DERMAL AND OCULAR EXPOSURE DURING THE SPRAY APPLICATION OF SELECTED INDUSTRIAL CHEMICALS

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by

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DECLARATION

I declare that this thesis contains no material which has been accepted for the award of any degree or diploma in any university or other tertiary educational institution; and that to the best of my knowledge and belief it contains no material previously published or written by another person except where due reference in made in the text of the thesis.

The experimental work described herein was carried out from 2001 to 2004 in the Department of Public Health, University of Adelaide. Some of the results of this thesis have been presented at the 21st Annual Conference of the Australian Institute of Occupational Hygienists (December 2003).

Experiments and studies on volunteer workers described in this thesis were carried out with the approval of the appropriate ethics committees of the University of Adelaide and Flinders University.

I consent to this thesis being made available for photocopying and loan if accepted for the award of the degree of Doctor of Philosophy.

Su-Gil Lee

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ABSTRACT

Use of chemicals may entail exposure by the dermal or ocular route, and there is a shortage of data pertaining to those routes. Spray application of chemicals poses a special problem since workers may experience significant skin, ocular and inhalational exposure.

This study addresses exposure during spraying of malathion and fenthion insecticides for fruit fly control and hexamethylene di-isocyanate (HDI) - based paint in the automotive and furniture industries. The research aims to characterize exposures and symptoms, and assess the adequacy of personal protective equipment under field conditions.

Pest control workers participated in an exposure simulation and were subsequently monitored during a fruit fly outbreak. Exposure assessment entailed air sampling, dermal exposure and biological monitoring. Sampling of lacrimal fluid was also conducted. Painters using isocyanates were assessed by dermal, air and ocular monitoring.

Health and work practice questionnaires were used for both groups, along with observation of job tasks and the work environment. Glove permeation tests, under conditions of variable use, temperature and active ingredient concentration were also conducted.

Questionnaire data did not suggest an excess of symptoms among fruit fly control workers, compared with controls. However, isocyanate-exposed painters experienced more skin and respiratory symptoms.

Insecticides were commonly detected in glove samples, on the forehead, and on the forearm, shoulder and chest regions. In the case of isocyanate spray painting, apprentices appeared to have higher skin exposures, associated with poorer work practice.

In general, glove performance was found to be influenced by glove type, thickness, repeated use and temperature.

Ocular exposure was detectable in many cases, but appeared to be strongly dependent on whether full face respiratory protection was worn.

Although there was evidence for dermal and inhalational exposure for workers exposed to malathion and fenthion, biological monitoring data are consistent with generally low uptake under the circumstances investigated.

Inhalational exposures to HDI-based paint aerosols were potentially significant, and there was evidence of exposure by the dermal and ocular routes.

Permeation and thickness data show that glove performance may deteriorate with increased usage and temperature, and it is suggested that attention be paid to differential wear patterns associated with the task and worker handedness.

TABLE OF CONTENTS

CHAPTER 4. GENERAL DISCUSSION

APPENDICES

LIST OF FIGURES

LIST OF PLATES

LIST OF TABLES

LIST OF STUDY GROUPS

Group 1:

Comprised fruit fly control workers participating in an exposure simulation at a government field research station in 2001

Group 2:

Comprised fruit fly control workers carrying out baiting work during an outbreak in Adelaide, South Australia in 2003

Group 3:

Comprised spray painters using isocyanate-based paints in private crash repair workshops, apprentice training facilities, and in outdoor (i.e. out of booth) and mobile touch up spray painting situations

Group 4:

Comprised spray painters using isocyanate-based spray paints in a furniture manufacturing company

ABBREVIATIONS

ACh	Acetylcholine
AChE	Acetylcholinesterase
ACGIH	American Conference of Governmental Industrial Hygienists
ADI	Acceptable Daily Intake
AM	Arithmetic Mean
AS	Australian Standard
AS/NZS	Australian/New Zealand Standard
ASTM	American Society for Testing and Materials
ATSDR	Agency for Toxic Substances and Disease Registry
BALF	Bronchoalveolar Lavage Fluid
BCPC	British Crop Protection Council
BEIs	Biological Exposure Indices (ACGIH)
BM	Biological Monitoring
BS	British Standard
BSS	Balanced Salt Solution
BT	Breakthrough Time
CAT	Catalase
CFR	Code of Federal Regulations
CI	Confidence Interval
CNS	Central Nervous System
CVS	Cardiovascular System
DEDTP	Diethyldithiophosphate

DEHP	Diethylhexyl Phthalate
DEP	Diethylphosphate
DETP	Diethylthiophosphate
DDT	Dichlorodiphenyltrichloroethane
DHHS	Department of Health & Human Services, U.S. Public Health Service
DMDTP	Dimethyldithiophosphate
DMP	Dimethylphosphate
DMTP	Dimethythiophosphate
DNA	Deoxyribonucleic Acid
DNP	2,4-Dinitrophenol
DREAM	A Method for Semi-quantitative DeRmal Exposure AssessMent
DS	Desorbing Solution
DTNB	Dithiobis(2-nitrobenzoic acid)
EC	Electrochemical Detector
ECD	Electron Capture Detector
EN	European Committee
EPA	U.S. Environmental Protection Agency
FDA	U.S. Food and Drug Administration
FEV_1	Forced Expiratory Volume in One Second
FIVES	Fluorescent Interactive Video Exposure System
FRC	Forced Residual Capacity
FVC	Forced Vital Capacity
GC	Gas-Chromatography

GC-ECD	Gas-Chromatography with Electron Capture Detector
GC-FPD	Gas Chromatography with Flame Photometric Detector
GC-TSD	Gas Chromatography with Thermionic Specific Detection
GI	Gastrointestinal
GM	Geometric Mean
HVLP	High-Volume Low-Pressure (spray painting system)
HDA	Hexamethylene-diamine
HDI	Hexamethylene Diisocyanate
HDI-IC	HDI Isocyanurate Trimer
HDI-BT	HDI Biuret Trimer
HPLC	High Performance Liquid Chromatography
HPLC/MS	High-Performance Liquid Chromatography/Mass Spectrometry
HPLC-UV	High Performance Liquid Chromatography with Ultra Violet Detector
HPLC-EC	High Performance Liquid Chromatography with Electrochemical Detector
HSE	U.K. Health and Safety Executive
IDLH	Immediately Dangerous to Life and Health
IFA	Immunofluorescence Analysis
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IPA	Isopropyl Alcohol
IPDI	Isophorone Diisocyanate

IR	Infrared
IRIS	Intergrated Risk Information System
LD_{50}	Lethal Dose (50% population of test animals)
LOAEL	Lowest-Observed-Adverse-Effect Level
LOD	Limit of Detection
MCF7	Human Breast Adenocarcinoma
MDA	Malondialdehyde
MDHS	Methods for the Determination of Hazardous Substances (UK HSE)
MDI	Methylene Bisphenyl Diisocyanate
MP	Mobile Phase
MRL	Minimal Risk Levels for Hazardous Substances
MSDS	Material Safety Data Sheet
MTA	Motor Trade Association, South Australia
NCI	U.S. National Cancer Institute
NIOSH	U.S. National Institute for Occupational Safety and Health
NOAEL	No-Observed-Adverse-Effect Level
NOHSC	National Occupational Health and Safety Commission (Australia)
NTE	Neuropathy Target Esterase
OA	Occupational Asthma
OECD	Organisation for Economic Cooperation and Development
OEL	Occupational Exposure Limit
OHS	Occupational Health and Safety
1-2MP	1-(2-methoxyphenyl)piperazine

OP	Organophosphate
OR	Odds Ratio
OSHA	U.S. Occupational Safety & Health Administration
PBPK	Physiologically Based Pharmacokinetic
PChE	Plasma Cholinesterase
PCNA	Proliferating Cell Nuclear Antigen
PID	Photo Ionization Detector
PIRSA	Primary Industries and Resources, South Australia
PPE	Personal Protective Equipment
PR	Permeation Rate
PTFE	Polytetrafluoroethylene
PVC	Polyvinyl Chloride
RBC	Red Blood Cell
REL	Recommended Exposure Limit (US NIOSH)
RfD	Oral Reference Dose
SA	South Australia
SCE	Sister Chromatid Exchange
SIR	Standardized Incidence Ratio
SOD	Superoxide Dismutase
STEL	Short Term Exposure Limit
STD	Standard Deviation
TAFE	Technical and Further Education
TDI	Toluene Diisocyanate
TGA	Therapeutic Goods Administration

TLC	Total Lung Capacity
TLV	Threshold Limit Value (ACGIH)
TSD	Thermionic Specific Detection
TWA	Time-Weighted Average
UV	Ultraviolet
VC	Vital Capacity
VOCs	Volatile Organic Compounds
WHO	World Health Organization

CHAPTER 1. GENERAL INTRODUCTION

1.1 Introduction

For hundreds of years, it has been recognized that workers' health may be compromised by work practices and conditions, and, in particular, chemical exposure. For example, Paracelsus (1493-1541) wrote about miners' diseases, and, in 1700, Ramazzini wrote "De Morbis Artificum" describing 53 occupational groups and the diseases they experienced. Since then, work conditions have clearly improved, but there remain situations where there is potential for chemical-induced occupational mortality and morbidity.

In Australia, the National Occupational Health and Safety Commission (NOHSC) has estimated around 2,200 deaths per year due to occupational exposures to hazardous substances (Kerr *et al.*, 1996; Morrell *et al.*, 1998). There has been debate about the precise figures (Christophers and Zammit 1997). However, two more contemporary studies, from Finland (Nurminen and Karjalainen, 2001) and USA (Steenland *et al*, 2003), using a similar approach to Kerr, estimated a higher incidence of deaths resulting from occupational diseases. If the attributable fractions from these studies are directly substituted into the NOHSC profile, the revised estimates are 3,200 and 6,100 using the US and the Finnish fractions respectively.

Gun *et al* (1996) reviewed the occurrence and causes of occupational injury and disease in South Australia. Apart from the continuing burden of asbestos-related disease, acute injury and skin disease are probably the most common problems associated with chemical exposure. Large numbers of workers are potentially exposed. To take one example, there are approximately 2,000 hairdressing salons in South Australia using various dyes, detergents and spray-on products.

Overall, chemical exposure represents a significant public health issue, and there is an ongoing need to reduce occupational and environmental health risks that arise during the manufacture, processing, use and disposal of chemicals. Various legislative arrangements exist in Australia, notably the regulations, codes of practice and guidance documents relating to the control of hazardous substances.

The National Code of Practice for the Control of Hazardous Substances (NOHSC, 1994a) outlines how to identify, assess, control and review risks to health from exposure to hazardous substances in the workplace. Under the Hazardous Substances Regulations are three main strands, i.e. information provision, risk assessment and hazard control.

Information provision includes:

- Material Safety Data Sheets (MSDS)
- Labels
- Emergency information

Risk assessment involves:

- Process review, including the identification of hazardous substances
- Exposure assessment and comparison with exposure criteria
- Assessment of the effectiveness of controls
- Consideration of the work-relatedness of any reported health effects

Hazard control, based on a hierarchy of controls, includes:

- Design or engineering solutions (elimination, substitution, minimization, isolation, ventilation)
- Administrative controls (training, policies and procedures, and work practices)
- Use of appropriate personal protective equipment

The National Occupational Health and Safety Commission (NOHSC, 1994b) and other agencies provide guidance on the minimization of occupational health risk due to exposure to hazardous substances. A key component of risk assessment is exposure assessment, which entails establishing the pattern of use of the chemical(s) and identifying sources/routes of occupational exposure. Exposure assessment is often qualitative or semi-quantitative, i.e. there is insufficient information available to provide reliable quantitative estimates.

1.2 Exposure Pathways for Chemicals

1.2.1 Introduction

Chemicals enter the body by three main routes, i.e. the lungs (inhalation), the skin (dermal absorption) and the mouth (ingestion). Ocular exposure and injection may also occur in some situations. The internal organs most commonly affected are the liver, kidneys, heart, nervous system (including the brain) and reproductive system. The relative extent of exposure by various routes is not always well understood.

Inhalational exposure assessment has been the traditional focus of attention, and relevant standards have been in existence for most of the 20th century. However, dermal exposure may be more important in many cases (Fiserova-Bergerova, 1993; Boeniger, 2003; Semple, 2004; Van Hemmen, 2004). In recognition of this, the American Conference of Governmental Industrial Hygienists (ACGIH) and other standard setting bodies, have introduced skin notations. At present, there are no dermal exposure standards or ocular standards, although some attempts have been made to develop quantitative dermal occupational exposure limits (Bos *et al*, 1998; Brouwer *et al*, 1998), complementary to inhalational exposure limits.

Dermal exposure can lead to adverse health effects, such as dermatitis, irritation, sensitization and systemic effects. Some chemicals, e.g. organic solvents, cause dehydration and/or defatting of the skin, making it a less effective barrier. In the case of the eye, chemical exposure to the eye can lead to a wide range of effects on the eye and adjacent structures. These effects include lacrimation, ciliary muscle effects, and conjunctivitis, to mention just a few (Piccoli *et al*, 2003).

In general, the respiratory, dermal and ocular structures may be considered as both a target organ and a portal of entry.

1.2.2 Dermal Contact

Once dermal contact occurs, the chemical may penetrate the skin, remain on the skin or evaporate, as in the case of many volatile substances.

The skin is the largest organ of the human body by area (Plate 1), and comprises the epidermis and dermis. The stratum corneum, the upper most layers of the epidermis

and dermis provide the barrier function for the skin (Schaefer and Redelmeier, 1996; Pugh *et al.*, 1998).

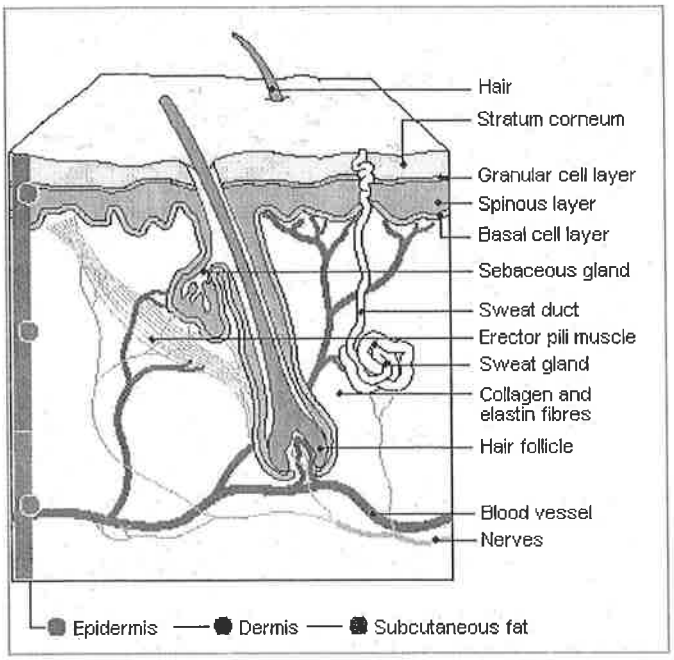


Plate 1: Structure of The Human Skin

(Sourced from: Skin biology and structure, www.mydr.com.au/default.asp?Article=3718)

Basically, there are three main pathways through the stratum corneum, namely the trans-appendageal route, the intercellular route through the lipid domain between the corneocytes and the intracellular route through the corneocytes. The trans-appendageal route entails the sebaceous ducts, hair follicles and sweat ducts. According to some researchers, lipophilic chemicals use the intercellular route as the main pathway (Montagna and Lobitz, 1964; Schaefer and Redelmeier, 1996). Even if there is no active transport mechanism, chemical absorption is controlled by permeation. The rate of permeation depends on the concentration gradient, and thus immersion in a liquid chemicals is much more hazardous than sparse droplet deposition, which is in turn, less hazardous than gas or vapor dermal exposure. Occlusion of liquid chemical in gloves may be tantamount to direct liquid immersion and potentially represents a serious dermal exposure risk. The combination of elevated temperature and increased blood flow to the skin in hot weather may exacerbate dermal absorption and/or accelerate diffusion rates.

