levels of HDI were taken in and around the spray painters breathing zone and since there was great variation in the frequency with which the respirators were worn, it would be impossible to calculate the actual exposure levels found inside the mask.

Airflow pattern tests were conducted simultaneously whilst HDI samples were being taken. The results were similar to those found in the previous study in that the horizontal and vertical side draft booths showed the presence of severe turbulence. The measurement of turbulence was a subjective measurement based purely upon observation since there were no instruments available to measure turbulence. As mentioned in the results section, turbulence may have been caused by defective spray booth door seals causing air leaks within the booth and also blocked and partially blocked filters in the ventilation outlets (Table 4.21).

No measurements were taken of the concentrations of organic solvents within the spray booth as samples of organic solvents taken in the fist study were found to be considerably lower than the respective TLV values and as stated in the review of the related literature (paragraph 1.4.4), it was felt that there was no need to repeat this evaluation in the follow-up study.

For this reason DeVillbiss a leading manufacturer of spray booths and spray booth equipment, have introduced a new spray - gun design called the "duo - tech" system (De Villbiss, 1990). This design addresses the problem of " bounceback" caused by the operation under a low volume high pressure system, by replacing the conventional spray gun with one that operates at high volume low pressure, thereby reducing the excessive overspray in the spray booth. In both studies all atomising spray guns were of the conventional high pressure, low volume type. In the USA, the South Coast Air Quality Management District in California has effectively banned the use of conventional spray-guns which give rise to bounce-back since it is a legal requirement that the spray gun transfer efficiency shall not be < 65% (Devilbiss Technical Publication - Catalogue -undated).

From the results of this follow-up study, it is apparent that the initial recommendations made by the first study to the Department of Labour regarding the stricter implementation of specified control measures have not been enforced. This is despite the fact, that there has been a tightening up of the South African legislation on the protection of the worker from occupational health exposures at the workplace, through the promulgation of the Hazardous Chemical Substances Regulations, 1995. This unfortunately has led to the further deterioration in the respiratory health status of the spray painters due to chronic HDI exposures, and unlike some overseas countries, routine lung function testing including peak flow measurements are not undertaken in an attempt to identify potential asthma sufferers.

5.7 LIMITATIONS OF THE STUDY

Spirometer accuracy even with the best quality control programmes may be a significant source of variability. The American Thoracic Society accuracy requirements for FVC and FEV_1 are ± 3% of the reading. For example, an individual has a stable FEV_1 on two separate tests, then allowing for instrument variation, one reading could be 4.12 litres (+3%) on one occasion and the other reading 3.88 litres (-3%) on another occasion. The difference between these two results represents a 240 ml. change in the FEV_1 reading or about 10 times the expected decline in FEV_1 for non-smokers. This significant change in FEV_1 is still within the ATS accuracy requirements. Diem *et al,* observed a survey bias of 130 ml. that could not be explained despite the best equipment and quality control procedures being used (Diem *et al,* 1982.)

In longitudinal studies as opposed to cross - sectional studies, reference can be made to base line data in order to notice and compare within each individual, any changes that are taking place. However the relative high variability associated with short term measurements in Δ FEV_1 make accelerated declines difficult to detect.

This study has, as previously stated, shown large baseline declines in FEV_1 over and above that which is normally accepted. However due to the inherent variability in the administration and the performance of spirometric testing , one must always view lung function results with caution. Reference is therefore made to Clement and Van de Woestjien who studied 2406 members of the Belgian Air Force for 3 to 15 years and concluded that at least 6 to 8 years of a follow-up period is required to appreciate with precision, the rates of decline in FEV_1. In addition to this follow-up period, spirometry examinations should be performed annually in order to detect any survey biases and determine the stability of FEV_1 measurements (Clement and Van de Woestijne, 1982).

Due to economic and logistical reasons this study was only conducted over a 4 year follow-up period of investigation on an original cohort of 40 spray painters and therefore acknowledges the fact, that there are certain built in limitations for example small sample size, which may have contributed to variability in the data. From a statistical point of view it was difficult, in some instances because of the relatively small sample size, to show statistical significance at the 95% confidence limit.

5.8 FUTURE RESEARCH

5.8.1 Introduction

The study has attempted to provide certain answers to a number of questions concerning the spray painters respiratory health status in relation to HDI exposure. There are still a number of unanswered questions which require further investigation. It is a fact that better clinical tools for the early recognition of occupational asthma can lead to better and earlier preventative strategies and prognostic indicators as well as provide a means for improving the clinical treatment of patients. Research examining important biomarkers of occupational asthma will allow better identification of this disease. Biomarkers include sputum examination or nasal lavage analysis.

5.8.2 Immunology

From the immunological aspect, Chan-Yeung reported that for both large and small molecular weight compounds it has not been established, whether or not nasal clinical sensitisation occurs before patients develop asthma. She reports that this possibility should receive priority in future prospective workplace investigations. Evaluation of the nose will in addition to immunological sensitisation, provide for the examination of various affector cells, mediators and cytokines elaborated as a result of the reaction (Chan-Yeung, 1995).

5.8.3 Spray Booths

" Bounce back " has been discussed under paragraph 5.6 General. It has been mentioned both in the original and follow-up studies and merits further study. Since the design protocol did not include the evaluation of the spray gun type and its usage, it is suggested that further studies should examine this phenomenon in more detail. By measuring the pressure inside the spray gun and other factors one can relate this to the transfer factor. The transfer factor quantifies the amount of paint emitted from the spray gun as a percentage transferred and deposited onto the sprayed surface. The more paint that is transferred onto the article being sprayed, the less returning into the spray painters " breathing zone" and being wasted in the form of spray mists or overspray. In California it has been made a legal requirement for the transfer factor to be at least 65%. The author has noted that despite high air velocities found within the spray booth, spray mists have on occasions been observed returning into the operator's breathing zone. Perhaps the need for an adequate transfer factor should become the basis for a legal requirement in terms of South African legislation, as it has both health and economic advantages ?

5.8.3 Future longitudinal studies using spirometry

Longitudinal studies of the long- term effects of HDI exposure in automotive spray painters should continue beyond the 4 year follow- up period as was the case in the present study. Whilst classic occupational asthma may be recognised and result in the removal of the worker from exposure, the decline in spirometry in this study in workers not recognised as asthmatics, is of concern.

CHAPTER SIX

SUMMARY AND RECOMMENDATIONS

6.1 SUMMARY

In Chapter 1 in the introduction to the review of the related literature, a comprehensive review was given on the health effects of isocyanates on spray painters. Most of the literature available related to the health effects of TDI with relatively few references to HDI. However despite this fact, it was quite clear from some of the reviews that HDI was also a potential sensitiser and in some cases had caused isocyanate- induced asthma. Measurements of cross-shift changes in lung function showed abnormal decreases in certain exposed cases particularly in FEV_1 and with this in mind the first study examined these changes and attempted to relate them to the potential HDI exposure levels. Since this study revealed substantial cross-shift declines in FEV_1 (>250 ml) the author realised the importance of a follow-up study to investigate possible chronic changes or the long term effects on respiratory health. Furthermore the literature also referred to the immunological response in an attempt to discover possible mechanisms responsible for HDI induced asthma and hence the need to examine these mechanisms in the follow-up study.

In the Chapter 2 - The Problem and It Setting, a number of objectives were stated. The first objective was to relate cross-shift changes to HDI exposure and to examine any acute effects. The second objective examined possible immunological responses to HDI exposure while the third objective examined possible chronic effects as a result of long term cumulative exposure to HDI. The fourth objective was concerned with the environmental evaluation of the spray painters working conditions in order to explain how circumstances at the working environment may have contributed to respiratory disorders. The fifth and final objective then integrated all the other objectives to give an overall picture of the respiratory health status of the spray painters as referred to in the main problem statement.

Chapter 3 - Methods, examined scientifically approved methods of evaluating:-

- HDI concentrations within the spray booths,
- spirometric lung function techniques
- various immunological tests including RAST (HDI)

NIOSH approved methods were used to sample and analyse HDI concentrations within the spray booth and the ATS protocol was implemented in spirometric lung function tests using the ECCS predicted reference values. For the evaluation of immunological tests including IgE, RAST (HDI) a standard kit as supplied by the laboratory was used and PC_{20} was evaluated by using the protocol as specified by Hargreave (Hargreave, 1984).

Chapter 4 and 5 presented and discussed the finding of the results and are summarised below:-

Objective 1:

Although there was no statistical correlation between drop in FEV_1 and HDI concentration measured within the booth, decreases in lung function was greatest in the exposed group followed by the partially and non-exposed groups. The difference between the pre and post test measurements were found to be statistically highly significant ($p< 0.0001$). When comparing both groups, the paired t-test rejected the null hypothesis H_0 that there was no difference between the "exposed group" of spray painters and the "never exposed" control group, at the 5% level of significance, with reference to the cross-shift change in FEV_1. This was also the case when examining the two groups regarding incidence of symptoms such as eye irritation and dermatitis.

Objective 2:

The measurement of IgE levels, PC_{20}, Rast (HDI) and peak flow measurement were found to be unsuitable markers for predicting potential cases of HDI induced asthma.

Objective 3:

A proportionately large number of spray painters showed significant declines in baseline measurements of pre FEV_1 (viz > 90ml.) from the initial to the follow-up study. Non-smokers showed greater declines in FEV_1 over a work shift than did their smoking counterparts. These findings were contrary to those found in the related literature.

Objective 4:

The concentrations of HDI in the majority of the spray booths exceeded the prescribed legal standard of 0.07 mg/m^3 (STEL). Furthermore, spray booth efficiency was observed to be insignificant in removing the overspray from the subjects breathing zone due to the "bounce back" phenomenon. This highlighted the need for the low pressure high volume spray guns to replace the conventional high pressure atomising spray guns.

Objective 5:

This objective basically examined and collated all of the above findings in order to formulate certain recommendations and rectify existing inadequacies identified in the spray painting industry. These recommendations have been listed in 6.2 below.

6.2 CONTROL MEASURES

Occupational asthma has become an important disease that merits high priority and urgent action. Recent achievements have facilitated preventative actions and it must be remembered that prevention in the occupational setting, is a multi-diciplinary enterprise needing the commitment of the industrial hygienist, engineers, chemists, and allergologists in addition to health personnel. Since one of the foremost principals of occupational hygiene is prevention, the following measures are discussed with a view to eliminating or at the least reducing, the hazard as far as "reasonably practicable".

This is a minimum requirement under current South African legislation in terms of the Hazardous Chemical Substances Regulations, 1995 framed under the Occupational Health and Safety Act of 1993 (Act No 85 of 1993). Generally there are three distinct preventative measures of action against occupational asthma which may be conventionally grouped as primary, secondary and tertiary.

6.2.1 Primary prevention

In accordance with the basic principals of Industrial hygiene, the substitution of isocyanate-based paints for a less toxic water-based paints is another alternative in preventing isocyanate-induced asthma in exposed persons . A number of overseas paint manufacturers have been experimenting with water-based paints, which are considered to be more environmentally friendly, than the isocyanate/ solvent based paints.

The main advantages of water-based paints, apart from producing a high quality paint finish are :-

1) a considerable reduction in the amount of organic solvents used.
2) less toxic to the working and external environment.
3) they are neither combustible nor explosive and
4) they will be able to satisfy many future environmental regulations.

A major disadvantage is, that the water-based paints are difficult to apply under conditions of high humidity. This is particularly important as far as Kwa Zulu Natal is concerned, as the relative humidity can be particularly high, especially in summer months. More research is required in the development of water based paints.

Primary preventative action prevents occupational exposure of the subject by reducing for example the HDI exposure levels as low as practicable through the use of an efficient down draught booth, low pressure high volume spray guns and in addition, the wearing of an SABS approved respirator by the worker.

6.2.2 Secondary prevention

This aims to detect asthma as early as possible in the patient and then take appropriate and timely action to minimise duration and severity. Secondary prevention would include immunological and lung function testing of the patient. However in the case of HDI exposure and as shown by this study, lung function testing in comparison to immunological testing, appears to be the more suitable predictor of occupational asthma. The primary and secondary measures would therefore be implemented at the workplace.

6.2.3 Tertiary prevention

Tertiary prevention in occupational asthma, although sometimes carried out by physicians with specialist expertise in occupational medicine, is essentially the same effective management programme of any type of asthma.

6.3 RECOMMENDATIONS

In view of the above findings and in order to reduce exposure levels to as low as practicable, this study recommends the implementation of an occupational hygiene programme which will incorporate the following specific measures:-

1. The provision of an efficient down draught booth together with regular monitoring including measurement and recording of HDI concentrations, air flow and turbulence testing to be carried out within the booth.

2. The spray gun is to be of the " high volume low pressure" type in order to increase the transfer factor and decrease the amount of overspray (bounce back) returning into the operator's breathing zone.

3. The wearing of SABS approved positive pressure airline masks (high protection factor) when spray painters are applying paints containing HDI.

4. Pre- employment and routine medicals including spirometric lung function testing to be carried out together with the completion of a standardised health questionnaire. The medicals are to be conducted on an annual basis, unless symptoms arise in which case such medicals should be conducted more frequently.

5. The introduction at the Technical Colleges of a comprehensive training programme where apprenticed spray painters may be trained in the safe handling of HDI.

6. Enforcement of current legislation by Inspectors of Occupational Safety.

Finally, based on the findings of both studies, the Department of Labour has requested the author to submit Guidance Notes on the "Safe handling of Hexamethylene Diisocyanates ". These notes are primarily for the spray painting industry to assist employers and employees in complying with the legal provisions of the Hazardous Chemical Substances Regulations, 1995 framed under the Occupational Health and Safety Act, 1993. Copies of these Guidance Notes have already been distributed free of charge, to local industry. However it is recommended where possible, that all spray painting establishments throughout South Africa should be issued with a copy of these Guidance Notes (refer Appendix A).

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PERSONAL COMMUNICATIONS:

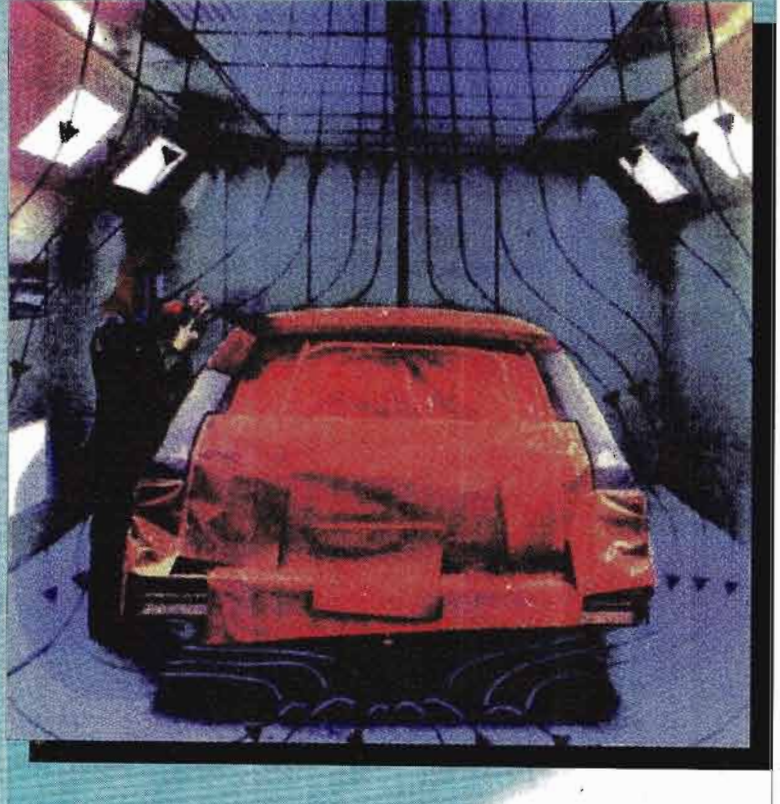
Mr R Ferrie, AECI, Fax No. 041424 -012 dated 7.09.89

Prof. Troskie, Head of Department of Statistics, University of Natal, Durban.

Miss.E Gouws, Medical Research Council, Umbilo Road, Durban.

Professor M Becklake, Respiratory Epidemiology Unit, Department of Epidemiology and Biostatistics Mc Gill University , Montreal , Quebec , Canada .

Case study
HEXAMETHYLENE DIISOCYANATE



A CASE STUDY AND GUIDANCE NOTES FOR SPRAY PAINTING ESTABLISHMENTS

EXAMPLE

Your workplace uses a brand-name two pack paint system containing hexamethylene diisocyanate (HDI) for spray painting vehicles. The spraying is carried out in a spraybooth next to a mixing/colour matching area, which is not ventilated. Workers wear half-face respirators while spraying, but not while mixing and matching. Clean-up is carried out in an open vessel, and solvent-soaked rags are disposed of in an open bin beside the mixing table.

A spraypainter spends up to 6 hours a day working in this area.

While any form of spray painting can pose a health hazard, your major concern here is a risk of exposure to isocyanate. You must assess this risk, and where necessary, take steps to control it, in line with Regulation 10 for Hazardous Chemical Substances 1995. (HCSR)

THE HAZARDOUS SUBSTANCES REGULATION APPLY BECAUSE:

- the Material Safety Data Sheet (MSDS) states that the hardener contains hexamethylene diisocyanate (HDI), a hazardous substance;

  (Your supplier should have given you an MSDS the first time the product was delivered).
- the MSDS also contains health hazard information;
- the labels for the product state that the hardener contains HDI;
- the labels include health and safety phrases;
- hexamethylene diisocyanate is listed in Table 1 (Page 1) for occupational exposure limits of the HCSR

THE REGULATION UNDER ISOCYANATES WILL ALSO APPLY EVEN IF:

- You haven't received an MSDS but the supplier has told you that the HDI is a hazardous substance.

  NOTE: If you don't get an MSDS and you think a product could be hazardous, it is your duty to ask.

TO COMPLY WITH THE REGULATIONS:

- make sure all employees who may be exposed to HDI have easy access to the MSDS;
- check that all containers are labelled with product name and health safety phrases;
- Do not accept delivery of unlabelled containers.
- if hardener is poured from bulk container into smaller containers that they may be stored for more than 1 day, label them;
- don't alter information on the MSDS.

You can change the order, or copy parts of it to use elsewhere, but the content must stay the same.

IF YOU HAVEN'T ALREADY DONE SO, START A HAZARDOUS SUBSTANCE REGISTER

Record that a substance containing HDI is at your workplace. Include a copy of the MSDS.

The register must be accessible to any of your employees who may be exposed to the paint.

1 THE STEPS YOU MUST TAKE ARE:

1. **Assessment**

   You need to assess the risk of exposure to HDI in your workplace.

   You won't be able to do this accurately without:

2. **Monitoring**

   which measures how much exposure to HDI your workers receive.

3. **Health Surveillance**

   which tells you if their health is possibly already affected by exposure to HDI.

When you have assessed the risk you can apply:

4. **Control**

   to make sure that exposure to HDI is stopped, or kept within safe limits.

2 ASSESSMENT (Regulation 5)

Risk assessment will enable you to find out:

- which workers are exposed to HDI;
- information about the health effects of HDI and the levels of exposure that cause them;
- whether monitoring or health surveillance is required;
- the kinds of work which may cause exposure to HDI;
- whether any of your workers are already showing effects from exposure;
- whether any exposure controls are already in place.