The main components of the stratum corneum are 40% protein, 40% water and 20% lipids (Schaefer and Redelmeier, 1996). It is composed of corneocytes (horny layer cells), and flattened non-nucleated keratinocytes (Touitou *et al.*, 2000). The underlying viable epidermis consists of keratinocytes, melanocytes, merkel cells and langerhans cells. (Montagna and Lobitz, 1964; Schaefer and Redelmeier, 1996). Metabolic enzymes exist in the epidermal layer.

In a human study (Williams, 1993), methyl ethyl ketone (MEK) was rapidly absorbed through the skin into the blood. Due to the solubility in water, MEK absorption through sweaty skin was faster. Even though inhalational exposure was low, i.e. about 10% of the amount applied to the skin, 90% was excreted in the urine as both MEK and its metabolites, and suggesting a significant dermal metabolism.

There have been several *in vitro* and *in vivo* studies of skin permeability (Morimoto *et al.*, 1992; Kao *et al.*, 1985; Beckley-Kartey *et al.*, 1997; Tupker *et al.*, 1997; Bronaugh *et al.*, 1982). There are also predictive models to support understanding of skin penetration (Tsuruta, 1990; Potts and Guy, 1992; Auton *et al.*, 1994; Leung & Paustenbach, 1994; Bookout *et al.*, 1996; Wilschut *et al.*, 1996; Kissel, 2000). These mathematical models are based on physicochemical properties of the compound.

1.2.3 Ocular Contact

The eye is composed of derivatives of surface ectoderm (corneal epithelium and conjunctiva) and of mesoderm (choroids, iris and ciliary body stroma) (Plate 2). The eye contains vascular areas and an aqueous system.

The ocular surface is moisturized at all times. The sebaceous meibomian glands in the lids create the outermost lipid layer, which is typically less than 0.1 micron thick. This layer prevents evaporation of the tear film and lubricates the eyelid. Meibomian lipids are composed of waxy and cholesterol esters (Holly and Lemp, 1987). The aqueous layer constitutes around 90% of the thickness of the tear film and is generated by the main lacrimal gland and the accessory lacrimal glands of Krause and Wolfring (Bron, 1985). The innermost layer of the tear film is the mucous layer, secreted by goblet cells. This hydrated glycoprotein layer makes the corneal surface hydrophilic and thus wettable and decreases surface tension of the tear film. The breakup of tear film is by

contact between the lipid and mucous layers or local breakdown of the mucous layer (Lin and Brenner, 1982; Sharma and Ruckenstein, 1982).

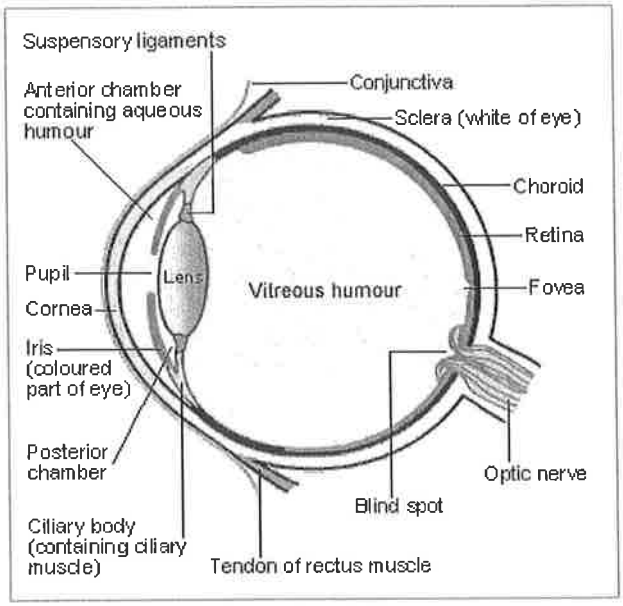


Plate 2: Structure of The Human Eye

(Sourced from: Structure of the eye, www.mydr.com.au/default.asp?Article=3429)

Chemical absorption through the eye may entail absorption through any or all of the ocular structures including eyelids, mucous membrane, conjunctiva and eyeball, although common terminology refers to the exposed eyeball and conjunctiva.

Chemicals absorbed through the eye may enter the bloodstream (Grant, 1974; Klaassen *et al.*, 2001). Systemic effects from ocular exposure may also be via nasal and alimentary mucosa. However, it has been found that short term effects are most common, and usually mediated by the interaction of the chemicals with the ocular surface. The principal mechanisms have been summarized by Piccoli *et al* (2003).

The lacrimal gland produces water in response to stimuli on the ocular surface and in so doing changes the lacrimal film composition. Blinking can also alter the precorneal tear film, protecting the outer eye from external factors.

There appears to be limited information regarding ocular exposure to industrial chemicals, as well as the relationship between dose, response and exposure limits.

1.3 Classes of Chemicals that may be Significantly Absorbed through the Skin and Eye

There are potentially many substances that may be absorbed through the skin. The ACGIH Threshold Limit Values (TLV) Booklet (2001) identifies varied classes of substances, such as alcohols, nitriles, organochlorine insecticides, aromatic amines, organophosphate insecticides, phenols, sulphoxides, carbamates, hydrazines and glycol ethers. Of the substances, dimethyl sulphoxide is notable in that it is used as a carrier for chemicals that are meant to be absorbed through the skin.

Approximately 27% of substances on the ACGIH TLV list have a skin notation indicating the significance of the issue.

In respect of ocular exposure, approximately 3% of the ACGIH TLVs are explicitly based on eye effects, e.g. silver, methyl silicate, naphthalene, disopropylamine, diquat, methanol, triethylamine and hydroquinone (Klaassen *et al.*, 2001). However, many or most of the substances on the TLV list may cause eye irritation, as a secondary effect.

The amount of absorption through the eye is particularly poorly understood, and there is a need for further research.

1.4 Assessment of Chemical Exposure

Although inhalation has traditionally considered to be the main route of exposure, skin absorption can be important (Semple, 2004), and variety of direct and indirect approaches have been developed to assess the significance of the dermal route. This section outlines some common techniques for chemical exposure assessment, including the use of biological monitoring as an integrated measure. It does not specifically consider ingestion or injection.

1.4.1 Inhalational Exposure Assessment

If inhalation is the only significant route of entry into the body, then the results of air sampling in the "breathing zone" may provide a good indication of personal health risk. Typically, a lapel-mounted sampling head (e.g. sorbent tube or particle filter) is

connected to a calibrated battery-powered air sampling pump, and this arrangement is worn throughout the relevant time period, often an 8-hour shift or 15-minute short term exposure period.

Air sampling approaches, equipment and analytical procedures are well documented (Lioy and Lioy, 2001; OSHA, 1993; NIOSH, 1994a).

1.4.2 Dermal Exposure Assessment

A range of dermal sampling methods has been described (Ness, 1991; McArthur, 1992; Fenske, 1993; Ness, 1994), but these are generally considered semi-quantitative.

Surface Monitoring

Surface monitoring, including vacuuming of surfaces, may serve to indicate the potential for dermal exposure to chemicals. It is, however, an indirect measure and relies on an understanding of skin contact time and transfer efficiency.

Surface monitoring for radioactive contamination has been widely used for decades, but has been relatively uncommon for general chemicals (Fenske, 1993).

In some cases, surface monitoring data can display good correlations with reported symptoms, e.g. surface monitoring of deposited glass fibres may be better correlated with reported dermatitis than air monitoring (Ness, 1994).

An important application of surface monitoring is in respect to demonstrating the adequacy of work practices, housekeeping and cleanup procedures. Thus, a number of surface contamination standards have been developed, e.g. 0.2 mg/100 cm^2 for sodium fluoroacetate (LaGoy *et al.,* 1992).

Fenske (1993) has highlighted several complications. For example, the reliability of surface wipe sampling depends on surface characteristics, contaminant loading, sampling media, and procedures.

Skin Wiping

Skin wiping is a convenient method of assessing dermal exposure.

Whatman Smear Tabs were used by Smith *et al.* (1982) for polychlorinated biphenyls (PCB) and by Wolff *et al.* (1989) for polycylic aromatic hydrocarbons (PAH).

Different types of prepacked hand wipes (i.e. Wash 'n' Dri Soft Cloths, Moist Toweletters, Washkin's Hospital Packettes, Walgreen's Brand Wet Wipes, Lehn and Fink's Wet Ones and Baby Size Wet Ones) have been evaluated (Que Hee *et al.*, 1985). In the study of lead contamination, the effectiveness of wiping depends not only on the type of wipe, but also on the number of repetitive wipes. Commercial paper towel premoistened with benzalkonium and alcohol were used for wiping hands, fingers and palms at a battery plant (Chavalitnitikul *et al.*, 1984). Commercial baby wipes have also been used for skin wiping (NIOSH, 1992).

Groth *et al.*, (1992) used wipers with polyethylene glycol (PEG) for methylene dianiline (MDA), because MDA is soluble in PEG and PEG is soluble in water.

However, skin cleaning should be conducted prior to wiping, because there may be pre-existing chemical residues in the layers of the skin (i.e. stratum corneum). Such pre-contamination should not be removed by waterless cleaners containing lanolin, or abrasive cleansers. In addition, skin barrier cream should not be used on the day of sampling, because it may contain lanolin resulting in the acceleration of the penetration of contaminants (Ness, 1994). Skin wipes may not collect all contaminants deposited, because contaminants can penetrate into the epidermis during exposure (McArthur, 1992). Volatile components may also evaporate from the skin surface.

Wiping with solvents may pose a risk to the worker, especially during time-consuming wiping activities associated with fingers and fingernails.

Skin wiping is not operator independent, and can vary with skin characteristics. Wiping has been reported to underestimate exposure, compared with hand washing and a glove method (Fenske *et al.*, 2000). However, much better recoveries were found in another study when isopropanol was used as the solvent instead of a water-surfactant mixture (Geno *et al.*, 1996).

Overall, skin surface contamination assessment is problematic and better methodologies are required (Fenske, 1990; Schröder *et al.*, 1999; Liu et al., 2000).

Skin Washing

Skin washing is one of the most common removal methods. This method has been used for washing the hand, wrist, arm, foot and ankle. However, this method cannot be used for pesticides which have high rates of dermal absorption. The hand washing procedure has been standardized (EPA, 1986).

Durham and Wolfe (1962) used polyethylene bags and this was more reliable than the swab method. However, physical characteristics of chemical substances should be considered, such as whether they are soluble or degraded by solvents (Davis, 1980). Durham and Wolfe (1962) reported that the recovery rates of parathion from the hand were 77% - 94% for the first rinse, 89% - 98% for the second rinse and less than 5% for the third rinse. They recommended three rinses to reach a high efficiency.

The efficiency range for chloropyrifos using water-alcohol mixtures was 23% to 96% (median 73%) (Brouwer *et al.*, 2000a).

The Cup Method, being a modified aerosol spray delivery system, has been used (Keenan and Cole, 1982). When the actuator button is pressed, the propellant is sprayed onto the surface of the skin and the rinse liquid from the contaminated skin surface is collected in a bottle. It has been suggested (Ness, 1994) that this method would provide more accurate results compared with hand washing or skin wiping.

The Pouring Method is essentially a hand wash involving a stream of solvent (Keenan and Cole, 1982; Davis *et al.*, 1983; Kangas *et al.*, 1993; Knaak *et al.*, 1986). Even though this method is not standardized, it can provide faster sampling collection than the bag method (Ness, 1994).

Washing techniques are not easily applicable to the assessment of total body exposure (Brouwer *et al.* 2000a), as they may affect the integrity of the skin, and may provide an underestimation, e.g. in the case of pesticides.

Removal efficiency should be studied as a part of quality assurance (Fenske & Lu, 1994; Brouwer *et al.*, 2000a) with a number of variables, such as the field conditions,

exposure patterns, relevant time of residence of the contaminant on the skin and relevant levels of skin loading present.

Adhesive Methods and Tape Stripping

As a surface sampling technique, adhesives have been used to measure skin contamination by solid substances. Lepow *et al* (1975) measured the exposure levels of lead from contaminated soil on the palms of children using preweighted self-adhesive labels.

In order to collect fibres causing itching and localized rashes in a data processing computer room, transparent tape was used on the skin (NIOSH, 1984a). Wheeler and Stancliffe (1998) used adhesive tapes (e.g., Scotch Tape® and forensic tape) and demonstrated that this technique had more efficiency for solids than wipe sampling.

It is a useful assessment method for the determination of the amount and distribution of chemicals in the stratum corneum (Dick *et al.*, 1997; Nylander-French, 2000). The chemical concentration profile within the layers decreases with the increase in tape stripping application (ECVAM, 1999). In a recent study, tape stripping was used to assess dermal exposure during aircraft maintenance. Naphthalene was used as a marker for JP-8 (Chao and Nylander-French, 2004).

Fluorescence

Some compounds are naturally fluorescent, e.g. polycyclic aromatic hydrocarbons, and the extent of surface and skin contamination can be assessed with a hand held UV light in a dark room.

Brouwer *et al* (1999, 2000b) studied dermal exposure from contaminated surfaces by using fluorescent tracers. A Fluorescent Interactive Video Exposure System (FIVES) was introduced by Roff (1997) and Cherrie *et al* (2000). By using fluorescent tracers, they were able to identify primary and secondary sources of contamination.

The method, however, is costly and has not been widely used.

Skin Patches, Pads and Clothing

Simple methods involving pads, patches and clothing have been used to measure the potential for dermal exposure, e.g. from residue transfer or aerosol deposition.

In assessing the deposition of pesticides on the skin, Fenske (1990) used surgical gauze patches. Charcoal cloth was used by Cohen and Popendorf (1989) to measure potential dermal exposure to a range of solvents.

It is a useful approach in judging the effectiveness of personal protective clothing against chemicals, and in the determination of where the main exposure occurs on the body.

As a direct detection method in workplaces using isocyanates, Permea-Tec^{TM} Pads were used by Rowell *et al.* (1997) to evaluate the exposure of the skin under protective gloves.

Skin patch sampling usually only addresses a small section of the body (Soutar *et al.*, 2000). Therefore, the results should be interpreted with care. Furthermore, the characteristics of skin patches differ from skin, e.g. when the skin is sweating, wrinkling and calloused. Adsorption and absorption of chemicals should be considered (Dost, 1995), and the collection efficiency of the sampling medium should be determined before collecting samples.

Gloves and socks are complementary to patches and pads, and, like them, may overestimate the potential for exposure due to absorptive properties (Fenske *et al.*, 1989; Fenske *et al.*, 2000; Soutar *et al.*, 2000).

However, in some tasks, the gloves may interfere with normal work and underestimation has also been reported (Zweig *et al.*, 1985).

Protocols have been developed for the estimation of total dermal exposure, e.g. based on patches or the use of overalls (WHO, 1986; Chester, 1995). Cattani *et al.*, (2001) used data from overalls, patches and gloves to assess total potential dermal exposure for workers using chlorpyrifos in termite control.

Dermal Exposure Assessment Toolkits and Models

A *Der*mal *E*xposure *A*ssessment *M*ethod (DREAM) was developed by Van-Wendel-De-Joode *et al.,* (2003) and provides a systemic description of dermal exposure pathways and a guide to the most appropriate measurement strategies.

This semi-quantitative method considers company, department, agent, job, task, exposure route, exposure module, exposure status, physical and chemical characteristics, exposure part and protective condition.

Dermal risk assessment toolkits have been developed (Schuhmacher-Wolzi *et al.*, 2003; Oppl *et al.*, 2003, Warren *et al.*, 2003). The toolkits consider the hazardous properties of the chemical in use, exposure conditions, and control status to assess dermal risks in workplaces. However, input data are not always reliable (Marquart *et al.*, 2003; Van Hemmen *et al.*, 2003).