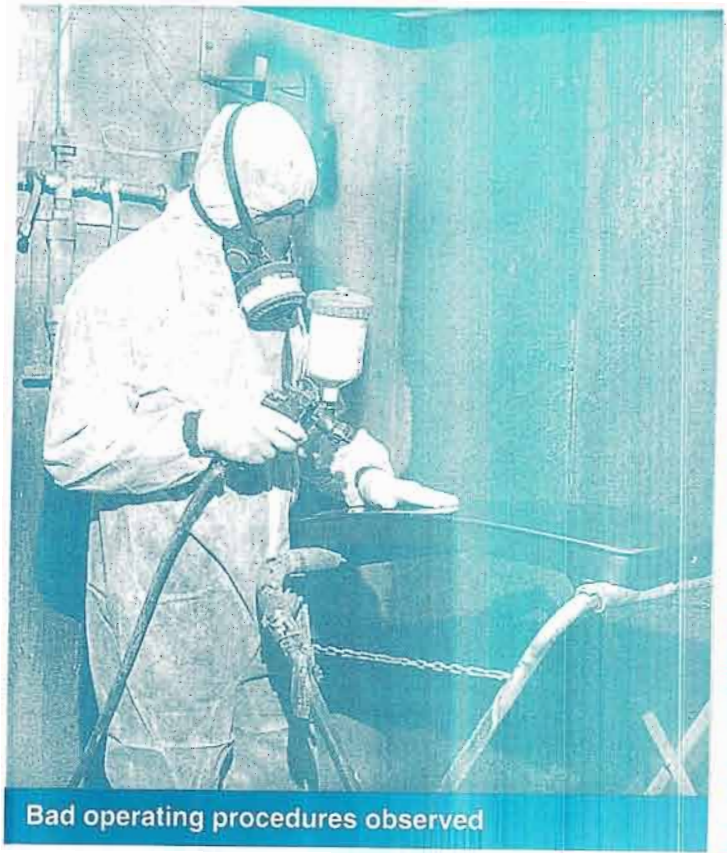
Make an assessment of the operating features of the workplace.

Look carefully for all the ways HDI could possibly enter the body. The routes of entry listed in the MSDS will help you.

You will find:

- the spraypainter mixing paint is exposed to vapours;
- skin exposure is possible if gloves are not always worn;
- workers are exposed to booth aerosol and vapours during spraying and colour matching, and painter uses inadequate respiratory protection;
- further skin exposure is possible to both HDI and solvents during clean-up operations.

These observations will enable you to decide that your employees are exposed to a hazardous substance.



Bad operating procedures observed

Carefully examine the controls that are in place.

Ask the following questions:

- Is there a skin hazard?

  The workers are not always protected from skin contact.

  The answer is "Yes".

- Is there a breathing hazard?

  Workers are sometimes exposed to vapours and paint aerosol.

  Workers don't use breathing protection as recommended by the MSDS.

  The mixing area is not ventilated.

  There have been reports of breathing symptoms.

  The answer is "Yes".

- Is air monitoring required?

  N.B.: The spraybooth is ventilated and half-face breathing masks are used. **However, for spray painting the MSDS and industry codes of practice require the highest level of respiratory protection - positive pressure air supplied full face respirators.**

APPENDIX: AIR MONITORING (Regulation 6)

Monitoring for isocyanates is referred to under Regulation 6. This provides some details of how that kind of monitoring can be carried out and by whom. Since monitoring is often critical in determining the most economical and effective way of controlling the risk, it requires reasonable attention to detail.

Who can do monitoring? {Regulation 6 (1) (c)}

To monitor for isocyanate vapour and isocyanate in aerosols, the employer will probably need to use outside expertise e.g. from an occupational hygienist employed by an "approved inspection authority".

Who does the employer need to monitor?

Monitoring of isocyanates needs to be conducted on those tasks which the risk assessment identifies as having significant risk. In this case study, workers undertaking paint mixing and colour matching required monitoring. Clean-up was also monitored, although by this stage there is usually little paint remaining.

What kinds of monitoring will be needed?

Monitoring for isocyanates may require more than one kind of measurement. Reference to Hazardous Chemical Substances Regulation 1995 reveals that isocyanate have two different exposure standards i.e.;

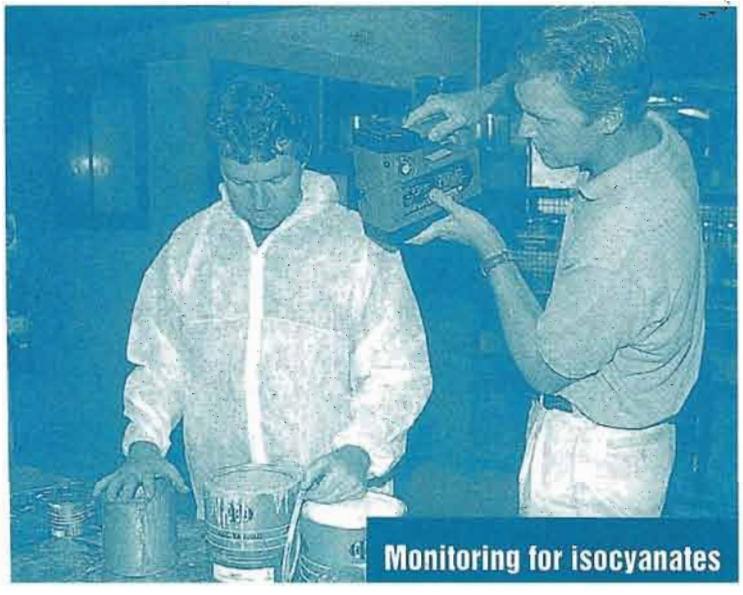
- Time Weighted Exposure Average Standard TWA 0.02 mg/m^3 (typically shift exposure)
- Short Term exposure Limit STEL 0.07 mg/m^3 (over periods of no greater than 15 minutes)

The different types of exposure standards are important in terms of ensuring that the national exposure standard for the relevant period is not exceeded. Their purpose is to ensure that any employee is exposed to neither unacceptable short term concentrations of the isocyanate nor to excessive concentrations over a longer period.

All air monitoring will be done in the breathing zone of the operator.

There is currently only one practical method for monitoring airborne isocyanates.

A direct reading monitor.



Monitoring for isocyanates

How to monitor for isocyanates

This type of meter is expensive. It is useful only for organisations with a rather large number of workplaces requiring monitoring, or for consultants doing these tests. Measurements of low isocyanate concentration levels takes place during a fixed four minute sampling period. Because it is a direct reading instrument, it can be used for Short Term exposures, and for TWA exposures when the meter has data logging or if you use appropiate multi-sampling strategies. (see illustration bottom left hand corner).

Acknowledgements

These guidance notes have been drawn up to assist both employers and employees in complying with the legal requirements on handling and application of hexamethylene diisocyanate (HDI) under the new Hazardous Chemical Substances Regulations 1995.

Whilst every effort has been made to ensure that this publication meets with the legal requirements, Polycon and its staff cannot be held liable due to any errors or omissions which may have occurred in the interpretation or in the publication of this document. Persons who require further clarification on procedures or legal requirements, should consult their local Inspector of Occupational Safety at the nearest Department of Labour office.

Polycon wishes to acknowledge the following persons for their comments and assistance in the compilation of these guidance notes.

B.W. Randolph, Senior Lecturer
Department of Environmental Health
Technikon Natal
PO Box 950
Durban 4000

TECHNIKON NATAL

Prof. UG Lalloo, Principal Physician
Head Respiratory Unit
University of Natal Medical School
719 Umbilo Rd. Durban 4001

Dr D Grantham, Principal Adviser
Division of Workplace Health and Safety
Queensland Government
Brisbane Australia

Ms Faiza Sali, Chief Inspector
Department of Labour
Pretoria.

SPONSORS,

In the mixing area, it is difficult for workers to wear breathing protection. They're possibly inhaling hazardous solvents from the paint and cleaning solutions. You need to know how much, **accurately**, so that you can take steps to prevent their exposure, or reduce it to an acceptable level. A general rule is that a risk is significant if the airborne concentration is one half the **Occupational Exposure Level. You won't know what the airborne concentration is until you measure it!**

The answer is "Yes". Air monitoring is necessary in the mixing and colour matching areas.

Unless you have experience in air monitoring, employ an expert to do it for you.

- Is health surveillance required?

Hexamethylene diisocyanate (HDI) is listed under "isocyanates".
The answer will be "Yes", if the risk to the worker's health from exposure is judged to be significant.

If you consider that the risk to your employees' health is significant, you must enter details into the Risk Assessment Record.

3 THE RISK ASSESSMENT RECORD

EXAMPLE your entry could look something like this:

Date of Assessment	20.3.95
Product Name	Hardener XYZ Paint System - contains hexamethylene diisocyanate.
Review Statement	XYZ Hardener contains HDI; MSDS is in the register and workplace; health information on respiratory and skin effects noted; label (and MSDS) note that substance has health effects (skin and respiratory) and that certain controls are to be used; employees are exposed (mixing, colour matching, mixing and cleaning; health surveillance required by Regulation; controls to be reviewed and upgraded.
Degree of Risk	Significant Risk
Control Measures	For skin protection, protective gloves needed; continue use of overalls and face shields; inhalation protection via air supply mandatory for spray painting; use booth extraction for painting and exhaust extraction for mixing, colour matching and cleaning.
Monitoring Required	Air monitoring required for spray painting, mixing, colour matching and clean-up; monitoring by consultant. Monitoring to be undertaken during first shift 7 April, 1995 and again after controls implemented.
Health Surveillance Required	Health surveillance required for all painters using this paint system.

4 MONITORING FOR ISOCYANATES (REGULATION 6)

HDI belongs to a group of chemicals known as isocyanates, so you will need to employ someone to monitor for isocyanates in your workplace, in the mixing, colour matching and clean-up areas in particular. The purpose of the monitoring will be to measure the airborne concentration so that you will know how to control it.

Refer to the Appendix for detailed methods.

How often should you monitor?

You will need to decide if you should monitor only once or at regular intervals.

There are three ways to approach monitoring:

(i) You can monitor once, and then decide on the control

(ii) You can apply control measures and then monitor at regular intervals to see if they are working properly.

(iii) You can use (i) and (ii) in sequence.

For isocyanate it's advisable to use option (iii).

Monitoring would need to be done again if there was a substantial change in your workplace, or your work practices, which can lead to an increase in exposure to HDI or other hazardous substances.

Monitoring results

The results of the monitoring could look like this:

Location/operation	Concentration of isocyanate mg/m^3	Does it exceed the exposure standard for the relevant
Mixing paint system	<0.003	no
Clean-up	<0.003	no
Colour matching (spraying outside the spraybooth) Tasks lasting approximately 5 minutes - no RPE	0.10	yes, exceeds STEL

RPE = Respiratory Protective Equipment

All samples were obtained in the breathing zone of the worker, and monitored by the instruments indicated in the Appendix.

You can use these results to help you decide about controls. To make this decision, you'll need to know something about the national exposure standards for isocyanates. (Page 1 of Regulations for Hazardous Chemical Substances 1995)

For isocyanates:

Time Weighted Average Exposure Standard = 0.02 mg/m^3

Short Term exposure Limit (STEL) = 0.07 mg/m^3

It's obvious that one of the short term exposures in your workplace exceeds the STEL, so some form of control is necessary. A copy of the results should go in the record, and all workers must be given acess to it, on request. The spray painter who was monitored must be given copy of his individual results.

5 CONTROL OF EXPOSURE

Once your risk assessment and air monitoring are complete, you can take steps to control the level of exposure to HDI and other substances.

(a) You can prevent the exposure.

(b) If this is not practicable, you can reduce the exposure as much as you can , **at least** to a level below the occupational exposure level (OEL-CL).

In your workplace, HDI can enter the body in two ways:

- through the skin;
- by inhalation;

In three separate work situations:

- mixing and clean-up
- colour matching;
- spray painting.

Deal with each situation separately.

Mixing and Clean-up

Air monitoring tells you that exposure to HDI by inhalation is not significant. However, other solvents that are used here can enter the body by inhalation and through the skin. Controls are needed to minimise exposure to these.

Colour Matching

Air monitoring shows you that short term exposures are more than the national standard. Control is needed, either by ventilation or PPE (personal protective equipment). Exposure must be reduced to 0.07 mg/m^3 or less {Option (b) above}. Skin protection must be maintained.

Spray Painting

Because of the extreme inhalation hazard identified in the MSDS and the Risk Assessment, inhalation of aerosols and vapour must be **prevented** {Option (**a**) above}.

Means of control

The Regulation allows the use of PPE only where it is not practicable to control exposure to a substance by other means.

A down draft spray booth operator wearing full face positive air pressure mask

Your options are limited:

- you can provide an air line respirator for spray painting inside an approved spray booth
- you can provide an extraction booth for colour matching;
- you can require workers to wear gloves for all operations.

How soon must controls be installed?

You must install controls as soon as practicable after the risk assessment. There is no fixed time: a spray painting booth may take some months to build. In the meantime you must provide an alternative means of control, such as air line protection.

The change from half-face filter respirators to positive pressure air supplied equipment should not take longer than a few weeks.

Gloves and eye protection should be provided within a week.

Maintenance of control

The Regulation requires you to maintain controls effectively.

The time between overhauls will vary with different items of equipment. Consult the operations' manual or consult the manufacturer or supplier for maintenance advice and schedules.

Remember: Correct maintenance of the air line respiratory protection for the spray painter in the booth is essential.

6 HEALTH SURVEILLANCE

Health surveillance is very important in that the improper use and handling of HDI may result in the spray painter contracting.

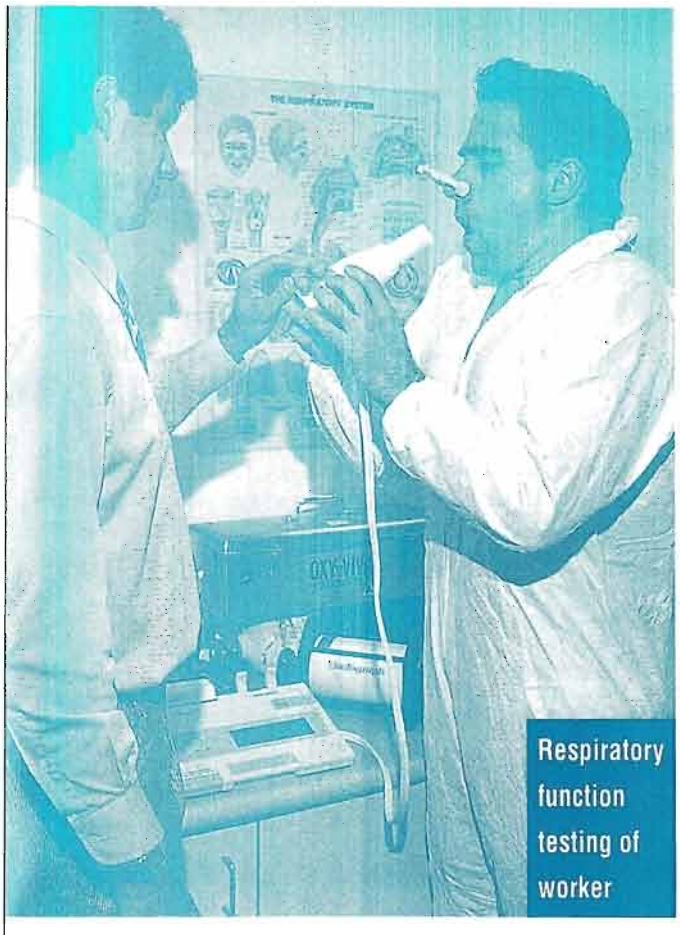
(i) Isocyanate - Induced Asthma
(Schedule 2 Compensatable Disease)
(ii) Sensitisation to HDI
(iii) Chemical Bronchitis
(iv) Reduced Lung Function

Health surveillance is to protect both the short term and long term health of your employees. It will reflect how effective control measures have been.

Health surveillance is mandatory for (HDI) here because it is a member of the isocyanate class of hazardous substances listed in Table 1 and because risk was found to be significant.

When your employees are to undergo health surveillance you must consult them on the choice of a doctor, who will:

- conduct a physical examination of the respiratory system and skin;
- carry out respiratory function tests;
- take a respiratory questionnaire.



Respiratory function testing of worker

You must then:

- pay for the doctor
- obtain the doctor's health surveillance report and keep it as a record;
- make sure the workers whose health has been under surveillance get a copy of the report.

The health surveillance report will advise you on the need for action regarding exposure to isocyanate. It reports on whether the medical tests were satisfactory or otherwise, and outlines any further action needed, such as repeat testing or removal from exposure.

Note: The doctor will make medical records about individual workers. **These records will include any symptoms of asthma, dermatitis or other skin conditions, and any evidence of sensitivity to isocyanate exposure. These records are confidential and are not part of the Health Surveillance Report. You will not be able to obtain details of any employee's medical record without that person's written consent.**

7 KEEPING RECORDS Regulation 9

Because there is a significant risk from exposure to isocyanate, you must keep the following records for 30 years:

- the assessment of the various spray painting operations;
- the result of the assessment i.e. what controls you introduced;
- the air monitoring results.
- health surveillance reports regarding the spray painters.
- any review assessments.

8 INDUCTION AND TRAINING

As an employer, you are required to provide induction and training to all workers about the health hazards of the substances to which they may be exposed.

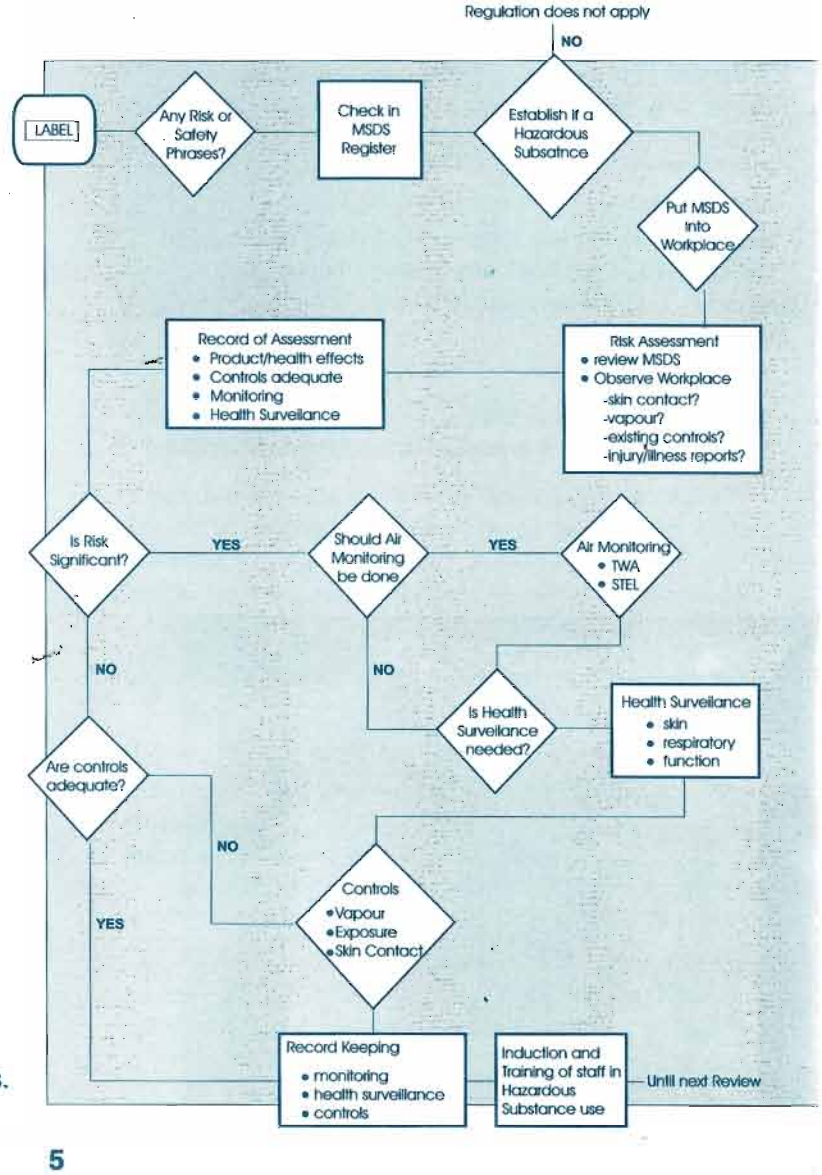
In the case of high risk substances such as isocyanate, this should include:

- health effects and symptoms;
- the need for health surveillance.
- respiratory protection training;
- skin protection requirements.

Training should also be provided in the use of associated solvents.

Keep record of all induction and training given.

Flow chart for this Risk Assessment and Control



APPENDIX B

THE RESPIRATORY QUESTIONNAIRE/LUNG FUNCTION

ANSWER COLUMN

Record number | | | | | | | | |

A. IDENTIFICATION DATA

1. Surname .....

   English ..... Ethnic .....
   First Name First Name

2. Address: .....

   .....

   .....Code: .....