In order to address these issues, exposure surveys have recently been conducted (Hughson and Aitken, 2004; Kromhout *et al.*, 2004; Rajan-Sithamparanadarajah *et al.*, 2004).

Other approaches have been used:

The European Predictive Operator Exposure Model, known as EUROPOEM has been developed for operator exposure assessment in pesticide application work (NOHSC, 1997). Like DREAM, the assessor's expertise is an important consideration. A Pesticide Handlers Exposure Database (PHED) has been used in the US and Canada (PHED, 1992)

The knowledge-based EASE model (Estimation and Assessment of Substance Exposure) was designed for assessing exposure to new and existing chemicals in the European Union. The model ranks the workplaces in broad bands of exposure, and, therefore, it always assumes homogeneous exposure within the workplace (Vermeulen *et al.*, 2002).

1.4.3 Ocular Exposure Assessment

Possible sampling approaches include wiping around the eye or washing the eye surface. An indirect approach might entail measuring the level of surface contamination inside or outside eye protective devices.

However, there did not appear to be any published literature on ocular exposure assessment methods.

1.4.4 Biological Exposure Assessment

Biological monitoring (BM) is used to assess the amount of chemical that an individual has been exposed to by all routes - inhalation, ingestion and skin absorption. The objective of BM is to prevent excessive exposure to chemicals, and is complementary to ambient methods, e.g. air and surface sampling (Lauwerys and Bernard, 1985; Ho and Dillon 1987; Bernard and Lauwerys, 1989)

BM can sometimes be used to evaluate the contribution from non-occupational sources, or to perform a retrospective evaluation of exposure.

There are various BM techniques available for looking at chemical exposure, particularly for those workers wearing personal protective clothing or for those doing strenuous physical activities, or working under hot conditions and so on.

The significance of BM in the context of dermal exposure assessment has been discussed by Fenske (1993). For example, correlations between data from patch samples with those from urine samples. However, BM does not provide information on exposure routes or body locations of exposure. Therefore, the amount of contamination on skin surfaces should be determined (McArthur, 1992).

1.4.5 Evaluation of Chemical Protective Clothing

There are numerous methods for evaluating the performance of chemical protective clothing (NIOSH 1990). For the purpose of this thesis, discussion will be restricted to gloves and, in particular, methods for the determination of permeation resistance.

Glove Testing

Several standard test methods for permeation have been introduced, e.g. the American Society for Testing and Materials (ASTM) F739 (1986, 1996) and European Committee for Standardization (EN) 374 (1994) methods.

Cells for permeation testing are commercially available.

In Australia, Bromwich (1998) developed a simple test cell for chemical protective clothing, yielding improved assembly time, flexibility, response time and cost.

AS/NZS 2161 part 10.3-2002 for the determination of resistance to permeation by chemicals has been adapted from the European (CEN) Standard EN 374-3:1994. Mäkelä *et al* (2003a) made a comparison of the two standard methods (ASTM F739 and EN 374). However, there was no statistical difference between ASTM F739 and EN 374 when a gaseous collection medium was used.

1.5 Selection of Chemicals and Processes

1.5.1 Industrial Processes where Skin and Eye Exposure is Likely

There are a number of situations where significant dermal and ocular exposure can occur, for example manual cleaning and dipping processes, chemical transfer and mixing, particularly in confined spaces (Warren *et al*, 2003)

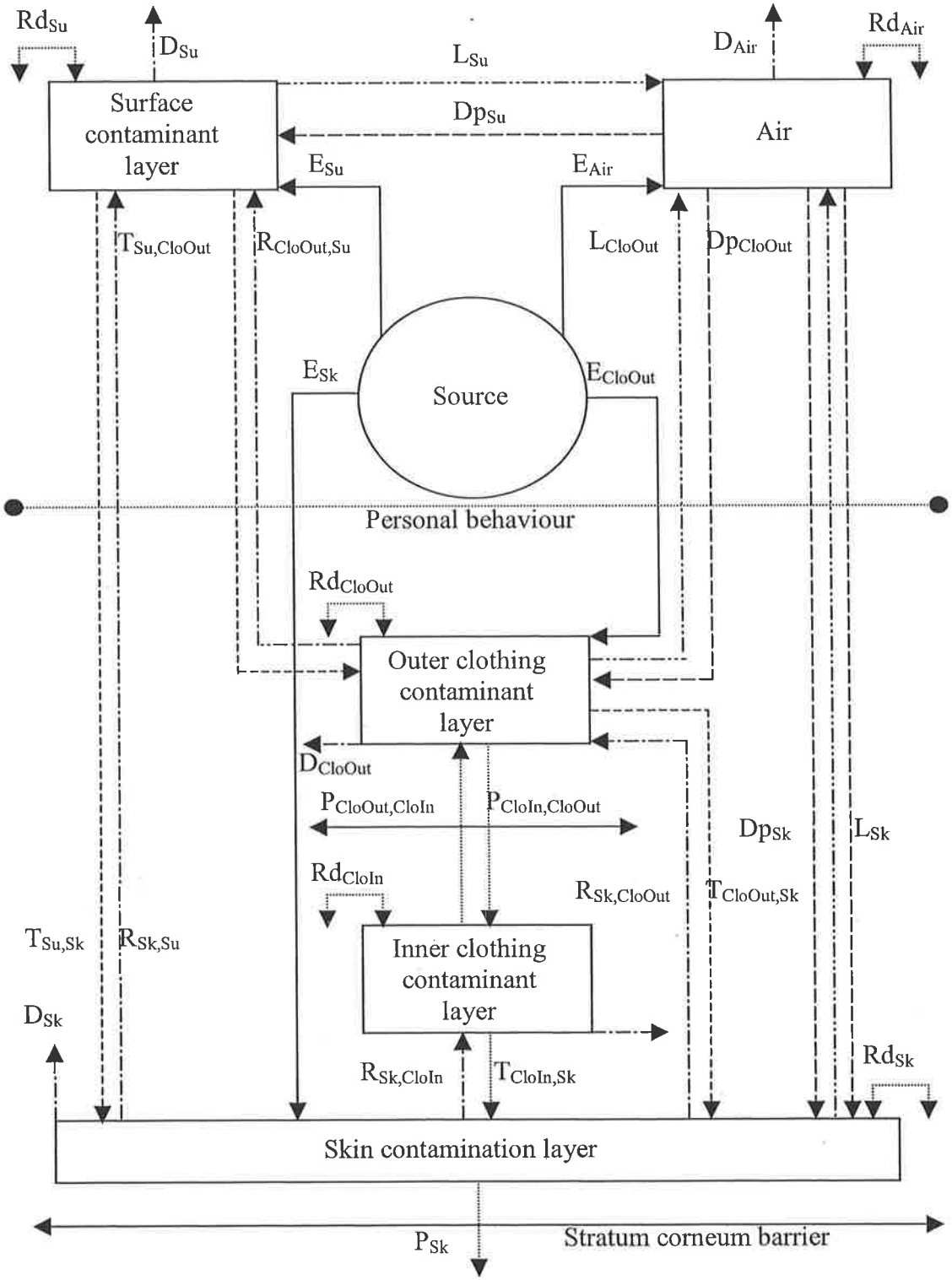
The eyes are of particular concern, as ocular exposure can occur via splashing, rubbing of contaminated hands on eyes or direct absorption from atmosphere.

The spray application of substances probably represents an extreme case since there is a deliberate generation of airborne particles that can potentially be inhaled or deposited on the skin or eyes.

1.5.2 Modeling of Skin and Eye Exposure during Spray Application

Various protocols and models of dermal exposure have been developed (Spear *et al.*, 1977; Fenske *et al.*, 1986a, 1986b) and these have commonly been applied to pesticide workers (NOHSC, 1997; Cattani *et al.*, 2001).

However, it has only been recently that a conceptual model has been developed (Schneider *et al*, 1999; 2000; Semple, 2004) (see Figure 1 and Table 1).



Overview of the conceptual model, compartment and rate constants.
E=emission (·····); Dp=deposition (——); I=resuspension or evaporation (– – –); T=transfer (— —);
R=removal (— · —); Rd=redistribution (·····); D=decontamination (— — —); P=penetration and permeation (·····).

*** Source: Schneider T., Vermeulen R., Brouwer D.H., Cherrie J.W., Kromhout H. and Fogh C.L., (1999) *Conceptual Model for Assessment of Dermal Exposure*, Occup Environ Med, 56, 756-773.**

Figure 1: A Conceptual Model of Dermal Exposure

Table 1: Compartment Descriptors for Conceptual Model

Compartment	Definition of metric	Symbol	Relation	Units
Source	Mass of harzardous substance available for emission	M_S		g
	Concentration of a hazardous substance in the source	C_S		$g.g^{-1}$, $g.m^{-3}$
Air	Mass of substance in the air compartment	M_{Air}		g
	Volume of the air compartment	V_{Air}		m^{-3}
	Concentration of hazardous substance in the air	C_{Air}		$g.m^{-3}$
Surface contamination layer	Mass of hazardous substance in the surface contamination layer	M_{Su}		g
	Concentration of a hazardous substance on the surface	C_{Su}	$M_{Su}/ (M_{Su}+M_{Other})$	$g.kg^{-1}$
	Area of surface which is contaminated with hazardous substance	A_{Su}		cm^2
Outer clothing contaminant layer	Mass of hazardous substance in the outer clothing contamination layer compartment	M_{CloOut}		g
	Concentration of a hazardous substance in the outer clothing compartment	C_{CloOut}	$M_{CloOut}/ (M_{CloOut} + M_{OtherOut})$	$g.kg^{-1}$
	Area of the outer clothing which is contaminated with hazardous substance	A_{CloOut}		cm^2
Inner clothing contaminant layer	Mass of hazardous substance in the inner clothing contamination layer compartment	M_{CloIn}		g
	Concentration of a hazardous substance in the inner clothing compartment	C_{CloIn}	$M_{CloIn}/ (M_{CloIn} + M_{OtherIn})$	$g.kg^{-1}$
	Area of the inner clothing which is contaminated with hazardous substance	A_{CloIn}		cm^2
Skin contamination layer	Mass of hazardous substance on the skin surface	M_{Sk}		g
	Concentration of a hazardous substance in the skin contaminant layer	C_{Sk}	$M_{Sk}/ (M_{Sk}+M_{Other})$	$g.kg^{-1}$
	Area of the skin which is contaminated with hazardous substance	A_{Sk}		cm^2

M_{Other}= mass of all other substances in a particular compartment

Source: Schneider T., Vermeulen R., Brouwer D.H., Cherrie J.W., Kromhout H. and Fogh C.L., (1999) *Conceptual Model for Assessment of Dermal Exposure*, Occup Environ Med, 56, 756-773.

Fundamental predictive models of inhalational exposure in spraying processes have been developed by Flynn and co-workers, and these have been validated in simple laboratory-based scenarios (Carlton and Flynn, 1997; Flynn *et al.*, 1999). No such model exists for dermal exposure, although Semple and coworkers (2001) described a semi-empirical dermal model for spray painters, and Hughson and Aitken (2004) reported on dermal exposure results for selected dermal exposure operations (DEO), including spraying. Warren *et al* (2003) published default dermal exposure values for risk assessment toolkits. For spraying, the two principal mechanism of exposure were

aerosol deposition on skin, and surface contact, representing exposure via intermediate contaminated surfaces.

With regard to ocular exposure, there do not appear to be any models, although the three principal dermal exposure mechanisms may be applicable, i.e. direct contact, surface contact and aerosol deposition (Warren *et al.*, 2003). The fundamental models for inhalational exposure during spraying may be useful in respect of providing input data for the broader semi-empirical models. However, owing to the complexity of spraying processes, e.g. object shape, orientation of the sprayer relative to mechanical ventilation systems, droplet size etc, there is a need to conduct direct measurement in most situations (Brouwer et al., 2000b). Processes associated with spraying, such as mixing and cleanup may represent simpler dermal exposure assessment situations, and for these tasks the direct contact mechanism, e.g. exposure from splashing, may be important.

1.5.3 Selection of Chemicals for this Research

Given the potential for the skin and eye exposure in spray processes, it was considered worthwhile to look at local industries where spray processes occur. Two situations were selected for this study:

1. The use of organophosphate (OP) pesticides (e.g. malathion and fenthion) in Mediterranean fruit fly eradication
2. The use of hexamethylene diisocyanate (HDI)-based aliphatic isocyanates in automobile repair and furniture industries.

The situations and chemicals were selected due to the availability of populations of workers, the potential severity of health effects and the lack of specific exposure data elsewhere (see later).

South Australia (SA) has a large agricultural industry, including fruit production which is potentionally threatended by fruit fly. Periodic infestations have been eradicated through monitoring and application of OPs.

Similarly, SA has a large number of such small and medium size furniture and motor vehicle-related industries, where the use of isocyanate-based two-pack spray paints is common.

OP Pesticides (Malathion; MAL & Fenthion; FEN)

In order to control the Mediterranean fruit fly and protect SA's $250 million horticultural industry, a standard eradication program has been implemented by Primary Industries and Resources South Australia (PIRSA, 2001) and involves OP pesticides, such as malathion (MAL) and fenthion (FEN).

Malathion (diethyl dimethoxythiophosphorylthio) succinate; CAS No. 121-75-5) is applied in a protein bait which attracts and kills fruit fly. Fenthion (O,O-dimethyl-O-4-methylthio-m-tolyl phosphorothioate; CAS No. 55-38-9) is applied to wet all foliage surfaces of potentially affected fruit trees and shrubs in domestic gardens. For malathion (MAL) bait spraying, spray workers use a single 14 litre backpack spray unit (knapsack) containing MAL diluted in water. Diluted solutions of fenthion are applied to trees or foliage by using air pressure equipment or a hand pressure spray gun.

The spray workers typically wear respiratory protective equipment (half-face mask) and protective clothing (overalls, gauntlets, boots, sunglasses with side-shields and hats) for in field applications.

Plate 3: Spray Worker Applying Pesticide

During the applications, the spray workers can be contaminated by airborne fumes/vapors, solution leakage from the knapsack and spray gun nozzle, and contaminated surfaces. However, exposure to the chemicals can be reduced by wearing appropriate PPE. Plate 3 is a photograph of the spray application of fruit fly bait.

Exposure to such pesticides via dermal absorption, inhalation and ingestion can lead to adverse health effects, such as dermatitis, irritation, sensitization and systemic effects. These can be short or long term effects (Reeves *et al.*, 1981; Mahiey *et al.*, 1982; Albright *et al.*, 1983; Gosselin *et al.*, 1984; Wali *et al.*, 1984; Balaji and Sasikala, 1993; EPA, 2000a, 2000b; PIRSA, 2001; Giri *et al.*, 2002; Hayes, 1982, 1990; Brunetto, 1992).

Isocyanate (Hexamethylene Diisocyanate; HDI)

Spray painters are an occupational group at potentially high risk of respiratory and skin disorders. For example, Ucgun *et al* (1998) concluded occupational asthma was a common among automobile and furniture painters.

Isocyanates, usually as oligomers of HDI or isophorone diisocyanate are present in the hardeners of two-pack polyurethane paints, routinely used in most crash repair workshops (Mohanu, 1996).

Following mixing of the hardener with paint resin and *reducer* solvent, the paint slowly cures, and must be sprayed onto the object, typically within 15-30 minutes. However, once cured the aliphatic polyurethane coating displays exceptional durability and resistance to yellowing.

Two-pack spray painting is generally conducted in a spray booth, and usually involves coloured undercoats and clear top coats.

In crash repair shops using isocyanate-based paints, the main activities are surface preparation, paint mixing, compressed air-assisted spraying, drying, wet or dry rubbing, and cleanup. The spray painting is generally accomplished with either a conventional (high-pressure induced venture or gravity feed) or an HVLP (high-volume low-pressure) spray gun.