3. Work number: ..... Height: .....

4. Year of birth: ..... Weight: .....

5. Sex:

Male	1
Female	2

6. Ethnic Group:

Black	1
Coloured	2
White	3
Asian	4

7. Date: .....

8. Factory: .....

9. Shift (Put in/show all shifts in the company):

1.	1
2.	2
3.	3
Other	4

B. SMOKING

1. Do you smoke?

YES	1
NO	2

If 'YES' go to question 3. If 'NO' go to question 2.

2. (i) Have you ever smoked?

YES	1
NO	2

If 'YES' go to question (ii).
If 'NO' go to question 8.

(ii) How long ago did you stop smoking:

Less than 1 year	1
years (number)	

(iii) How long did you smoke for? .....years

(iv) Do you smoke:

Cigarettes	1
Pipe only	2
Cigarettes & pipe	3

(v) How many cigarettes did you smoke each day?

Less than 10	1
Between 10 - 20	2
Between 20 - 30	3
More than 30	4

(vi) Pipe smokers: How much pipe tobacco did you smoke in a week? .....

(vii) Did you inhale?

YES	1
NO	2

3. For how many years have you smoked? .....years

4. Do you smoke:

Cigarettes	1
Pipe only	2
Cigarettes & pipe	3

5. How many cigarettes do you smoke each day?

Less than 10	1
Between 10 - 20	2
Between 20 - 30	3
More than 30	4

6. Pipe smokers: How much pipe tobacco did you smoke in a week? .....

7. Do you inhale?

YES	1
NO	2

8. What do you usually use to cook your food with at home?

Electrical stove	1
Gas stove	2
Paraffin stove	3
Wood stove	4
Other	5

C. I AM NOW GOING TO ASK YOU SOME QUESTIONS MAINLY ABOUT YOUR CHEST.

COUGH

1. Do you usually cough when you wake up in the morning? (excluding clearing throat)

YES	1
NO	2

2. Do you usually cough a lot during the day or night?

YES	1
NO	2

If the answer to any of the above is YES ask the next question.

3. Do you cough like this on most days for as much as three months a year?

YES	1
NO	2

PHLEGM

1. Do you usually bring up phlegm from your chest when you get out of bed in the morning?

YES	1
NO	2

2. Do you bring up phlegm on most days for as much as three months a year?

YES	1
NO	2

If the answer is 'YES', ask the next question.

3. For how many years have you been coughing up this amount of phlegm?

Less than 1 year	1
More thaan 1 year but less than 3	2
More than 3 years	3

D. BREATHLESSNESS

1. Do you suffer from any shortness of breath?

YES	1
NO	2

2. Do you suffer more from shortness of breath than other people?

YES	1
NO	2

3. Which of these activities makes you feel short of breath?

Running	1
Heavy work	2
Walking up a hill or up stairs	3
Walking on flat ground	4

TIGHTNESS

1. Does your chest ever feel tight or your breathing become difficult?

YES	1
NO	2

2. Is your chest tight or your breathing difficult on any particular day of the week?

YES	1
NO	2

3. If 'YES' then ask which day/s of the week this usually is: _____

Monday	2
Tuesday	4
Wednesday	8
Thursday	16
Friday	32
Saturday	64
Sunday	128

4. Is this tightness worse:

Before work	1
During work	2
After work	3

WHEEZING

1. Does your chest ever sound wheezy or whistling?

YES	1
NO	2

2. Do you suffer from attacks of shortness of breath with wheezing?

YES	1
NO	2

If 'NO', then go to Section F

3. How many years ago did these attacks start? ..... years

4. Do you still get these attacks?

YES	1
NO	2

5. Did you ever have these attacks before working with spray paints?

YES	1
NO	2

6. Are these attacks worse at any particular time of day?

YES	1
NO	2

If 'YES', are the attacks worse -

Before work	1
During work	2
After work	3

7. Are these attacks worse on any particular day of the week?

YES	1
NO	2

If 'YES', mark the days:

Monday	1
Tuesday	2
Wednesday	4
Thursday	8
Friday	16
Saturday	32
Sunday	64

8. Are these attacks worse during any particular season?

YES	1
NO	2

If 'YES', mark the season/s:

Spring	1
Summer	2
Autumn	4
Winter	8

9. When you are on holiday, do these attacks occur -

as often as at work	1
less than at work	2
more than at work	3

E. THE FINAL QUESTION ARE ABOUT PAST ILLNESSES

1. How many days sick leave have you had in the last 12 months?

..... days

2. How many of these were for chest illnesses? ..... days

3. Have you ever been treated for:

	Yes	No	Unsure
Tuberculosis	1	2	3
Other chest problems	1	2	3

4. In the last two years, have you ever been treated in hospital for any chest complaints?

YES	1
NO	2

(TB, pneumonia, stabbed chest, chest operations, asthma, bronchitis).

F. GENERAL

1. Do you suffer from any skin irritation?

YES	1
NO	2

2. If 'YES', give dtails (eg. dermatitis on hands, etc)

.....

3. Do you suffer from eye irritation?

YES	1
NO	2

G. OCCUPATION

(Record on dotted lines the number of years during which the subject has worked in any of these industries)

Have you ever worked in a dusty job? .....

In a coal mine? .....

In any other mine? .....

In a quarry? .....

In a foundry? .....

In a pottery? .....

In a cotton, flax, or hemp mill? .....

With asbestos? .....

In any other dusty job? .....

If 'YES' specify: .....

Have you ever been exposed regularly to an irritating gas or to chemical fumes? .....

If 'YES', give details of nature and duration:

.....

.....

Opinion and diagnosis: .....

.....

.....

APPENDIX C

ECCS regression equations for reference values.

Lung function Parameter	Smoking Status Smokers Non Smokers Ex-Smokers	Year	Sex	Regression Equation
FVC (l)	- do -	1977	M	5.52H - 0.028A - 3.82
FEV_1 (l)	- do -	1977	M	4.06H - 0.038A - 2.0
FEV_1/VC (%)	- do -	1977	M	-0.25A + 86.84
MMEF (l/s)	- do -	1977	M	2.32H - 0.06A + 1.76
PEF (l/min)	- do -	1977	M	5.48H - 0.041A - 1.58
MEF (l/s) 75% FVC	- do -	1977	M	3.58H - 0.041A + 2.8
MEF (l/s) 50% FVC	- do -	1977	M	2.8H - 0.058A + 1.54
MEF (l/s) 25% FVC	- do -	1977	M	1.22H - 0.041A + 1.03

(Quanger, PH (ed), 1983)

M = Males
H = Standing Height (metres)
A = Age (years)

APPENDIX D

Written Patient Consent Form
B.H.R. Test

1. Introduction:

In 1988 and during early 1993 you participated in a study to evaluate the health effects of paint spray containing a substance called isocyanate. This involved lung function testing at your workplace.

As a follow up to the above study we would like to carry out a further test known as a B.H.R. or bronchial-hyper-responseness test to see if you are showing signs of being or becoming asthmatic.

However, before agreeing to take this test you will be given a full explanation of what is involved. If you are worried or do not understand anything please do not feel embarrassed to ask questions. Approximately 20 spray painters will be taking part in this test.

2. What tests are involved:

(a) The study involves inhaling in stages solutions of histamine in increasing concentrations. Histamine is a substance/chemical that can cause narrowing of the tubes in your lung. At each stage your lung function will be carefully monitored. Should the lung function levels fall below a certain predetermined level the test will be stopped.

Upon completion you will be given "fenoterol" (medication that causes opening of the airways) to inhale and then be discharged only after a repeat lung function test indicates a return to normal.

What Side Effects Might Be Experienced:

The possible side effects include tightness of chest, cough and headache which occur temporarily with inhaled high concentrations of histamine. This will be relieved after inhalation with a bronchialdilator.

Please remember our first concern in this test is your well being.

(b) As a further confirmatory test the RAST or Radioallergosorbent test will be conducted. In this instance a 5 ml sample of venous blood is required from

your forearm in order to submit it for analysis at the laboratory.

This test will determine if your blood reacts with the chemical - hexamethylene diisocynate found in the spray paint.

The blood sample will be taken by a registered medical practitioner.

3. Thank you

We would like to thank you for your interest even if you decide not to take part. There is no pressure on you to participate in the study and having agreed to participate you are free to withdraw at any stage for any reason.

If you do decide to take part ALL information relating to the study will be entirely confidential and you will not be identifiable in any respects of this study.

4. For the duration of the study, you will be under the care of Dr E. Irusen.

If you have any problems, or any questions during the study, please do not hesitate to contact him on 2504238 (University of Natal Medical School).

Dr E. Irusen/Mr B. Randolph has provided me with a copy of this consent form and has fully explained to me the nature and purpose of the study.

Dr E. Irusen/Mr B. Randolph has given me the opportunity to ask any questions concerning the study. It has been explained to me that I will be free to withdraw from the study at any time, without incurring displeasure and without any disadvantage.

I consent to participate in this study.

Patient's Signature ..... Date .....

Investigator's Signature ..... Date .....

Investigator's Name ...B. W. RANDOLPH.....
(Please print)

BHR REPORTING

(1) Baseline FEV1 : FVC - best of 3 attempts
<5% variability

(2) Phosphate buffered saline neb. x 2 min
- FEV1 @ 30 & 90 sec

Calculate 20% fall from lowest post saline

FEV1 - target to aim for.

(3) Nebulize with increasing concentrations of histamine recording FEV1 as indicated ie, if FEV1 @ 90sec < FEV1 @ 30 -repeat @ 180 sec every 2 min thereafter.

Stop if FEV1 drops by 20 % or less than 1 L

Time in seconds

Histamine	30	90	180	300	420
Baseline					
Saline					
0.015mg/ml					
0.03					
0.06					
0.125					
0.25					
0.50					
1					
2					
4					
8					
16					
32					

$$\frac{\text{Lowest Post Saline FEV1 - Lowest Post Histamine FEV1}}{\text{Lowest Post Saline FEV1}} \times 100$$

= % fall in FEV1

NAME OF FIRM: ..... REF.NO: .....

ADDRESS OF FIRM: .....

..... DATE: .....

EMPLOYEE'S NAME AND ADDRESS: .....

.....

..... TELEPHONE NO: .....

MANAGER'S NAME: ..... TELEPHONE NO: .....