The spray painters typically wear overalls or disposable coveralls, disposable gloves, boots, a full face-airline mask or a half face air purifying mask. They are potentially exposed to isocyanates from airborne contaminats (dusts, mists or vapors), contaminated surfaces and clean up proceses. Plate 4 illustrates spray painting with isocyanates.

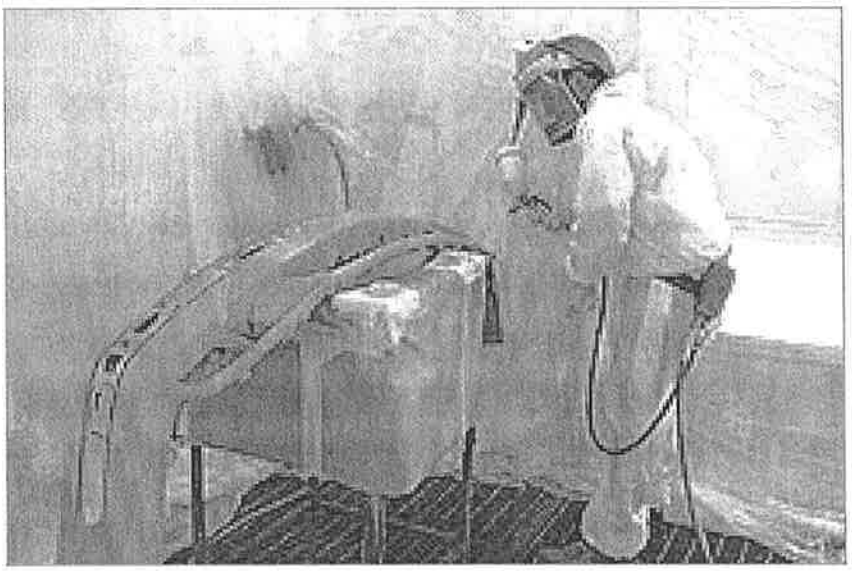


Plate 4: Spray Painter Applying Isocyanates

1.6 Organophosphate Pesticides (MAL, FEN) Used for The Control of The Mediterranean Fruit Fly

This section introduces the specific procedures, toxicology and previous research.

1.6.1 Introduction

Pests are any organisms adversely affecting human interests, e.g. destroying crops, decreasing harvests and spreading disease. Pesticides such as fumigants, herbicides, insecticides and rodenticides may be used to control pests (Arnold, 1992; EPA, 2001). Of the pesticides, insecticides are subdivided into inorganic insecticides, chlorinated hydrocarbons, carbamates, synthetic pyrethroids and other botanicals, and organophosphates (Dent, 1991).

The widespread use of pesticides has the potential to result in human exposure and adverse effects. According to Edmiston and Maddy (1987), 2,099 illnesses or injuries were reported by the Worker Health and Safety Branch of the California Department of Food and Agriculture in 1986. Around 51% were related to pesticide exposure.

Fruit fly are major pests of horticultural crops in Australia (Smith, 1997). They are generally found hovering near decaying vegetation and overripe fruit as well as in the home, especially when vegetable or fruit materials are present after major home canning efforts. Fruit flies target apricots, peaches, nectarines, apples, pears, citrus and guava. In order to control fruit flies, there are several control methods, including cover sprays, protein bait sprays, traps, fruit removal and sanitation.

Fruit fly, of which there are over 80 species, were introduced into Australia over fifty years ago. These include the native Queensland fruit fly in the eastern states and the Mediterranean fruit fly in Western Australia and South Australia. Since 1897, a policy of fruit fly eradication had been established.

In 1947, the first outbreak of fruit fly occurred in SA. Several mechanisms were suggested to control the extent of fruit fly infestation in SA, such as the removal of fruit from backyards and the disposal of fruit/plant material. At that time, lure traps and bait spraying were performed to eradicate fruit flies.

Earlier programs used DDT or other organochlorine chemicals that were available at the time, but DDT was banned in Australia in 1985, due to concerns about environmental and human toxicity. Since then, the organophosphates have been applied for pest control in a program of work which is administered and controlled by the Department of Primary Industries and Resources South Australia (PIRSA).

In SA, fruit fly outbreaks are discovered by a system of vigilant householder reporting larvae found in fruit and a network of over 3,800 fruit fly trapping sites across the State. Outbreaks in metropolitan Adelaide are controlled by the imposition of a strict quarantine upon affected areas, and a control program including the use of the organophosphorus insecticides (OPs) MAL and FEN.

As mentioned, the responsibility for the control and eradication of outbreaks of fruit fly rests with PIRSA which has legislated authority to enter private premises to apply insecticides and remove infested fruit (Fruit and Plant Protection Act 1992), although the co-operation of the community is essential for the effectiveness of the control program.

In general, when there is an outbreak of fruit fly, PIRSA establishes two boundaries. From the outbreak centre, an area within 200m radius is subject to intensive treatment using MAL/protein baiting, and insect pheremone traps are used to monitor fruit fly numbers. Traps are used between 200m and 1.5km to ensure the outbreak does not spread. The PIRSA officers are empowered to strip and remove all fruit from affected trees. They then spray all fruit trees and those of all trees within 200 metres as well as on the ground underneath and set pheromone traps every 1-2 weeks for six weeks.
In 2001, as a consequence of public concerns, PIRSA conducted a risk assessment of potential health effects resulting from exposure to MAL and FEN.

Organophosphate pesticides act through the inhibition of the enzyme acetylcholinesterase (AChE) leading to impairment of the nervous system. The inactivation of AChE can cause the accumulation of acetylcholine at the neuroceptor transmission site (DHHS, 1993). For instance, OPs cause target species to lose muscle coordination, convulse and die. Similar enzymes are found in mammals, including humans, and non-target toxicity is mediated through the same mechanism. The main symptoms in humans arise from AChE inhibition in the central nervous system (CNS) and at muscarinic and nicotinic nerve terminals in the periphery. Acute symptoms include headaches, skin irritation, stomach pains, vomiting, eye irritation and diarrhea. Possible chronic symptoms include neuropsychological outcomes, peripheral neuropathy and psychiatric illness (EPA, 2002a).

OP compounds have been investigated for genotoxic effects since they are weak alkylating agents (Fest and Schmidt, 1973) and have been found to be mutagenic in bacteria (Hanna and Dyer, 1975; Shirasu *et al.*, 1976; Waters *et al.*, 1980), although in other test systems, including human cells in vitro and sister chromatid exchanges, a cytogenetic measure of genotoxicity, results have been inconclusive (Collins, 1972; Ficsor *et al.*, 1977; Wild, 1975; Van Bao *et al.*, 1974; Hogstedt *et al.*, 1980; Nicholas

and Van Den Berghe, 1982). Human exposures *in vivo* have also yielded both positive and negative results (WHO, 1986), and these discrepancies may be associated with studies being poorly controlled with respect to other chemical exposures or variations in the formulation of pesticide used.

Public concerns about the effect of OPs exposure are related to the possible consequences of long-term exposure to low levels of OPs. In particular, a range of non-specific flu-like symptoms and partial paralysis were claimed to be associated with OP exposure in sheep farmers exposed to OP compounds in insecticidal dips (Independent, 1992). It is unclear whether these symptoms are manifestations of chronic OPs exposure at low concentrations or are associated with unreported high intensity exposures.

Biological monitoring techniques can be applied to workers exposed to OPs in order to assess the extent of their exposure. This has generally involved the measurement of peripheral cholinesterase enzymes which are inhibited by OPs, including red blood cell cholinesterase and serum (plasma) cholinesterase (Gage, 1955; Mason and Lewis, 1939).

The inhibition of these peripheral enzymes differs from that of those in the central nervous system but monitoring of the peripheral enzymes is a useful marker of acute toxicity (70% inhibition of plasma cholinesterase is generally associated with clinical effects) (Mutch *et al.*, 1992). Peoples and Knaak (1982) stated that the determination of plasma and red blood cell cholinesterase is the optimum method for organophosphate identification. Most organophosphates are readily hydrolyzed by the liver and as such exert their effect faster, however some of them are stored in the liver and release slowly therefore delaying its toxicity.

Peripheral lymphocyte neuropathy target esterase (NTE) activity has also been monitored as an indicator of delayed polyneuropathy (Mutch *et al.*, 1992; Lotti, 1986). Other biological monitoring strategies have been developed, including the measurement of urinary dialkyl phosphates and metabolites of OPs. These estimate the exposure level of OPs and the relationships between exposure, uptake and response (Davies *et al.*, 1979).

Recent work has suggested that workers wearing protective equipment exposed to OP sheep dip at concentrations which altered neither cholinesterase enzyme activities nor urinary levels of dialkyl phosphates cause significant changes in sister chromatid exchange frequencies in peripheral lymphocytes (Hatjian *et al.*, 2000).

MAL is a slightly toxic compound in EPA toxicity class III as a General Use Pesticide (GUP). The common name is "malathion" with the synonym of 0, 0-dimethyl S-(1, 2-dicarbethoxyethyl) phosphorodithioate. Registered trade names are Cekumal, Fyfanon®, Malixol® and Maltox® (Howard and Neal, 1992). The chemical formula is $C_{10}H_{19}O_6PS_2$.

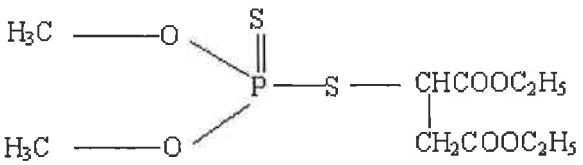


Figure 2: Chemical Structure of Malathion

Figure 2 represents the chemical structure of MAL. Physical and chemical properties have been reported in several publications (Matsumura, 1985; Howard and Neal, 1992; Budavari, 1996 CHEMWATCH, 2003a).

FEN is a moderately toxic compound in EPA toxicity class II as a Restricted Use Pesticide (RUP) due to the special handling warranted by its toxicity. FEN is one of the OPs used against sucking or biting pests, fruit flies, stem bores, mosquitoes and intestinal worms. FEN can be used in dust, emulsifiable concentrate, granular, liquid concentrate, spray concentrate and wettable powder formulations (Meister, 1992).

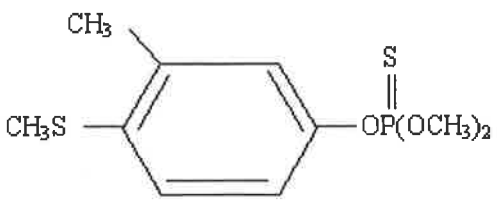


Figure 3: Chemical Structure of Fenthion

It is known as a 4-methylmercapto-3-methylphenyl dimethyl thiophosphate, Bay 29493, Baycid, Baytex, Entex, Lebaycid, Mercaptophos, Prentox FEN 4E, Queletox, S 1752, Spotton, Talodex and Tiguvon. However, FEN has not been one of the chemical approved by FDA, due to a large number of poisoning deaths. Figure 3 represents the chemical structure of FEN. Physical and chemical properties are described in many studies (Hayes and Laws, 1990; Meister, 1992; ICSC, 1993; CHEMWATCH, 2003b).

According to a Ministerial review of the PIRSA fruit fly eradication program (PIRSA, 2001) complaints from the SA public were significantly increased in 2000 and 2001. However, no specific symptoms were documented and the possibility of adverse health symptoms caused by exposure to MAL and FEN used for the Mediterranean fruit fly eradication in SA was thought to be low. Nevertheless, the application of FEN in cover spraying was temporarily halted following the release of the Report.

1.6.2 Overview of Health Effects

Organophosphorus insecticides generally elicit adverse health effects by inhibiting acetylcholinesterase (AChE) in the nervous system with subsequent accumulation of toxic levels of acetylcholine (ACh) as a neurotransmitter. Galloway and Handy (2003) reviewed the toxicological effects of OPs in terms of immune systems and functions. Immunotoxicity may be direct via inhibition of serine hydrolases or esterases in components of the immune system, through oxidative damage to immune organs, or by modulation of signal transduction pathways controlling immune functions. Indirect effects include modulation by the nervous system, or chronic effects of altered metabolism/nutrition on immune organs. Other side effects were decreased host resistance, hypersensitivity and autoimmunity. However, they suggested a selection of generic biomarkers to provide the evidence of human immunotoxicity.

With MAL, exposure can cause liver and kidney damage, and irritation to mucous membranes. It also acts as a cholinesterase (ChE) inhibitor and may cause seizure,

nausea, vomiting, airway obstruction, blood disorders, cardiovascular system injury, gastrointestinal disturbances, nervous system injury and/or increased mucous secretions in the lungs (EPA, 2002b).

Acute effects include the degradation of acetylcholinesterase in the tissues, headaches, dizziness, weakness, shaking, nausea, stomach cramps, diarrhoea and sweating. There are no data demonstrating carconogenicity. Chronic exposure can lead to the loss of appetite, weakness, weight loss and general feeling of sickness (ATSDR, 1998a, 2000; PIRSA, 2002).

FEN may cause seizure, nausea, vomiting, airway obstruction and/or increased mucous secretions in the lungs (Gosselin *et al.*, 1984), although chronic exposure symptoms and acute symptoms are qualitatively the same as with MAL. (PIRSA, 2002).

1.6.2.1 Absorption, distribution, metabolism and excretion

MAL

MAL is absorbed by the skin as well as by the respiratory and gastrointestinal tracts. In an oral animal study, more than 90% of MAL dose was excreted in urine within 72 hours, with most excretion in the first 24 hours. MAL did not appear in organs or tissues. The dermal absorption rate for malathion in humans is about 10% (Feldman and Maibach, 1970; ATSDR, 2000). Dermal absorption depends on skin characteristics in different exposed areas (Feldman and Maibach, 1974; Ravovsky and Brown, 1993; Dennis and Lee, 1999).

The major metabolites of malathion are mono- and di-carboxylic acid derivatives, and malaoxon is a minor metabolite. The principal toxicological effect of malathion is cholinesterase inhibition, due primarily to malaoxon and to phosphorus thionate impurities. However, over 80 % of the radioactivity in urine was represented by the diacid (DCA) and monoacid (MCA) metabolites. Only between 4 and 6% of the administered dose was converted to malaoxon, the active cholinesterase inhibiting metabolite of malathion. (Reddy *et al.*, 1989).

The elimination of a methyl group catalyzed by glutathione S-transferase increases MAL metabolism (Bhagwat and Ramachandran, 1975; Malik and Summer, 1982).

Urinary excretion was examined in several studies (Feldman and Maibach, 1974; Ravovsky and Brown, 1993; Dennis and Lee, 1999). Urinary samples provides the identification of metabolites mostly (Lechner and Abdel-Rahman, 1986).

FEN

Fenthion is moderately toxic if ingested, inhaled, or absorbed through the skin. It is oxidized to fenthion sulfoxide and the oxon derivative (Kitamura *et al.*, 2003a, 2003b). FEN and its metabolites were found in the fat of steers slaughtered 3 days after dermal application of fenthion (Hayes and Laws, 1990). FEN was detected from fat, gonads, kidney, muscle and liver (Puhl & Hurley 1982; Crosby *et al.*, 1990). In 1992, Weber & Ecker reported the similar results in terms of gastrointestinal absorption.

FEN was excreted from urine and faeces following oral exposure, and a range of activities were correlated with urinary output, such as brain acetylcholinesterase activity, erythrocyte acetylcholinesterase activity (Brady and Arthur 1961; Inukai & Iyatomi 1981; Puhl & Hurley 1982; Krautter, 1990; Doolottle & Bates, 1993).

1.6.2.2 Mechanism of toxicity

Cholinesterase is one of many important enzymes needed for the proper functioning of the nervous systems of humans. Stimulating signals are discontinued by a specific type of cholinesterase enzyme, acetylcholinesterase, which breaks down acetylcholine, ending the signal. If cholinesterase-affecting insecticides are present in the synapses, however, this situation is thrown out of balance. The presence of cholinesterase inhibiting chemicals prevents the breakdown of acetylcholine. Acetylcholine can then build up, causing overstimulation of the nervous system. Thus, when a person receives to great an exposure to cholinesterase inhibiting compounds, the body is unable to break down the acetylcholine (DHHS, 1993).