PERSONAL DETAILS

Height: .....cm

Age: .....years

TYPE OF TEST/EVALUATION COMPLETED

(a) Lung function PRE |__| POST |__|

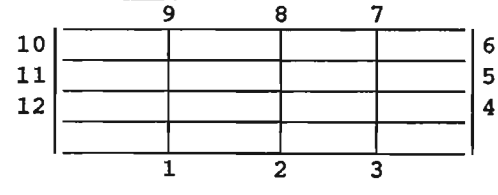
(b) Isocy. evaluation |__| Sample no. .....

(c) Flowrate = 1L/min Time = mins

(d) Total volume = litres

(e) Questionnaires: Lung function
Employee's quest.

SPRAY BOOTH



1 = 7 =
2 = 8 =
3 = 9 =
4 = 10 =
5 = 11 =
6 = 12 =

(a) Average movement = m/s (12 readings)
(b) Temperature = degrees Celcius
(c) Relative humidity= %

(d) Type: Vert D |__| Vert S |__| Horizontal |__| Other |__|

CALIBRATION

1 litre/minute
Battery charged

CALIBRATION

Before A) =
Before B) = Average A,B,C =
Before C) =

After A) =
After B) = Average A,B,C =
After C) =

Hot wire: Scale zeroed

RESPIRATORY PROTECTIVE EQUIPMENT

Type of mask: Condition: Good |__| Fair |__| Bad |__|

RESULTS (Comments) APPROVED YES |__| NO |__|

.....

TURBULENCE

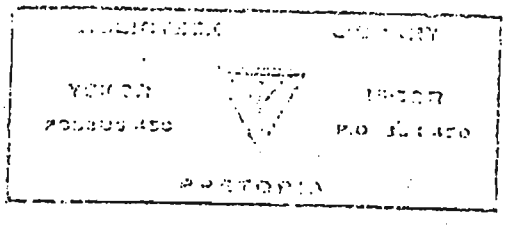
.....

NIOSH MANUAL OF ANALYTICAL METHODS

THIRD EDITION

Peter M. Eller, Ph.D., CIH
Editor

VOLUME 2



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control
National Institute for Occupational Safety and Health
Division of Physical Sciences and Engineering
Cincinnati, Ohio

February, 1984

FORMULA: RNCO

M.W.: varies

ISOCYANATE GROUP

METHOD: 5505
ISSUED: 2/15/84

OSHA: C 20 ppb (MDI and TDI)
NIOSH: 5 ppb/10 hr; 20 ppb/10 min (diisocyanates) [1]
ACGIH: C 20 ppb (MDI); 5 ppm (TDI)

PROPERTIES: depend on R- to which isocyanate group is attached; R- may be aromatic, aliphatic, monomeric or polymeric

SYNONYMS: various [1], including 4,4'-methylenediphenyl isocyanate (MDI; CAS #101-68-8); 2,4-toluene diisocyanate (TDI; CAS #584-84-9).

SAMPLING

SAMPLER: IMPINGER (solution of 1-(2-methoxyphenyl)-piperazine in toluene)

FLOW RATE: 1 L/min

VOL-MIN: 350 L
-MAX: 600 L

SHIPMENT: in vials; flammable liquid

SAMPLE STABILITY: $\geq$ 2 weeks

BLANKS: 2 to 10 field blanks per set + 1 initial reagent blank

ACCURACY

RANGE STUDIED: not studied

BIAS: not determined

OVERALL PRECISION (s_r): not evaluated

MEASUREMENT

!TECHNIQUE: HPLC, UV DETECTION
!
!ANALYTE: 1-(2-methoxyphenyl)piperazine
!
!PREPARATION: acetylate analyte; evaporate toluene; dissolve residue in methanol
!
!INJECTION VOLUME: 10 µL
!
!MOBILE PHASE: 50/50 acetonitrile/0.015 M sodium acetate; pH 6; 1.5 mL/min
!
!COLUMN: octylsilylated silica (C_8), 10-µm particle size, 25 cm x 4.2 mm
!
!DETECTOR WAVELENGTH: 254 nm
!
!CALIBRATION: solutions of 1-(2-methoxyphenyl)-piperazine in methanol
!
!RANGE: 0.24 to 3.5 µmol NCO group per sample
!
!ESTIMATED LOD: 0.2 µmol NCO group per sample
!
!PRECISION (s_r): 0.048 [2]

APPLICABILITY: This method is used to determine the total concentration of the isocyanate group, regardless of the molecule to which the isocyanate group is attached. Monomeric isocyanates can be individually determined with this sampling reagent [3]. Concentrations of ureas from monomeric isocyanates and 1-(2-methoxyphenyl)piperazine can be determined simultaneously. NIOSH has used this method to sample for isocyanate groups and monomeric 2,4-toluene diisocyanate in a urethane foam manufacturing plant.

INTERFERENCES: Phosgene, acid halides and possibly some esters will react with 1-(2-methoxyphenyl)piperazine, consume reagent, and cause a positive bias.

OTHER METHODS: P&CAM 141, 142, 326, and 347 [4,5,6] are for monomeric species only and which are subject to amine interference or use an unstable derivatizing agent. Recent reviews have been published [7,8].

REAGENTS:

1. Sampling medium:* 1-(2-methoxyphenyl)piperazine in toluene (see APPENDIX).
   NOTE: Reserve 10 mL of this solution for analysis (step 15).
2. Acetic anhydride.
3. Methanol.*
4. Acetonitrile.
5. Deionized water.
6. Pentane.
7. Sodium acetate, anhydrous.
8. Acetic acid, glacial.
9. Nitrogen.
10. Toluene.*
11. Calibration stock stolution, 1 µg/µL. Dissolve 1-(2-methoxyphenyl)piperazine in methanol.
12. Mobile phase. Dissolve 1.2 g sodium acetate in 1 L deionized water. Add 1 L acetonitrile. Add glacial acetic acid as needed to bring the pH to 6.0.

*See Special Precautions.

EQUIPMENT:

1. Sampler: midget impinger, 25-mL.
2. Personal sampling pump, 1 L/min, with flexible connecting tubing.
3. Glass-marking pen.
4. Liquid chromatograph with a UV detector, recorder, integrator and column (page 5505-1).
5. Ultrasonic waterbath.
6. Vials, 20-mL glass, with polypropylene-lined screw caps.
7. Vials, 4-mL glass, with screw caps.
8. Pasteur pipets, 7-cm glass, disposable.
9. Volumetric flasks, 10-mL.
10. Syringes, sizes appropriate for preparing standard solutions.
11. Pipets, 2- and 15-mL glass, delivery, with pipet bulb.
12. Hotplate.
13. Beakers, 250-mL.
14. Evaporator, Mini-Vap, 6 port, or equivalent.
15. Flask, filtration, 500-mL.
16. Funnel, Buchner, fritted glass, medium porosity, 100-mL.
17. Vacuum pump.
18. Flask, 50-mL, round bottom.
19. T-adapter, with stopcock.
20. pH meter.

SPECIAL PRECAUTIONS: Sample and standard preparation should be done in hood to avoid exposure to toluene and methanol vapors.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Transfer 15.0 mL sampling medium to an impinger. Mark the solution level on the impinger with a glass-marking pen.
3. Connect the assembled impinger to a sampling pump. If it is necessary to add solvent during sampling for proper impinger operation, add only toluene. Do not add more sampling medium.
   NOTE: If an area sample is being taken, the impinger may be packed in ice during sampling to retard toluene losses.
4. Sample 350 to 600 L of air at a sampling rate of 1 L/min.
5. Bring sample solution level back to the pre-sampling mark (15.0 mL) by adding toluene.
6. Transfer the sample solution to a 20-mL vial for shipment. Do not rinse the impinger.

SAMPLE PREPARATION:

7. Transfer a 2-mL aliquot to a 4-mL vial for evaporating.
8. Add 10 µL acetic anhydride. acetylate the 1-(2-methoxyphenyl)piperazine.
9. Evaporate to ne from sample under

10. Add 200 µL methanol after sample has reached complete dryness.
11. Agitate sample in an ultrasonic bath for 15 min to dissolve residue.

CALIBRATION AND QUALITY CONTROL:

12. Prepare working standards (25 to 450 µg/mL) by adding appropriate aliquots of calibration stock solution to 2 to 3 mL methanol in a 10-mL volumetric flask. Add 10 µL acetic anhydride. Mix and dilute to the mark with methanol.
13. Analyze working standards together with samples and blanks (steps 16 through 18). Prepare a calibration graph of area vs. amount (µg) of 1-(2-methoxyphenyl)piperazine per 15 mL original solution.
    NOTE: The amount present in an original 15-mL sample is 1.5 times the concentration of the analyzed solution: (0.2 mL/aliquot) • (7.5 aliquots/sample).
14. Prepare control samples by adding a known amount of a monomeric isocyanate to 15.0 mL sampling medium and performing steps 7-11 and 16-19.
15. Analyze three 2-mL aliquots of the sampling medium from the same batch used for sampling (Reagent 1.).
    NOTE: These are not the same as field blanks.

MEASUREMENT:

16. Set up the HPLC system according to manufacturer's recommendations and to the conditions given on page 5505-1.
17. Inject a 10-µL concentrated sample aliquot.
18. Measure peak area.

CALCULATIONS:

19. Read amount, M_S (µg), of 1-(2-methoxyphenyl)piperazine per 15 mL sample from calibration graph for each sample.
20. Calculate the initial amount of reagent, µg, present before sampling, M_I, by averaging the amount determined for the three samples prepared from sampling medium not taken into the field (step 15).
21. Calculate the concentration of isocyanate groups, C (µmol/m³), in the air volume sampled, V (L):

$$C = \frac{(M_I - M_S) \cdot 10^3}{(192.26) \cdot (V)}, \ \mu mol/m^3.$$

where 192.26 is the molecular weight of 1-(2-methoxyphenol)piperazine.

EVALUATION OF METHOD:

Lab-tested with 2,4-toluene diisocyanate spiked samplers with independent quantitation of isocyanate groups from measurement of isocyanate urea [2]. The average recovery for the sample preparation procedure of 1-(2-methoxyphenyl)piperazine, as the acetyl derivative, was determined to be 96% over a range of 8.2 to 813 µg per 15-mL sample. Toluene solutions of 1-(2-methyoxyphenyl)piperazine (15.7 µg per 15-mL sample) were stored at room temperature for two weeks with no loss of 1-(2-methoxyphenyl)piperazine. Precision was determined from the analysis of 21 samples which were prepared by adding known quantities of monomeric 2,4-toluene diisocyanate (0.24 to 3.2 µmole) to 1-(2-methoxyphenyl)piperazine in toluene (43 µg/mL).