Figure 4 shows the mechanism of action of OPs. When the depression of cholinesterase is 15-25%, slight poisoning will be recognized. For moderate poisoning and severe poisoning, the levels are 25-35% and 35-50% respectively. In other words,

if the level of cholinesterase in either plasma or RBC has dropped to 30%, the exposed worker should avoid further exposure (Jane 1987). If exposure to pesticides ceases, the inhibition of cholinesterase is reversible, and the activity of cholinesterase will return to normal. The accumulation of OPs leads a high degree of inhibition and increased signs of poisoning (Machin and McBride, 1989a, 1989b). In humans, the inhibition of cholinesterases in RBCs and plasma is associated with signs of poisoning, such as headaches, blurred vision or vomiting (Moeller and Rider, 1962).

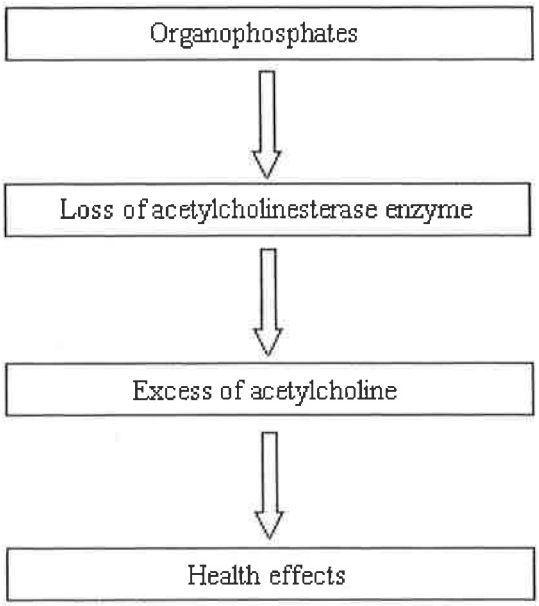


Figure 4: Toxic Mechanism of Organophosphates

1.6.2.3 Skin, eye and mucous membrane effects

MAL

There is a shortage of data about skin, eye and mucous membrane symptoms of humans exposed to MAL.

In animal studies, Relford *et al* (1989) reported mild dermatitis in mice with brief whole body immersion in a dip preparation composed of 8% MAL.

Ekin (1971) found pupillary constriction and blurred vision in humans. According to the study results, the known symptoms were from the stimulation of parasympathetic autonomic postganglionic nerves, common features of organophosphate poisoning. Ocular problems were found, e.g. swelling, irritation, blurring, double vision or poor

vision, mild redness of the periocular tissue and retinal degeneration in general human subjects and animals (Markowitz *et al.*, 1986; Dementi, 1993; Daly, 1996).

FEN

Dean *et al.*, (1967) recognized that the signs of acute poisoning by FEN in humans begins with blurred vision. There is a shortage of data relating to skin and mucous membrane symptoms following FEN exposure. In animal studies, no dermal sensitization was observed (Eigenberg, 1987a, 1987b). However, chronic active inflammation of the skin of the tail and hind limbs was detected (Christenson, 1990a).

1.6.2.4 Respiratory effects

MAL

In animal studies, known symptoms are hyperplasia of the olfactory and larynx epithelia, dyspnea and respiratory distress which may be caused by the stimulation of parasympathetic postganglionic nerves or diaphragmatic failure (Prabhakaran *et al.*, 1993; Beattie, 1994; Piramanayagam *et al.*, 1996).

FEN

From experimental animal studies, FEN exposure is associated with inflammatory changes of the respiratory tract and correlates with the magnitude of cholinesterase inhibition after dermal administration (Thyssen, 1978; Christenson, 1990b).

1.6.2.5 Genotoxicity and cancer

MAL

A range of in vitro and in vivo studies have examined the possibility of genotoxicity and cancer from FEN exposure. Griffin and Hill (1978) reported a break of purified colicinogenic plasmid E1 DNA from MAL. Sister chromatid exchanges were observed in human lymphoid cells and lymphocytes, in human fetal fibroblasts, and Chinese hamster ovary cells (Nicholas *et al.*, 1979; Nishio and Uyeki, 1981; Sobti *et al.*, 1982; Balaji and Sasikala, 1993). From in vivo studies, significant numbers of

chromosomal aberrations, abnormal metaphases were observed (Dulout *et al.*, 1983; Dzwonkowska and Hubner, 1986). Balaji and Sasikala (1993) reported that MAL causes a dose-dependent increase in chromosome aberrations as well as sister chromatid exchanges in human leukocyte cultures. Thus MAL may contribute to genotoxicity in humans. In 2002, Giri *et al.*, found significant increases of chromosome aberrations, sperm normalities without any affect of a number of sperm and the significant increase of SCE. They concluded that technical grade MAL may cause potential genotoxicity and germ cell mutagenesis.

From a human study, Reeves and coworkers (1981) found that blood disorders, acute lymphoblastic leukemia and aplastic anemia occurred after exposure to MAL. Cabello *et al.*, (2003) examined the possibility of MAL inducing the progression of malignant transformation of a human breast epithelial cell line, MCF 7. According to the results, MAL increased PCNA and induced MCF7 and atropine inhibited the effect of such substances.

FEN

The National Cancer Institute (NCI) (1979b) indicated FEN as a possible insecticide of carcinogenicity to male mice, when technical-grade FEN (0-1.0 mg/kg/day bw) was fed to rats for 103 weeks. However, no carcinogenic effect to rats and mice was found in a subsequent report (ACGIH, 1986).

1.6.2.6 Other effects

MAL

From a human study, Reeves *et al.*, (1981) found that blood disorders, acute lymphoblastic leukemia and aplastic anemia occurred after exposure to MAL. There are other symptoms related to MAL exposure in humans. The development of renal insufficiency occurred by exposure to MAL (Albright *et al.*, 1983). With organophosphate pesticides handlers for over 29 years, there were marked impairments of neutrophil chemotaxis and significant decrease of neutrophil adhesion (Hermanowicz and Kossman, 1984).

Significant symptoms were detected, e.g. diarrhoea, constipation or painful bowel movements, abdominal cramping, diarrhoea, nausea and vomiting (Healy, 1959; Amos and Hall, 1965; Markowitz *et al.*, 1986). Rupa *et al.*, (1991) found that the percentage of stillbirths and abortions are higher than an unexposed group.

There have been cardiovascular effect studies of MAL poisoning (Rivett and Potgieter, 1987; Crowley and Johns, 1996). In long-term studies, there is no report of adverse cardiovascular effects from rats and mice (NCI, 1979a; Slauter, 1994).

FEN

There are a range of animal study results for other symptoms, such as decreased fertility, decreased number of implantation sites per dam, decreased litter size, increased number of stillborn pups per litter, reduced viability index, decreased pup body weight, developmental toxicity, increased haemosiderosis, increased body weight, a slight increase in spleen weight with splenic congestion, extramedullary haematopoiesis and haemosiderosis, teratogenic effects (Doull *et al.*, 1963a, 1963b; Machemer, 1978a, 1978b; Shepard, 1984; Clemens, 1987; Kowalski, 1987; Kowalski *et al.*, 1989; Suberg & Leser, 1990).

In short-term studies, there were decreased activity and ataxia, hypertrophy or hyperplasia of the oesophageal glandular components (Hayes and Ramm, 1988; Hayes, 1989). In a chronic study, no clinical sign of peripheral neuropathy or myopathy and no pathophysiological findings indicative of any reversible neurological deficits were observed (Misra *et al.*, 1985, 1988).

1.6.3 Exposure Criteria

MAL

The Acceptable Daily Intake (ADI) of MAL is 0.02 mg/kg, and 1.6 mg/day is the value for 80kg adults. It is based on a No-Observed-Adverse-Effect Levels (NOAEL) of 0.23 mg/kg/day. The Lowest-Observed-Adverse-Effect Levels (LOAEL) was 0.34 mg/kg/day (Moeller and Rider, 1962).

According to Daly (1996), a chronic oral MRL is 0.02 mg/kg/day. It was based on a NOAEL of 2 mg/kg/day for the inhibition of plasma and red blood cell cholinesterase

activities in humans. The LOAEL was 29 mg/kg/day. The Oral Reference Dose (RfD)was defined with 0.02 mg/kg/day by IRIS (2001). It was based on 0.23 mg/kg/day of a NOAEL for the inhibition of plasma and red blood cell cholinesterase activities in humans and the LOAEL was 0.34 mg/kg/day.

The TWA Australian occupational exposure standard (OES) is 10 mg/m^3 (NOHSC, 1995a). The American Conference of Governmental Industrial Hygienists (ACGIH, 2001) Threshold Limit Value (TLV-TWA) is 10 mg/m^3 with skin notation, based on cholinergic effects.

Red cell and plasma cholinesterase activity levels are recommended for biological monitoring of workers using organophosphate pesticides.

There should be a repeat test if there is a 20% depression of cholinesterase activity. In addition, if cholinesterase activity has fallen by 40% or more, the worker should be moved to the area which is free of the organophosphate pesticides until the level returns to baseline levels (NOHSC, 1995b).

FEN

The Australian Therapeutic Goods Administration (TGA) has established an ADI for FEN of 0.002 mg/kg/day for a 70-year lifetime (PIRSA, 2001). The World Health Organization ADI is 0.007 mg/kg/day.

Several animal studies have assessed acute toxicity levels in terms of oral, dermal and inhalation (Doull *et al.*, 1961, 1963a; Klimmer, 1963, 1971; Mobay Chemical Corporation, 1981a, 1981b; BCPC, 1983; Meister *et al.*, 1984; Bailey, 1987, 1988; Suberg & Leser, 1990; NIOSH, 2002).

The TWA OES is 0.2 mg/m^3 (NOHSC, 1995a). ACGIH recommends the same value with a skin notation, based on cholinergic effects. There is no carcinogen classification (PIRSA, 2002; EPA, 2002b).

1.6.4 Previous Research

The pesticides (MAL and FEN) were examined partly due to concerns about occupational exposure during the Mediterranean fruit fly eradication programs.

In order to understand the risks of adverse health effects, related studies should be reviewed. However, in the case of MAL few comparable studies have been published.

MAL: Health Effect Assessment

There is a shortage of published literature on adverse health symptoms potentially caused by MAL exposure during Mediterranean fruit fly eradication programs (Dept. of Preventive Medicine, 1992; Kahn *et al.*, 1992; Schanker *et al.*, 1992; Thomas *et al.*, 1992; MMWR, 1998).

The Department of Preventive Medicine at the University of Southern California (1992) identified an association between abortion and exposure to MAL, applied to control the Mediterranean fruit fly. In this study, 933 pregnancies were surveyed. It was found that the risk of gastrointestinal disorders in children exposed to MAL during the second trimester of pregnancy was over two and one-half times more than for children who are not exposed to MAL during pregnancy. However, there was no relationship between MAL exposure and adverse health symptoms, such as spontaneous abortion, intrauterine growth retardation, stillbirth or most categories of congenital abnormalities.

During the period of the study, no investigation of subtle neurological disorders such as language delays, attention deficits, learning disabilities, hyperactivity or conduct disorders was conducted.

Relationships between allergic skin reactions (urticaria, angioedema and nonspecific skin rash) and immediate or delayed types of hypersensitivity reactions potentially arising from repeated exposure during MAL baiting were studies by Schanker *et al.* (1992). For this study, ten subjects were selected, but only one case represented a possible immediate IgE reaction to MAL baiting.

Acute health effects from the spray application of MAL bait were assessed by Kahn *et al.* (1992). Self-reported symptoms from on-site health interviews were headaches (20.6%), shortness of breath (7.6%), cough (9.7%), watering eyes (13.9%), difficulty

breathing (4.2%) and skin rash (4.6%). No acute health effects were reported from the surveillance of hospital data, review of ambulance dispatches and a review of emergency treatment. In addition, no significant acute morbidity was reported from personal interviews conducted before and after MAL bait spraying.

Thomas *et al.,* (1992) investigated 7,450 women pregnant during a period of MAL application. There was no evidence for an association between MAL exposure and spontaneous abortion, intrauterine growth retardation, stillbirth or congenital abnormalities. However, a moderate relation between stillbirths and exposure accumulated up to 1 month before death was found.

A study of potential health effects arising from MAL exposure was conducted in Florida (MMWR, 1998). The public was surveyed via telephone hotlines. Of the 230 calls, 123 individuals were identified as possible cases with adverse health symptoms. Of the 123, 72% were female (median 46.5 years), 7% were children (≤5 years), 16% were older people (≥65 years) and 3% were people whose health symptoms could be related to their work, such as pesticide workers or gardeners.

The following distribution of symptoms was reported:

71% respiratory (dyspnea, wheezing, coughing and upper respiratory tract pain and irritation);

63% gastrointestinal (nausea, vomiting, diarrhea, melena and abdominal cramping);

60% nervous (headaches, vertigo, ataxia, peripheral paresthesia, disorientation and confusion);

23% skin (erythema, pruritis and burning sensations);

19% of the eyes (lacrimation, conjunctivitis, blepharitis and blurred vision).

More than one symptom or experience was reported by some people. It was suggested the symptoms were likely to be related to MAL exposure, even if only small quantities of MAL were applied in the eradication program.

Taylor (1963) suggested that children under the age of seven are more sensitive to the anticholinesterase effect than adults. However, good evidence for this assertion was lacking.

Biological Monitoring

Biological effect monitoring strategies have been developed, using endpoints related to genotoxicity. There have been several *in vivo* studies with humans exposed to MAL (Van Bao *et al.*, 1974; Titenko-Holland *et al.*, 1997; Singaravelu *et al.*, 1998; Windham *et al.*, 1998). When an exposed group was compared with an unexposed group, no differences were seen in proliferation or micronucleus levels in lymphocytes (Titenko-Holland *et al.*, 1997; Windham *et al.*, 1998). However, according to Singaravelu *et al.*, (1998), there was a significant difference in chromatid aberrations, in the case of individuals exposed to MAL for 11-20 years, when compared with an unexposed group. These biological effect approaches have advantages in representing integrated pesticide exposures over weeks to months and have been shown to be very sensitive markers of exposure (Hatjian *et al*, 1993).

Exposure Assessment/Work Practices

MAL and FEN exposure levels were reported from several studies (Garrod *et al.* 1998; Tuomainen *et al.* 2002; Machera *et al.*, 2003).

Twenty surveys from 15 sites spraying remedial pesticide were conducted to measure surface deposition and inhalation exposure levels (Garrod *et al.*, 1998). Coveralls, protective gloves and socks were surveyed for deposition rates. The applied pressures were 320 and 1050 kPa. Deposition rates of coveralls were between 27.4 and 6550 mg/minute (209 mg/minute-median). On the body, the depositions on the legs, the arms, the torso and the head were 75%, 11%, 12% and 2% respectively. Beneath protective gloves, the exposure levels of the hands were between 0.2 and 358 mg/minute (5.8 mg/minute-median). According to the observation of the authors, skin contact arose from contaminated surface or outside of the gloves during their removal. Also, it was thought that the contamination of hands might contribute the contamination of inside gloves. For inhalation exposure, TWA ranged between 4.33 and 1320 mg/m^3 (53.5 mg/m^3-median) in survey.

Potential dermal exposure and biomarkers (MAL monocarboxylic acid, MMA) in urine were measured from pesticide (MAL) applicators (Tuomainen *et al.*, 2002). The workers applied MAL to roses in green houses. The urine was collected within 24 hours after starting the application. Dermal monitoring was conducted during the application as well. Several parts of the body were measured, such as the upper limbs (19%), the lower limbs (48%), the hands and chest (30%) and back and head regions (3%). From the urine samples, small amounts of MMA were detected. Also, the excretion of MMA was extremely fast at 6-7 hours after the application.

From this study, a range of factors influenced exposure, such as working skill, behavior, time, area and tool (spray gun) and spray volume and density. In addition, the leaking and spillage of spraying solution from hoses were also observed.

Whole body dosimetry has been applied to MAL spray applicators to determine potential dermal and inhalation exposure levels (Machera *et al.*, 2003). The proportions of pesticide deposition on the body were 0.05 and 0.07% of the applied spray solution with low-pressure knapsack (3 bar), and 0.09–0.19% of the spray solution applied with tractor-generated high pressure (18 bar). For air monitoring and hand monitoring, XAD-2 sampling tube and cotton/rubber gloves were used respectively. It was found that dermal (hands) exposure and inhalation exposure are related to the application pressure.

FEN: Health Effect Assessment

Several case studies looking at health symptoms associated with FEN exposure have been published (von Clarmann & Geldmacher-von Mallinkrodt, 1966; Dean *et al.*, 1967; Wadia *et al.*, 1977).

Dean *et al.*, (1967) reported on a man who had taken an unknown quantity of FEN. He suffered from significant respiratory difficulty, even after 72 hours of emergency treatment. Wadia *et al.*, (1977) studied patients poisoned by FEN. There was no pulmonary oedema after FEN poisoning.

FEN is able to irritate eyes and mucous membranes. A FEN formulation was ingested by a man and adverse symptoms were observed 45 minutes later (von Clarmann & Geldmacher-von Mallinkrodt, 1966). Cyanotic mucous membranes and no reactions to pain or light on the pupil were observed with recovery after 8 days of treatment.

Biological Monitoring

In order to assess overall exposure levels, biological monitoring can be conducted via urine and blood samples. Urinary metabolites for OPs and cholinesterase activity can be monitored. Several researchers have reported biological monitoring data for MAL (Moeller and Rider, 1962; Wester *et al.*, 1983) and FEN (Elliot & Barnes, 1963; Taylor, 1963; Pickering, 1966; Fytizas-Danielidou, 1971; Wolf *et al.*, 1974; Simmon *et al.* 1977; Mahiey *et al.* 1982; Misra *et al.*, 1985, 1988; Brunetto *et al.*, 1992; Cocker *et al.* 2002).

Elliot and Barnes (1963) observed that individuals exposed to a high quantity of FEN used for malaria eradication causes slight plasma cholinesterase depression.

An individual taking 60 g of a FEN formulation called ENTEX ® (95-98% pure) was observed (Pickering, 1966). He suffered from clinical conditions for six days after the accident. But after the poisoning, the depression of blood cholinesterase activity was sustained by 22 days. Workers who controlled the mosquito were exposed to FEN via skin (3.6-12.3 mg/h) and inhalation (< 0.02-0.09 mg/h) during chemical application (Fytizas-Danielidou, 1971; Wolf *et al.*, 1974).

Brunetto *et al.*, (1992) reported the relationship between clinical signs, cholinesterase activity and FEN levels following oral ingestion of FEN. For this evaluation, plasma cholinesterase (PChE) activity and FEN concentration were examined during the therapeutic intervention to determine whether they are predictive of clinical outcome and the efficacy of treatment. However PChE activity was not sufficiently predictive of the likelihood of sudden relapses.

Several OPs including FEN were investigated, with the objectieve of estimating exposures through the skin (Cocker *et al.*, 2002). Urine and blood samples were collected and total urinary alkyl phosphates were measured. It was concluded that urinary alkyl phosphates were more suitable than ChE for occupational and environmental studies.

1.7 HDI-based Isocyanates in Automobile and Furniture Industries

This section introduces specific procedures, toxicology and previous research.

1.7.1 Introduction

Organic isocyanates are compounds containing the isocyanate group (-NCO). They react with alcohol (hydroxyl) groups to produce polyurethane polymers, for foams and paints. Polyurethane products are manufactured for several industries, such as cars, airplanes, furniture and bedding.

Table 2: Common Organic Isocyanates Diisocyanates and Physical Characteristics

Abbreviation	Chemical name	Formula
TDI	Toluene diisocyanate	$CH_3C_6H_3(NCO)_2$
MDI	Methylene bis (4-phenylisocyanate)	$OCN\text{-}C_6H_4\text{-}CH_2\text{-}C_6H_4\text{-}OCN$
HDI	Hexamethylene diisocyanate	$C_{15}H_{12}N_2O_2$
IPDI	Isophorone diisocyanate	$C_{12}H_{18}N_2O_2$

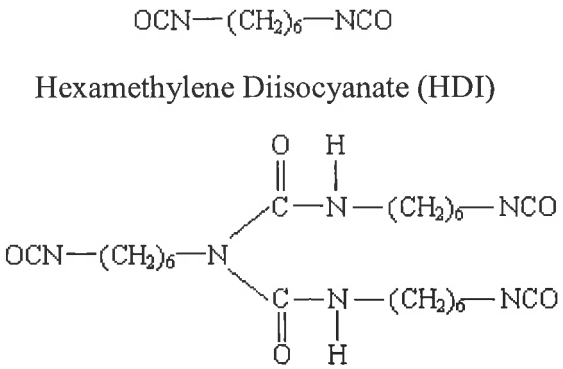
Isocyanate	Appearance	MW[1)]	B.Pt.[2)] (°C)	Vapour pressure (mm Hg)
TDI[3)]	colourless/pale yellow liquid, pungent odour	174	250[4)]	0.025 (25 °C)
MDI	brown, viscous liquid or white odourless flakes (pure)	250	314[5)]	0.00009 (25 °C)
HDI	colourless liquid	168	213	0.05 (25 °C)
IPDI	colourless/yellow liquid	222	158[6)]	0.003 (20 °C)
MIC	volatile liquid	57	38	348 (20 °C)

1) Molecular weight
2) Boiling Point
3) Commercial TDI is a liquid at room temperature and consists of 2,4 and 2,6 isomers in the proportion of 65:35 or, more commonly 80:20.
4) 80:20 mixture
5) Begins to decompose at about 232 °C
6) At 10 torr.

Common isocyanates used are methylene bisphenyl diisocyanate (MDI), toluene diisocyanate (TDI), hexamethylene diisocyanate (HDI) and isophorone diisocyanate (IPDI). See Table 2.

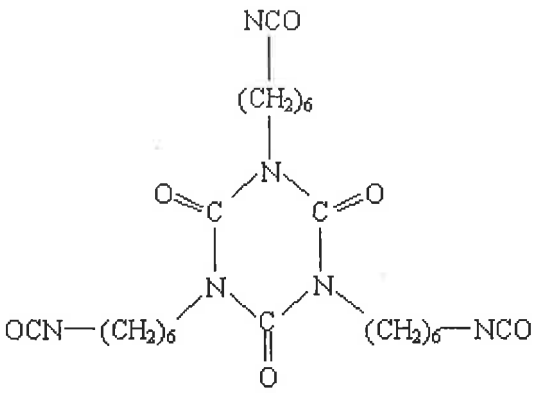
Isocyanates, dissolved in aromatic solvents, such as xylene and toluene, are found in hardeners of two-part paints and primers. Due to the inhalational hazard associated with monomers, most isocyanates are supplied as oligomers (prepolymers).

1,6-Hexamethylene diisocyanate (HDI), also known as Mondur HX and Desmodur H, is a common aliphatic diisocyanate. In HDI-based hardeners, the biuret and isocyanurate trimers are regularly used. (ATSDR, 1998a; OSHA, 1998). Figure 5 represents the chemical structures of HDI-based polyisocyanates. Physical and chemical properties are described in many studies (NIOSH, 1978; Lewis, 1993; Von Burg, 1993; HSDB, 1995).



Hexamethylene Diisocyanate (HDI)

HDI biuret trimer



HDI isocyanurate trimer

Figure 5: Chemical structures of HDI and HDI trimers

Approximately 50% of HDI prepolymers are biurets containing 0.7-1.6% monomer. The other 50% are isocyanurate trimers containing 0.2% monomer. However, even though high airborne levels of HDI oligomers can occur during spray painting, it is difficult to determine whether the monomer or polymer causes adverse health effects

(Huynh *et al.*, 1992). At the time of manufacture, monomer content is less than 0.7% based on resin solids. However, after 3-6 months storage, the free monomer content may rise to a maximum of 1.6% (EHSD, 2001).

Exposure to HDI-based products is common in spray painters working in the automobile industry and in furniture manufacture in SA and elsewhere.

An estimated 153,000 auto body repair workers have the potential for some exposure to paint containing HDI in the UK (Meredith *et al.*, 1991). The Motor Trade Association (MTA) represents over 1,400 businesses in SA. Approximately 20% of these are directly involved with crash repair (Mohanu, 1996).

Automotive refinishing includes autobody repair/paint shops, production autobody paint shops, new car dealer repair/paint shops, fleet operator repair/paint shops and customade car fabrication. According to Heitbrink (1995), the major air contaminant in automobile shops and refinishing industries was polyisocyanates.

In the case of the furniture industry, it was reported that continuous exposure to isocyanates increased the risk of developing respiratory symptoms for workers in companies using large quantities of isocyanate-paints (Mastrangelo *et al.*, 1995). Talini *et al.* (1998) examined exposed spray painters and unexposed workers (woodworkers and assemblers). Significant adverse health symptoms were noted for isocyanate-exposed workers.

1.7.2 Overview of Health Effects

The focus of this subsection is on HDI-based products.

Little information about the toxicokinetics of HDI has been available. HDI can be hydrolyzed in aqueous media, even if the process is slow. 1,6-hexamethylene diamine (HDA) is the major urinary metabolite.

According to Tse and Pesce (1979), free HDI may combine with serum proteins.

HDI can have effects on various tissues and organs in the human body. This effect may occur within a short period of time (acute effect) or over a long period of time by repeated exposure (chronic effects). According to ATSDR (1998b), known acute symptoms are likely to be shortness of breath, burning sensation of respiratory passages, nausea, headaches and increased proneness to accidents. An allergic

respiratory reaction similar to an asthma attack can occur in some individuals with prolonged or repeated previous exposure or a large single exposure to HDI. Several respiratory toxicological symptoms were observed with exposures over 0.0006 ppm of HDI (monomer) (Von Burg, 1993). The observed signs are burning and irritation of the nose, throat and mucous membranes of the lungs, cough, laryngitis, bronchitis, tightness of the chest, hoarseness, pulmonary edema, emphysema, car pulmonale and asthma-like syndrome. It is known that HDI biuret and trimer can cause respiratory and immunological reactions which are similar to the HDI monomer in human and animal studies (Belin *et al.*, 1981; Weyel *et al.*, 1982; Alexandersson *et al.*, 1987; Ferguson *et al.*, 1987; Usui *et al.*, 1992).

Acute skin contact may cause rashes, blistering and reddening of the skin. Repeated skin contact may cause skin sensitization. Long term diverse adverse health efects are possible; kidney and liver dysfunction with possible central nervous system effects, allergic, asthma, shortness of breath, wheezing, bronchitis, coughing, redness, irritation and skin damage. Evidence is lacking on carcinogenesis.

Ocular exposure to airborne isocyanates can cause eye irritation and temporary blurred vision. Direct contact with the eye may cause damage to the cornea.

1.7.2.1 Absorption, distribution, metabolism and excretion

The main absorption of HDI is by inhalation or skin contact. When inhaled, HDI binds to human tissues, proteins and DNA, forming adducts which may cause adverse health effects.

HDI monomer may be metabolized by hydrolysis to amines excreted from urine (Berode *et al.*, 1991). Liu *et al.*, (2004) suggested that the metabolism of HDI biuret aerosol can follow a similar mechanism to that of HDI monomer. However, HDI is reactive and unstable and high analytical sensitivity is required (Streicher *et al.*, 2002).

Brorson *et al.*, (1990a) examined the urinary metabolite, 1,6-hexamethylene diamine (HDA), after oral administration of HDI. The half-life of HDA in urine was between

1.1 and 1.4 hours. Brorson *et al.*, (1990b) detected the accumulative excretion of HDA after acute respiratory exposure. When urinary samples were collected immediately after the exposure, HDA started to accumulate in urine. In a recent study, the urinary HDA concentration decreased to the pre-exposure levels 20 hours after cessation of exposure. (Liu *et al.*, 2004).

1.7.2.2 Mechanism of toxicity

Even though there is no specific information on the mechanism of toxicity, Karol (1986) and Von Burg (1993) have suggested that the mechanism is likely to be related to the reaction with biological macromolecules and various proteins in the body.

1.7.2.3 Skin, eye and mucous membrane effects

It is well known that isocyanates cause skin irritation and affects mucous membranes. Hardy and Devine (1979) reported on severe chemical conjunctivitis following splashes in the eye. Stadler and Karol (1985) found that the greater the dose of HDI, the more intense of erythema ($p < 0.05$). Mobay Corporation (1981b) reported severe congestion, skin thickening, moderate to severe erythema and slight corrosion. Karol (1986) stated isocyanates may cause contact dermatitis or skin sensitization. However, skin sensitization may occur as a result from a spill or other accidents. After skin sensitization, subsequent exposure can cause rash, itching, hives or swelling of the arms and legs.

Severe eye symptoms were found from animal studies, e.g. lacrimation, a slit-shaped opacity of the cornea, severe conjuntival inflammation, corneal injury, damage of iris, moderate corneal injury and iris, inflamed eyelids, moderate eye irritation to the conjunctiva, and severe damage of the cornea, iris and conjunctiva. (Haskell Laboratory, 1961; Mobay Corporation, 1966; Mobay Corporation, 1981a, 1984, 1989).

1.7.2.4 Respiratory effects excluding asthma

Inhalation of isocyanates mainly causes respiratory effects, such as chemical bronchitis with initial symptoms of throat irritation, laryngitis, coughing, and chest pain or tightness (Phillips and Peters, 1992). A symptomatic change in lung function was also reported (Musk *et al.*, 1988).

Symptoms also included mild respiratory distress, marginally decreases body weight, increasing lung weights, increased recruitment of alveolar marcrophages, focal interstitial fibrosis with round-cell infiltrations, bronchiolo-aveolar proliferations, unequivocal changes in respiratory patterns and a bronchial influx of eosinophilic granulocytes (Pauluhn and Mohr, 2001; Pauluhn *et al.*, 2002). However, HDI-monomer induced more specific IgG antibody than HDI-homopolymer (Pauluhn *et al.*, 2002).

In short term exposures, acute symptoms were chest tightness, cough, shortness of breath wheezing, malaise, chill, pulmonary irritation, lung weight, lavage fluid protein, recover of neutrophils in lavage fluid, proliferative (Belin *et al.*, 1981; Banks *et al.*, 1986; Hagmar *et al.*, 1987; Vandenplas *et al.*, 1993; Baur *et al.*, 1994; Akbar-Khanzadeh and Riva, 1996; Lee *et al.*, 2003). For longer durations, the Haskell Laboratory (1961) found bronchitis, bronchopneumonia and also respiratory impairment with labored breathing and irritation.

Lung function and blood tests implemented by Malo *et al.*, (1983) suggested a bronchial reaction (decreases in FEV_1/FVC ratios as well as a late obstructive and restrictive breathing defect) after exposure.

1.7.2.5 Occupational asthma

Isocyanates have long been suspected as being causes of occupational asthma. Meredith *et al.* (1991) argued that the diisocyanates used in a variety of applications in many industries can be a main cause of OA. Occupational asthma is induced by sensitization to variety of substances (Chan-Yeung and Lam, 1986) without specific mechanisms (Karol, 1988; Kennedy *et al.*, 1989; Deschamps *et al.*, 1998).