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[3] Warwick, C. J., D. J. Bagon and C. V. Purnell, Analyst, 106, 676-685 (1981).
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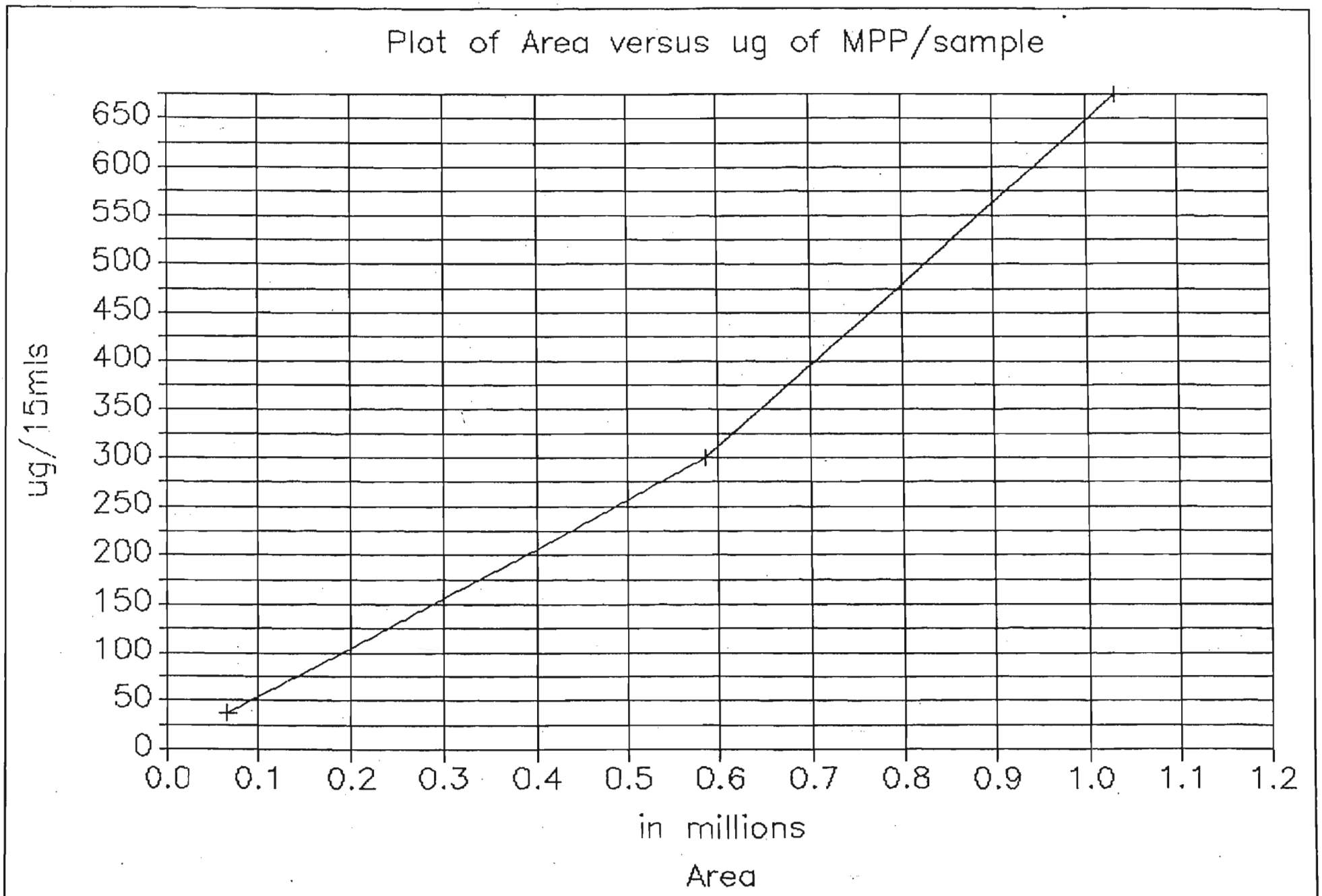
[7] Melcher, R. G., Anal. Chem. 55, 40R-56R (1983).
[8] Purnell, C. J. and R. F. Walker, Anal. Proc. 18, 472-478 (1981).

APPENDIX:

PURIFICATION OF 1-(2-METHOXYPHENYL)PIPERAZINE AND PREPARATION OF SAMPLING MEDIUM:
Place 25 g 1-(2-methoxyphenyl)piperazine (yellowish white solid) in a 250-mL beaker. Add approximately 125 mL pentane. Bring to a boil on a hotplate and allow to boil until all but a small amount of yellow oil is in solution. The 1-(2-methoyphenyl)piperazine will melt as it is warmed in the pentane. Decant the solution into a clean beaker, cover with a watchglass and then cool in the freezer for 2 to 3 hrs. White fluffy crystals will form. Filter with a Buchner funnel. Transfer the crystals to a 50-mL round bottom flask and dry briefly under vacuum to remove final traces of pentane. Store the hygroscopic crystals in an air-tight container in a refrigerator. The melting range of the crystals is 26-29 °C.

Prepare the sampling medium using the purified 1-(2-methoxyphenyl)piperazine. Dissolve this reagent in toluene at a concentration of 43 µg/mL.

METHOD WRITTEN BY: Martha Seymour and A. W. Teass, Ph.D., NIOSH/DPSE.


Plot of Area versus ug of MPP/sample
ug/15mls
650
600
550
500
450
400
350
300
250
200
150
100
50
0
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
1.2
in millions
Area

umole/samp as MPP	ıle/m^3	As Des N75 mg/m^3	As PolyIsoCyanates mg/m^3	As Free HDI mg/m^3	As TDI mgm/m^3
1.28	75.57	19.27	14.45	0.10	
2.05	58.70	14.97	11.23	0.07	
1.56	82.13	20.94	15.71	0.10	
0.94	46.81	11.94	8.95	0.06	
0.83	55.48	14.15	10.61	0.07	
2.96	197.65	50.40	37.80	0.25	
1.33	88.42	22.55	16.91	0.11	
1.87	312.08	79.58	59.68	0.40	
1.98	329.42	84.00	63.00	0.42	
Oregon Range	7-12.2	Average	3.78		
1.56	74.30	18.95	14.21	0.09	
1.40	66.87	17.05	12.79	0.09	
0.94	34.68	8.84	6.63	0.04	
0.83	33.29	8.49	6.37	0.04	

27-Mar-93				
450std	1,389,440	13,967		
200 Std	770,241	9,155		
25 Std	117,342	1,590		
Control #18	1,383,683	14,303.00		
MPP10393	1,013,696	1,031,965		
REPEAT	1,062,158			
BRSTD	971,194		AirVol l	ug/sample
REPEAT	1,080,813			
BR1 15/2/93#008	563,920	468,045	17.00	247.00
BR2 19/2/93#1616MORGAN	352,165	679,800	35.00	395.00
BR3 26/2/93#032	457,170	574,795	19.00	300.00
BR4 4/3/93 #017C LARCHER	686,199	345,766	20.00	180.00
BR5 6/3/93 #35 C Downes	719,741	312,224	15.00	160.00
BR6 16/3/93 ASHOOK#31	142,172	889,793	15.00	570.00
BR7 Std	976,885	55,080		
BR8#38 P Kinlock	553,465	478,500	15.00	255.00
Br#18 2/4/93	388,451	643,514	6.00	360.00
	359,897	672,068	6.00	380.00
Standard	912,354	1,096,381		
06-May-93	1,280,408			
Randolph004/1 P Naidu	342,012	570,342	21.00	300.00
Randolph4/2	401,159	511,195	21.00	270.00
Randolph #29 S Peterson	566,949	345,405	27.00	180.00
25/05/93				
BRSTD 2/6/93	986,303	934,389		
BR Std	898,312			
BR std	918,551			
BR006 S Dorkin	627,687	306,702	25.00	160.00

APPENDIX H

EMPLOYEE'S QUESTIONNAIRE - CONFIDENTIAL

ANSWER COLUMN

Date: .....

Record number | | | | | | | | |

PERSONAL PARTICULARS:

1. Name of company: .....

2. Address of premises: .....

   .....

3. (a) Name of employee: .....

Population Group	
Coloured	1
White	2
Black	3
Indian	4

   (b) Age of employee: .....

   (c) Height of employee: .....

   (d) Weight of employee: .....

4. Length of service with present employer as spray painter:

Years		

5. Length of previous service as spray painter:

Years		

6. Total number of years in trade (4) + (5):

Years		

7. (a) Were you previously employed in any work where you were exposed to possible dust, fumes, gases, vapours, eg. mines, foundry, brick manufacturer?

YES	1
NO	2

   (b) If 'YES' to (a) above, how many years?

0 - 5	1
6 - 10	2
11 - 15	3
16 - 20	4

RESPIRATOR

8. Do you regard the use of a respirator when spray painting as a necessity?

YES	1
NO	2

9. What type of respirator, if any, do you regard as suitable for use with the twin pack paints?

No respirator	1
Dust mask	2
Cartridge mask	3
Air line mask	4
Self purifying mask	5

10. Has your employer provided you with a respirator?

YES	1
NO	2

11. If 'YES'. What type of respirator has he provided?

Dust mask	1
Cartridge mask	2
Air line mask	3
Self purifying mask	4

12. Does the abovementioned respirator provide you with eye protection?

YES	1
NO	2

13. (a) Are there any health risks involved with spray painting?

YES	1
NO	2

(b) To what degree in your opinion are you at risk in contracting a disease, for example, induced asthma, sensitisation, dermatitis, from spray painting?