Isocyanates are currently the most common causes of occupational asthma (Park, 1997; Park and Nahm, 1996). Agencies, such as HSE, OSHA and NIOSH, have

expressed concern about the potential health risk that may result in workers exposed to HDI. Piirila *et al.* (2000) reported on a long-term follow-up study covering the period 1976-1992. Of 245 new cases of asthma caused by diisocyanates, a high percentage of cases were induced by HDI (39%) and MDI (39%), with others being TDI (17%).

Symptoms may occur within a few days or weeks after exposure to isocyanates and symptoms or reactions can last several months or years after the end of exposure (Fabbri and Mapp, 1992).

Deschamps *et al* (1998) suggest that isocyanate asthma may be induced via several mechanisms, notably immunological, pharmacological and/or irritative. It is thought that asthma is multifactorial and there is no general agreement on mechanisms.

In a recent study, Di Stefano *et al* (2003) studied occupational asthma in industrialized countries in terms of serum specific IgE to isocyanates. However, isocyanate-specific IgE could not provide a complete understanding.

It is known that the respiratory tract is the primary route of sensitization. However, according to recent animal studies, dermal exposure to isocyanates may cause respiratory sensitization (Karol *et al*, 1981; Erjefalt and Persson, 1992; Rattray *et al.*, 1994).

1.7.2.6 Genotoxicity and cancer

There was no evidence of human carcinogenic potential from HDI exposure. Animal studies have also been negative (Mobay Corporation, 1989).

1.7.2.7 Other effects

In a study by the Haskell Laboratory (1961), very significant respiratory impairment and cyanosis were observed during exposure. But no changes in blood chemistry, serum chemistry and hematology were reported (Mobay Corporation, 1988, 1989). Karol *et al.*, (1984) reported no significant change in plasma cholinesterase by inhalation.

In an intermediate-duration study, decreased kidney weight was observed, and in a chronic-duration study, no significant change of kidney weight was detected (Mobay Corporation, 1984, 1989). Inflammation of the stomach mucosa, and diarrhoea have been reported (Haskell Laboratory, 1961; Mobay Corporation, 1984, 1989).

1.7.3 Exposure Criteria

The National Occupational Health and Safety Commission Occupational Exposure Standard (NOHSC, 1995a) is designed to prevent respiratory sensitization. The 8-hour time weighted average (TWA) value for all isocyanates (as -NCO) is 0.02 mg/m^3. The 15 minute STEL for all isocyanates (as -NCO) is 0.07 mg/m^3. TLV-TWA is 0.034 mg/m^3 (ACGIH, 2001).

1,6-Hexamethylene diamine (HDA) is a biomarker of short-term exposure to HDI (Brorson *et al.*, 1990a, 1990b; Dalene *et al.*, 1990, 1994) but there are no exposure standards.

1.7.4 Previous Research

For this study, articles were reviewed in terms of ambient monitoring including PPE monitoring, surveys (health symptoms), biological monitoring and working conditions (e.g. spray booth).

Exposure Assessment/Work Practices

A number of studies provided exposure data and information on protective equipment usage (Pisaniello and Muriale, 1989a; Janko *et al.*, 1992; Heitbrink *et al.*, 1993a; Cooper *et al.*, 1993; Cushmac *et al.*, 1997; Liu *et al.*, 2001b, 2004).

Pisaniello and Muriale (1989a) found personal exposures associated with operations where dusts or aerosols are not generated, such as paint mixing and spray gun washing, to be very low, typically 1 $\mu gNCO/m^3$. No measurements exceeded 2 $\mu gNCO/m^3$, even when sampling directly over open containers of hardener.

For the spraying of two-pack (primer/filler)undercoat, breathing zone concentrations ranged from 7 to 180 μgNCO/m^3 ; for solid colours (topcoat), 8 to 3500 μgNCO/m^3 and for the spraying of a clearcoat (topcoat), 9 to 550 μgNCO/m^3.

In an inhalational exposure study, Heitbrink *et al.,* (1993a) reported exposures between 17-190 μgNCO/m^3 using NIOSH Method 5521. Cooper *et al.,* (1993) reported on control technologies for autobody repair and painting shops. In the case of small painting tasks, spray booth air velocities were often too low to control air contamination. Also, inappropriate usage and knowledge of respiratory protection was observed.

Cushmac *et al.,* (1997) reported the usage of respiratory protection. Full face air and half face air purifying respirators with organic vapor cartridges and pre-filters for mists, were not used appropriately. They were not maintained properly or were kept in poor storage conditions.

From the study conducted by Janko *et al.,* (1992), 0.001 ppm of HDI monomer (GM) and 0.7-12.2 mg/m^3 of HDI polyisocyanate (GM 3.8 mg/m^3) were measured from spray painting in an industrial spray operation. In autobody shops, HDI monomer (GM) and HDI polyisocyanates (GM) were 0.014 mg/m^3 and 1.67 mg/m^3 respectively. Liu *et al.,* (2004), using the *Isocheck* treated-filter method for HDI biuret aerosol, reported exposure levels (GM) for monomer, oligomers and total reactive isocyanate group of 53.8 μg/m^3, 98.7 μg/m^3 and 58.2 μgNCO/m^3 respectively.

Liu *et al.,* (2001b) reported on quantitative levels of surface contamination and skin contamination in autobody shops, and the effectiveness of PPE. From 20 shops, high contamination levels of surface were measured from hardener containers (2.9-108.1 μg/in^2), bench top (0.8-25.9 μg/in^2), rulers (0.5-6.3 μg/in^2) and gloves (0.11-4.7 μg/in^2). From the skin, the average exposure levels of monomer and oligomer were 0.3±2.9 μg/in^2 and 0.01±3.1 μg/in^2 respectively. Under PPE, levels of 0.5±2.3 μg/in^2 were found, suggesting inadequate protection. In addition, they concluded that due to painting activity in auto body shops, surface contamination and skin exposure to isocyanates is common, and that skin exposure can contribute significantly to total isocyanate exposure can.

Health Effect Assessment

Symptoms were reported in several studies (Alexandersson *et al.*, 1987; Pisaniello and Muriale, 1989a, 1989b; Torniling *et al.*, 1990; Parker *et al.*, 1991; Usui *et al.*, 1992; Mastrangelo *et al.*, 1995; Randolph *et al.*, 1997; Ucgun *et al.*, 1998; Talini *et al.*,1998).

Alexandersson *et al.,* (1987) observed respiratory symptoms. Significant difference was observed compared with controls (n=70). From the study, it was argued that peak exposures to isocyanate (HDI) might better relate to respiratory disease than 8-hour averages. However, no statistical significant spirometric change was observed during a week. Tornling *et al.,* (1990) conducted a followup study with similar conclusions.

A survey of isocyanates exposures in workshops was conducted in SA (Pisaniello and Muriale, 1989a). From the survey, respiratory and skin problems (cough, phlegm, short of breath, chest tightness and skin irritation or dermatitis) were found to be common among spray painters. The prevalences differed significantly from mechanics not exposed isocyanates.

From this survey work, poor work practices and inadequate personal respiratory protection were observed. Also, the lack of educational programs for employees and the difficulty of applying regulations to small business were evident (Pisaniello and Muriale, 1989b).

Mastrangelo *et al.,* (1995) surveyed furniture workers in the Veneto region of Italy. From the survey, it was reported that the risk of the development of occupational asthma could be increased by continuous exposure to isocyanates. Ucgun *et al.,* (1998) also surveyed the prevalence of occupation asthma among automobile and furniture spray painters in Turkey. They reported similar results.

In 1997, the respiratory health status and dermatitis among spray painters using HDI products were reported in a cross-sectional study (Randolph *et al.*, 1997). Chronic respiratory symptoms, cough, wheeze and wheeze with breathlessness were reported. Eye irritation (55%) and dermatitis of the hand (32%) were also reported, due to poor ventilation systems and PPE usage.

In 1998, Talini *et al.,* published a study investigating respiratory symptoms, asthma, atopy and bronchial responsiveness. For spray painters, the prevalence of attacks of shortness of breath with wheezing, dyspnoea and asthma-like symptoms plus non-

specific bronchial hyperreactivity were 13.5% (woodworkers: 7.7%, assemblers: 1.6%), 11.5% (woodworkers: 6.3%, assemblers: 1.6%) and 13.3% (woodworkers: 10%, assemblers: 4%) respectively. Also, a high prevalence of chronic cough, and wheeze were reported from spray painters. In this study, atopic spray painters were deemed to be at higher risk of OA than other workers.

Biological Monitoring

Biological monitoring data have been reported for spray painters using HDI products (Tinnerberg *et al.* 1995; Williams *et al.*, 1999; Liu *et al.* 2000, 2001a; Redlich *et al.* 2001, 2002; Wisnewski *et al.*, 2003; Liu *et al.*, 2001a, 2004).

Williams *et al.*, (1999) detected urinary HDA from 4 spray painters out of 22 workers working in motor vehicle repair shops. However, no HDA was found in the urinary samples of unexposed subjects. They concluded that exposure could occur even if the spray painters wore protective equipment and used appropriate extraction systems.

Interestingly, HDA was measured in the urine of a bystander, when spraying was conducted out of the booth.

Liu *et al.,* (2001a) studied urinary HDA as a biomarker of HDI from 10 small autobody shops. In the case of some of workers exposed to 0.17 mg/m^3 HDI, the maximum urinary HDA level was 27 μg/g creatinine. The measured average levels of HDA of spray painters, technical repairs and administrative workers were 1.44 μg/g, 1.3 μg/g and 0.88 μg/g respectively. As a result of this study, latex gloves were not recommended for spray painters using isocyanate (HDI).

Two studies were conducted by Redlich *et al.,* (2001, 2002). In 2001, a cross sectional study was conducted with 75 subjects. Two major observations were made for exposed workers, i.e. HDI-specific lymphocyte proliferation (30%) and HDI-specific IgG (34%). Although there was no relationship between asthma and HDI-specific IgE, there was an increase in methacholine responsiveness, HDI-specific lymphocyte proliferation, chest tightness and shortness of breath for the group exposed to HDI. In this study, it was suggested that subclinical diisocyanate asthma may be not easy to identify using conventional screening and diagnostic modalities.

In the one-year follow-up study (2002), 34 subjects staying at the same shops and 11 subjects who had left the shops were observed. There were significant differences, e.g. a history of asthma - 23 vs. 3% ($P < 0.05$), bronchial hyper-responsiveness - 23 vs. 9%, HDI-specific IgG - 64 vs. 29% ($P < 0.05$), and HDI-specific proliferation-S.I. 2.0 vs. 1.3 ($P < 0.05$). In this follow-up study, there were no statistically significant changes in physiology, and immunologic responses.

Wisnewski *et al.,* (2003) conducted the first study of immune response to HDI exposure in automobile body industry. Blood samples were collected from exposed workers and an unexposed group. For the exposed group, increased proliferation of specific cell types was detected. They were expressed by unique oligoclonal gamma/delta T-cells. It appears from this study that HDI can selectively stimulate gamma/delta T cells which potentially modulate the human immune response to exposure.

In a human study to assess respiratory exposure to HDI aerosol, urinary hexane diamine (HDA) was used (Liu *et al.*, 2004). The samples were collected from spray workers at 23 autobody shops producing HDI biuret aerosol and vapor. Before the urinary monitoring, baseline samples were collected. From the subjects, urinary samples were collected immediately post exposure and every four to five hours up to 20 hours post exposure. Baseline HDA concentrations were between 0.2 μg/g and 14.6 μg/g creatinine (GM; 0.7 μg/g). From the samples collected post-exposure, the range of HDA concentrations were between 0.4 μg/g and 101 μg/g creatinine.

The timing of the urine collection was important in the measurement of urinary HDA levels. Urine samples should be collected immediately post exposure. They suggested that HDA may be more indicative of HDI monomer than oligomers. More studies of HDI metabolism and individual variability in urinary HDA levels were recommended.

Control

In order to minimize exposure to isocyanate (HDI) during 2-pack spray painting, there is a significant reliance on spray booths (Heitbrink *et al.*, 1993b, 1995, 1996; Woskie *et al.*, 2004)

Six autobody shops were examined by Heitbrink *et al.*, (1995). In the spray booth, overspray concentrations were measured within spray painters' breathing zone in different spray booths (downdraft booths, semi-downdraft booths and cross draft booths).

According to the evaluation, spray booths were often inadequte to control HDI exposure from overspray. The major air contamination was polyisocyanate.

The extent of spray painter exposure depended on the type of spray painting booth and the choice of a spray painting gun. Of the three kinds of spray booths, downdraft booths were most effective (Heitbrink *et al.*, 1993b).

In the case of spray guns, HVLP spray painting guns was suggested rather than using conventional guns (Heitbrink *et al.*, 1996).

In a recent study, the determinants of isocyanate (HDI) exposure were evaluated in a large survey of painters (n=380) in auto body repair shops (Woskie *et al.*, 2004). In this study there were several influence factors, such as shop size, tasks (e.g. mixing, cleaning sanding and coating), income, spray location, workers position, an air purifying system (e.g. booth) and spray paint quantity.

The highest level of airborne polyisocyanate was 3119.6 $\mu gNCO/m^3$ and around 45% of the samples had over 220 $\mu gNCO/m^3$ from spraying inside the booth. It was found that there was no difference between using downcraft and semi-downcraft booths in terms of exposure.

1.8 Purpose of the Study and Research Questions

1.8.1 Purpose of the Study

Exposures can be identified and effectively controlled only as part of a systematic risk assessment/management program, which may encompass a combination of ambient, biological and biological effect monitoring strategies.

Ambient monitoring methods allow for the measurement of chemicals in air or on surfaces (including skin) to which workers are exposed, but provide limited information about the extent of uptake of these chemicals into workers' bodies.

Biological monitoring of chemicals or their metabolites potentially provides this information but fails to provide any evidence of effects associated with the uptake. Biological effect monitoring allows an estimate of some biochemical or cytogenetic response in chemical-exposed workers. It is important to note that these biological effect endpoints are not measures of disease, but are used as a signal function to indicate that some biological event has occurred. Ultimately, health questionnaires or medical monitoring, such as lung or liver function testing, can be used to assess clinically relevant disease resulting from exposure. Although biological and biological effect monitoring methods are most predictive of health risk, they are often invasive and currently only apply to a limited range of chemicals.

Consequently, their application in industry has been sparse. Ambient methods are more practical and acceptable to the workforce.

Significantly, such methods can be easily integrated into effective prevention and regulatory systems.

The sequence of hazardous chemical evaluation options may be considered as follows:

ambient monitoring (air, surfaces and other media) <> biological monitoring <> biological effects monitoring <> health effects or medical monitoring

Although chemicals are widely used in workplaces, relatively few compounds have been assessed for dermal and/or ocular exposure, and it is not known how many or what percentage of workers have significant chemical absorption through the skin or eyes (Boeniger and Klingner, 2002; Fenske, 1993; Dost, 1996; Schneider *et al.*, 2000; Nylander-French, 2000; Cherrie *et al.*, 2000). The area is still in its infancy, and many questions remain unanswered.

There appears to be a shortage of actual exposure data and a need to systematically develop and validate dermal/ocular exposure assessment methods and models. In the case of control by PPE, there is a lack of information on the performance and the effective service life of PPE, e.g. gloves, used to protect against chemical exposure.

In some cases, PPE can exacerbate chemical exposure, for example by occlusion.

Boeniger (1991) has suggested that the thumbs and forefingers might be particularly vulnerable. In the case of the pesticide sprayers, the palm may also be vulnerable.

1.8.2 Research Questions

In Australia, the control of the Mediterranean fruit fly involving the spray application of malathion and fenthion is only carried out in South Australia. At the commencement of this study, little or no exposure data were available. This is a significant shortcoming in the context of health risk assessment.