No risk	1
Slight risk	2
Moderate risk	3
Severe risk	4

14. How regularly, if ever, do you use a respirator?

Never	1
Rarely	2
Sometimes	3
Usually	4
Always	5

15. If the answer to question 14 is NEVER/RARELY/SOMETIMES, what are your reasons?

15.1	I do not consider it a necessity to use a respirator	1
15.2	I have up to now, not experienced any detrimental effects, eg. coughing, wheezing, smarting of eyes, etc.	2
15.3	The detrimental effect of exposure to gases, vapours are long term and are therefore of no immediate danger to my health	3
15.4	The use of a respirator is time consuming	4
15.5	It hinders/obstructs me from carrying out my work	5
15.6	It is uncomfortable to wear	6
	Other (specify):	

16. If the answer to either 15.1 or 15.6 above is 'YES', then is it because -

It does not fit properly?	
It is particularly uncomfortable due to high temperature, humidity, perspiration	
It interferes with my breathing rhythm	
It gives me a claustrophobic effect	
It interferes with my means of communication	
Other reasons (give details)	

17. **DUTIES OF EMPLOYER** (General Administrative Regulation 5)

17.1	Has your employer made available to you a hazard data sheet on twin pack paints?	YES	1	
		NO	2	
17.2	Has your employer made you aware of the dangers of using isocyanate containing paints?	YES	1	
		NO	2	
17.3	Has your employer discussed the functions and uses of the different types of respirators?	YES	1	
		NO	2	
17.4	Has your employer arranged for any safety training while you were learning the trade or an apprentice spray painter?	YES	1	
		NO	2	
17.5	Does your employer/manager/foreman insist that you wear the respirator at all times?	YES	1	
		NO	2	
17.6	If the answer to 17.5 is 'NO', does your supervisor leave it up to you whether you wear a respirator or not?	YES	1	
		NO	2	
17.7	Has disciplinary action been taken against you for not wearing a respirator?	YES	1	
		NO	2	
17.8	Are you prepared to take the responsibility and health risk by not wearing a respirator?	YES	1	
		NO	2	

18. (a) Have you refused to wear a respirator despite your employer's insistence?

YES	1	
NO	2	

(b) If 'YES', can you give the <u>two most important</u> reasons for refusing an instruction:

(1) .....

.....

(2) .....

.....

19. **Health questions**

(1)	Do you suffer from dermatitis or other skin irritations?	YES	1	
		NO	2	
(2)	Do you experience a burning sensation in your eyes?	YES	1	
		NO	2	
(3)	When last did you have a severe cough or lung complaint?	.....		
(4)	When last did you go for a medical check-up?	.....		

Type

Aliphatic polyisocyanate

Form supplied

Approx. 75% in 1-methoxypropylacetate-2/xylene (1:1) as well as solvent-free as ®Desmodur N 100 in special cases.

Uses

As the curing component for DD materials to formulate coatings with good colour retention and outdoor resistance.

Characteristic data

NCO content*	approx. 16.5%
Equivalent weight	approx. 255
Colour value, DIN 6162*	< 3
Flash point, DIN 53213	approx. 38 °C
Density at 20 °C, DIN 53217	1.07 g/cm^3
Viscosity at 23 °C*	225 ± 75 mPa·s
Content of monomeric diisocyanate	see under "Safety"

* supply specification

Solubility

Desmodur N can be thinned with e.g. ethyl acetate, butyl acetate, ethyl glycol acetate, 1-methoxypropyl-acetate-2, toluene and xylene. Desmodur N is insoluble in aliphatic hydrocarbons.

As they react with Desmodur N, solvents that contain reactive groups (e.g. alcohols, amines) must not be used. Desmodur N is sensitive to moisture, and PUR grade solvents should be used (< 0.05% water).

However, the solids content of such solutions should not be lower than 35–40%, otherwise turbidity and precipitation may occur after a certain time, despite compliance with the above.

Compatibility

Desmodur N 75 can be mixed together with a variety of other Desmodur types, such as Desmodur N 3200, N 3390, Z 4370, HL, IL, L.

Generally good compatibility is ensured with a variety of polyesters, polyacrylate polyols and polyethers.

Combinations with the polyesters of the Desmophen 650–690 series, Desmophen RD 181, the acrylates of the Desmophen A series and the Desmophen 550 U polyether are particularly suitable.

Crosslinking

For stoichiometric (equivalent) crosslinking (NCO:OH = 1:1) the equivalent weights in g of the corresponding polyols or polyisocyanates are combined.

Examples:

		* OH equivalent weight
Desmophen 650 or 651	– 100%	approx. 212
Desmophen 670	– 100%	approx. 395
Desmophen 680	– 60%	approx. 850
Desmophen 690	– 100%	approx. 850
Desmophen A 160	– 60%	approx. 1060
Desmophen A 165	– 65%	approx. 1000
Desmophen A 260	– 60%	approx. 800
Desmophen A 265	– 65%	approx. 770
Desmophen A 365	– 60%	approx. 607
Desmophen A 450	– 50%	approx. 1700
		** NCO equivalent weight
Desmodur N 75		approx. 255

i. e. 255 g Desmodur N 75, form supplied, require 212 g Desmophen 650 or 651 – 100% for stoichiometric crosslinking.

$$\text{* OH equivalent weight} = \frac{17 \cdot 100}{\%\ \text{OH}}$$

$$\text{** NCO equivalent weight} = \frac{42 \cdot 100}{\%\ \text{NCO}}$$

Application

For weather-resistant and colour-retentive outdoor coatings with very good resistance to solvents, chemicals and abrasion:

Desmodur N/Desmophen 650 or 651.

For coatings which ensure good flexibility even at low temperature but require forced drying:

Desmodur N/Desmophen 670.

For two-pack automotive repair coatings:

Desmodur N/Desmophen A 260, A 265 or A 365.

For industrial coatings:

Desmodur N/Desmophen A 160 or A 165.

To accelerate drying it is advisable to add approx. 0.3% Desmorapid PP when using polyesters as co-reactants at room temperature. When carrying out drying at elevated temperatures, the addition of approx. 0.2% zinc octoate (with 8% Zn) is recommended. Approx. 0.2% Dabco LV 33 should be added in the case of Desmophen A 365. The additions indicated are calculated on solid resin.

Drying can also be accelerated by raising the temperature.

It should be noted that adding a catalyst also reduces the pot life of the formulation. By selecting the right addition, however, the pot life can be adjusted without difficulty to suit the application method chosen.

The pot life is not only influenced by the catalyst addition but also by the binder content, temperature and type of solvent. Solvent mixtures should have a proportion of aromatic hydrocarbons of not higher than 30%. A relatively long pot life is obtained with solvents such as esters, ketones and ether esters.

Effective levelling agents have been found to be CAB 551-001 (Eastman Kodak) in an addition of approx. 0.2%.

Approx. 0.1–0.2% ®Baysilone Paint Additive OL 31 should be added to improve the smoothness of the film surface.

An addition of Desmodur N can markedly improve the properties (e.g. mar and solvent resistance) of other binders such as nitrocellulose/alkyd combinations (usually formulated using nitrocellulose chips rather than cotton), PVA copolymers, and alkyd resins.

Storage

Desmodur N is sensitive to moisture and should therefore be kept in tightly sealed containers. Stability for 6 months is guaranteed when the product is stored in its sealed original container.

Safety

On account of its content of solvents and polyisocyanate the product requires special care in handling.

The safety data sheet should be observed. This contains information on labelling, transport and storage as well as on handling, product safety and ecology. If not already recerved, it is available on request.

Attention is also drawn to Section F1, which comprises data supplementary to that given in our product information. Any existing national regulations on the handling of PUR coating materials and solvents should be observed.

The product is flammable, and the containers should therefore be kept away from ignition sources. Precautions against electrostatic pick-up should be taken. The product must only be handled in explosion-proof rooms.

Skin and eye contact with the product as well as inhalation of the vapours should be avoided. We recommend the wearing of safety goggles and protective gloves.

During spray application the respiratory organs should be protected from spray mist, and it is therefore essential to wear a respirator.

Immediately after production, and after short-therm storage, Desmodur N 75 has a content of less than 0.5% monomeric hexamethylene diisocyanate (HDI). Upon prolonged storage at room temperature or within several days at an elevated temperature (e.g. +50°C) the content of monomeric HDI may rise to max. 0.9%. This involves only a slight risk of irritation through inhalation. Hypersensitivity reactions are possible in isolated cases.

Bayer

Order-No.: LS 44016 e · Edition: 1.4.1986 (Edition: 1.4.1975 invalid) E 387 - 846 / 844 607

Printed in Germany

APPENDIX J

STRICTLY CONFIDENTIAL

UNIVERSITY OF NATAL

DEPARTMENT OF COMMUNITY HEALTH

SPIROMETRIC LUNG FUNCTION TEST AND A RESPIRATORY

HEALTH AND SAFETY QUESTIONNAIRES

INTRODUCTION TO THE STUDY:

My name is BERNARD WINSTON RANDOLPH and early in 1989, whilst completing a Master's Diploma in Public Health , I introduced myself as an Inspector of Occupational Health and Safety employed with the Department of Labour , Durban..
With your consent I conducted a lung function test which also required the completion of both a respiratory health and safety questionnaires.

Presently I am conducting a follow -up study to re - evaluate your present working environment and like the initial study , I will again require your consent in order to complete the study.

As before there are two questionnaires which I will ask you to complete and should you have any difficulty in answering any of the questions, I will assist you .

You are reminded that all information which you supply will remain " STRICTLY CONFIDENTIAL" .

Once again your co-operation is kindly requested and you are reminded that should you not wish to participate or to withdraw from the study at any time, you may do so, without any disadvantage or obligation.
Thanking you for your kind assistance.

B. W. RANDOLPH.

APPENDIX K

UNIVERSITY OF NATAL

FACULTY OF MEDICINE

INTER-OFFICE MEMORANDUM

TO: Mr B Randolph
Department of Community Health

FROM: Mrs S McDonald
PostGraduate Administration
Faculty of Medicine

22 December 1993

PROTOCOL: A FOLLOW-UP STUDY OF THE RESPIRATORY HEALTH STATUS OF AUTOMOTIVE SPRAY-PAINTERS EXPOSED TO PAINTS CONTAINING ISOCYANATES

The Post-graduate (Ethics) Committee has considered the abovementioned application and has found it ethically acceptable.

However, the Higher Degrees Committee have requested that "the rationale for the use of histamine challenge and the basis for the hypothesis be supplied in concise form".

S McDONALD (Mrs)
PostGraduate Administration

McD/ethics/accept