Occupational asthma is the most common compensable occupational lung disease in SA and isocyanate exposure is a significant cause (Gun and Langley, 1987; Gun *et al*, 1996). Owing to its extensive motor vehicle and furniture industries, South Australia has a large number of workers exposed to isocyanates, but the only exposure data relate to inhalation (Pisaniello and Muriale, 1989a). There is a need to better understand the dermal route as animal data suggest that it may contribute to respiratory sensitization. Ocular exposure may also be relevant.

This study seeks to extend knowledge of the extent, and determinants, of dermal and ocular exposure. It will provide new data relevant to selected industries of significance in SA.

It is also proposed to conduct research, which may lead to the development of new dermal/ocular exposure methods and glove performance evaluation opportunities.

Correlations between ambient exposures, biological measures, observed work practices and health questionnaire data will be used to develop an understanding of the etiology of chemical related disease. Importantly, this understanding would be of great value in terms of chemical hazard control. In the case of isocyanates, this study will build on local research investigating exposure levels and health status related to work practices and working conditions (Pisaniello and Muriale, 1989a)

The specific research objectives were as follows:

1. Evaluate dermal exposures, in total and in respect to particular areas of exposed skin, e.g. hands, and assessment of the opportunities of exposure;

2. Evaluate chemical contamination of the eye surface, arising from the spray application of chemicals;
3. Determine the prevalence of skin and eye-related symptoms, in absolute terms and in comparison with a control group of unexposed workers;
4. Compare measured exposures with observed work practice, equipment and control measures;
5. Evaluate, where feasible, of uptake using biological monitoring methods and correlation with ambient and dermal measurements;
6. Assess PPE service life, in particular repeated usage of gloves, in actual field use and in simulated laboratory experiments.

CHAPTER 2. DERMAL AND OCULAR EXPOSURE TO ORGANOPHOSPHATE PESTICIDES USED IN FRUIT FLY ERADICATION

2.1 Introduction

An introduction to OPs (MAL and FEN) used for the control of Mediterranean fruit fly has been given in Section 1.6 of Chapter 1.

For this study, experiments and observations were carried out at two sites (Lenswood and Thebarton, South Australia). In order to estimate exposure levels to the pesticides and adverse health symptom prevalences, questionnaire surveys and a range of sampling methods were applied (see Section 2.3). Glove testing was conducted to determine glove performance, i.e. breakthrough times and permeation rates. The results are described in Section 2.4.

A simulation field trial was performed at Lenswood in 2001 with the cooperation of PIRSA. In addition to air sampling, workers were asked to provide urine samples and blood samples, and dermal and ocular monitoring were conducted with approval of the Flinders Clinical Research Ethics Committee.

During a fruit fly outbreak in 2003, pest control workers were requested to provide their PPE (cotton gloves) and skin wipe samples for analysis. Ocular monitoring was also carried out after finishing the pesticide application. However, no air monitoring and biological monitoring were conducted because these had been performed as part of the earlier simulation field trial, and the main focus of this study was work practice and behaviour.

2.2 Study Populations

The PIRSA Fruit Fly Control Unit is responsible for spraying and other control operations in South Australia. In July 2001, Mediterranean fruit fly outbreaks were identified in three zones of the Adelaide metropolitan area. Pesticide application crews were deployed to apply MAL bait spray and FEN foliar cover spray to control fruit fly (Plate 5). As a result of public concerns about suburban pesticide use, and

concerns from workers regarding the extent of their pesticide exposure, PIRSA was asked to conduct a formal risk assessment relating to potential health effects resulting from exposure to organophosphates (OPs) pesticides (MAL and FEN) while spraying in the field.

Plate 5: Pesticides (MAL and FEN) Application During Simulation in 2001

Two opportunities were presented to collect data relevant to the risk assessment - A field simulation of OP applications in a PIRSA orchard in Lenswood in 2001 and an active OP spray program to control a fruit fly outbreak in metropolitan Adelaide in April 2003 (Plate 6).

Plate 6: Pesticide (MAL) Application During an Outbreak in 2003

2.2.1 Study Group 1 (Field Simulation Trial, 2001)

The fruit fly pest controllers were recruited through PIRSA, which provided the author permission to meet the workers and observe work practices. Exposures associated with the normal spraying process were simulated at the PIRSA field station at Lenswood, an Adelaide Hills location, in October 2001. For the assessment, a total of six volunteers were selected by PIRSA. They were all experienced pesticide sprayers. Three workers were selected to apply MAL baiting and another three sprayers were selected for FEN cover spraying. In the case of FEN cover spraying, a single motorized unit containing a diluted solution was used in the field. The area of bait spraying was approximately 25 m^2.

Technical grade MAL and FEN were used for spraying. To prepare for baiting operations, a team manager transferred concentrate of technical grade MAL and FEN from 25 L storage drums into a 5 L container, and this concentrate was provided to a group leader. When the team manager transferred the concentrate, he wore a half-face respirator fitted with organic vapor and particulate cartridges and protective gloves (*Protector Safety* cotton lined PVC protective gloves Cat No. IDD14), which were provided to the applicators as well.

With 5 L of technical grade pesticide, a group leader made working strengths solution using water. Technical grade MAL (58% purity) was diluted with water for spraying onto trees. The diluted MAL solution (1g in 100 ml in water) was applied (100 ml per tree). With technical grade FEN (55% purity) solution, the dilution was 0.05% (0.05g in 100 ml in water). Two percent vegetable protein extract was added for fruit fly attraction. While he diluted the concentrate in a 150 L container, he wore protective gloves.

The group leader transferred the diluted baiting solution into each knapsack (14 L) for each applicator. On average, the diluted solution was sprayed for 15 minutes.

Workers wore personal protective equipment such as overalls, goggles, cotton gloves, PVC gloves, half-face respirator with organic vapour and particulate cartridges, safety boots, socks and hat.

2.2.2 Study Group 2 (Fieldwork During Fruit Fly Outbreak, 2003)

As a result of an outbreak in April 2003, a two-week MAL baiting program was undertaken at Thebarton, an inner western suburb of Adelaide.

MAL bait spraying was conducted in teams, comprising one person for baiting application, one for door knocking and providing information and the team leader. Baiting sprayers used a knapsack and a spray gun. The capacity of the knapsack was 14 litres and approximately 12 litres of diluted solution was added for baiting each time. After a knapsack was filled by a team leader, each sprayer wore their knapsack on the back and sprayed the diluted solution using a spray gun operated by a piston.

The diluted solution (1g of technical grade MAL in 100 ml in water, 2% vegetable protein extract) was applied onto foliage, about 100 ml to each tree and bush. The application of spray baiting was carried out for approximately 3.5 hours per day for each sprayer.

Workers wore personal protective equipment such as overalls, shoes or boots, goggles, hat, cotton gloves underneath PVC gloves, and a half-face respirator with organic vapour and particulate cartridges.

2.3 Methods

2.3.1 Fieldwork Methods

For the fruit fly pesticide applicators, a range of methods were used:

Health and work practice questionnaire, personal air samples, ocular sampling, skin wipes, skin patches, PPE samples (gloves, socks, hats and overalls), urine (pre- and post-task) and blood (post-task).

2.3.1.1 Questionnaire survey (Study Group 2 only)

2.3.1.1.1 Development and pilot investigation

A small cross-sectional health study was conducted as part of the 2003 investigation.

For this purpose a questionnaire (Appendix 2.1) was developed to assess the prevalence of symptoms potentially related to the use of OPs (Cattani *et al*, 2001), and

to obtain information on work practices and experiences. It was piloted with a group of several PIRSA and University staff, not involved with the fruit fly outbreak.

A total of 27 male pest controllers were recruited by PIRSA for the two-week MAL baiting program. All agreed to participate in the survey and were privately interviewed with the questionnaire at the PIRSA depot, at the end of the two-week period of work. The vast majority of workers had prior experience in fruit fly control, but there had not been an outbreak in the previous 12 months.

An information sheet (Appendix 1.1), consent form (Appendix 1.3) and complaint form (Appendix 1.4) were provided and the project was explained by a member of the research team. The questionnaire included personal information (name, date of birth, sex, workplace, job title, work experience and educational status), health information (respiratory symptoms, skin symptoms, ocular symptoms, other unusual symptoms and smoking habit) and work practices (chemical usage and PPE usage).

A separate questionnaire was used to assess glove usage (see Appendix 2.4).

A control group of 91 unexposed male workers was used. The questionnaire for the control group included personal information (name, date of birth, sex, workplace, job title, duties, working period and outside spending), health information (skin symptoms, ocular symptoms, other unusual symptoms and smoking status) and chemical usage and work practices (chemical usage and PPE usage) (see Appendix 2.3). The control group was comparable with the pest control applicators in terms of socioeconomic status. Unexposed workers were recruited from blue-collar categories, such as maintenance and manufacturing.

2.3.1.1.2 Administration and human ethics

Details of the proposed study were provided to Human Ethics Committees, and the study was approved by the Human Research Ethics Committees of Flinders University (2001) and The University of Adelaide (2003). Notifications of the approvals were provided by letter in July 2001 (see Appendix 3.1) and in March, 2003 (see Appendix 3.2).

No workers actively spraying at the time of the study were excluded.

2.3.1.1.3 Data analysis

Personal information was kept secure and confidential. Only members of the study team had access the information. Data from the questionnaires and worksite observation forms were kept in a locked filing cabinet. Data from the questionnaires were entered into an Excel spreadsheet, and all information was coded. Names were removed from the entered data. Data files were kept on a computer requiring password access, or on floppy disks/CDROMs stored in a locked cupboard. Statistical analysis was performed by using Microsoft EXCEL on a personal computer. Reporting of statistics was in summary form with no individuals identified. A two tailed test of differences of proportions was used (Fleiss, 1981).

2.3.1.2 Worksite observations

From Schneider *et al* (1999), dermal exposure can be from emission, deposition, transfer. Work practices, including the use of PPE, were observed and noted during the 2001 field simulation and 2003 outbreak baiting program. General observations were conducted for work procedures, the working environment, chemical exposure source, area of contamination on the body, exposure state, cleaning procedures and the use of PPE.

2.3.1.3 Environmental measurements

2.3.1.3.1 Air monitoring (Study Group 1 only)

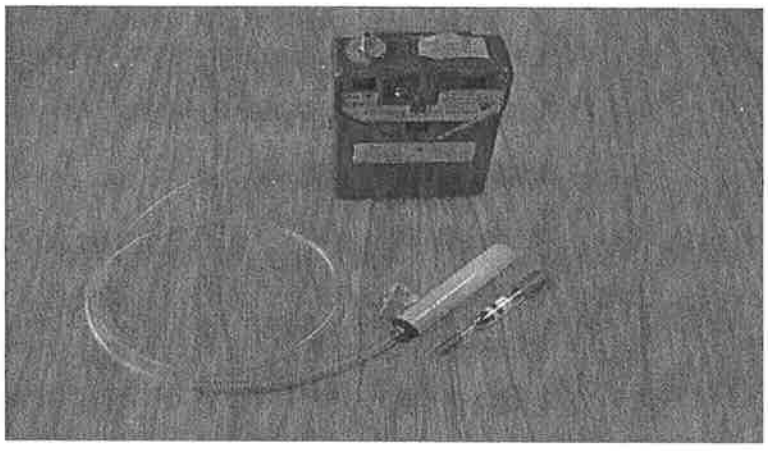


Plate 7: OVS- Sampling Tube for Air Monitoring of Pesticide Workers

Personal air monitoring for MAL and FEN was conducted at Lenswood in 2001 using OSHA Versatile Sampler (OVS) tubes

(a combined glass filter/XAD-2 sorbent system) connected to calibrated battery-powered air sampling pumps.

Plate 7 shows the air monitoring setup. The flow rate of the sampling pump was 1.5 L/minute and was checked before and after sampling with a calibrated rotameter. A thermoanemometer (DSE Q1411) and portable weather station were used to record both wind speed and temperature during the field simulation. (Model Number 102083, Climatronics Corporation, Bohemia, NY), [supplied by MEA instruments; Datalogging was with a Unidata Australia Starlogger Model 6004C].

As soon as sample collection was finished, each collected sample was stored in a separate container, and then kept in a freezer below –20°C. HPLC grade toluene was used to extract the samples. All extracted samples were evaporated down to 1ml and then transferred into separate vials. One microlitre samples were injected into a gas chromatograph (GC) for analysis (see Section 2.3.3 for analytical details).

2.3.1.3.2 Surface monitoring

The forehead of workers was dry wiped using 100% pure cotton pads (5 cm x 6 cm x 0.5 cm) following the period of baiting (see Plate 8).

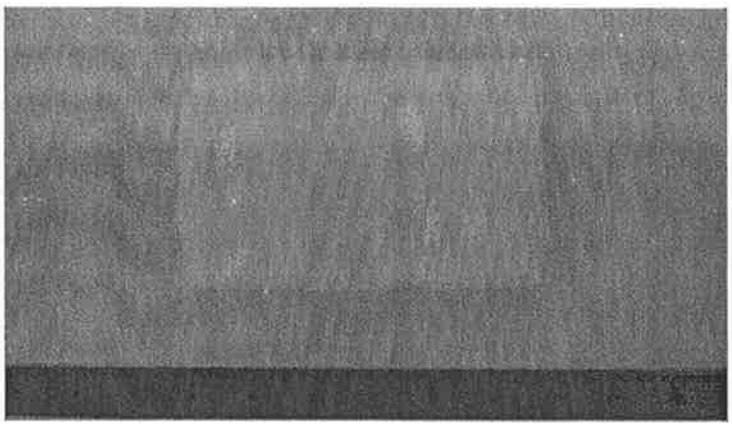


Plate 8: Cotton Pads for Dermal Monitoring and Surface Monitoring

2.3.1.4 Dermal and ocular monitoring

Most of the data relate to the field simulation experiment (Study Group 1). Here, samples of PPE were collected and analysed.

PPE samples comprised cotton inner gloves, socks and hats and full cotton overalls.

The body locations of PPE samples are shown in Figure 6.

Background levels of MAL and FEN were measured in each batch of cotton gloves, overalls, and other sampling media. No potentially-interfering residual pesticide was found.

After the simulation experiment, the cotton overalls were cut into approximately 20 cm x 8 cm sections (both front and back), and carefully stored in a freezer in individual containers. Areas were pre-selected for pesticide analysis based on field observations of work practices and judgement of sites most likely to be exposed to spray.

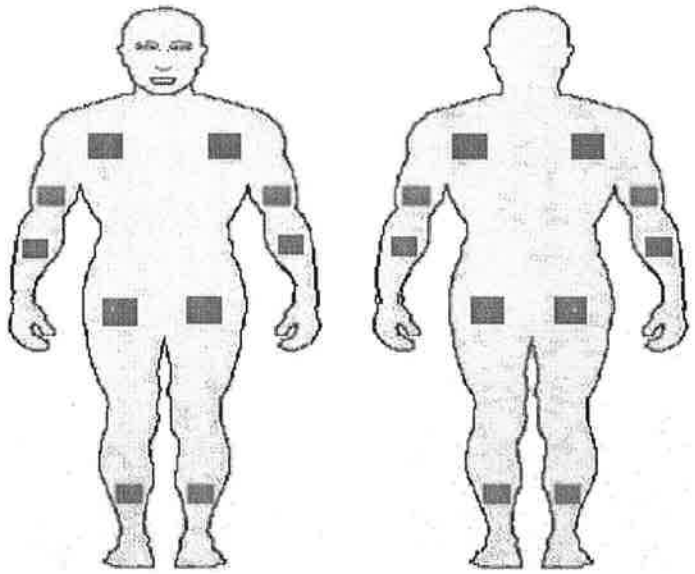


Figure 6: Dermal Exposure Sampling Positions

Ocular sampling entailed the administration of one or two drops of sterile liquid to each eye, immediately after the spraying activity. Excess liquid from the corner of each eye was absorbed onto a sterile cotton swab. *Allergan* "Refresh" eye drops, from individual sterile (single use) plastic ampoules (0.4 ml), were used. Plate 9 shows the swab and eye drop ampoules.

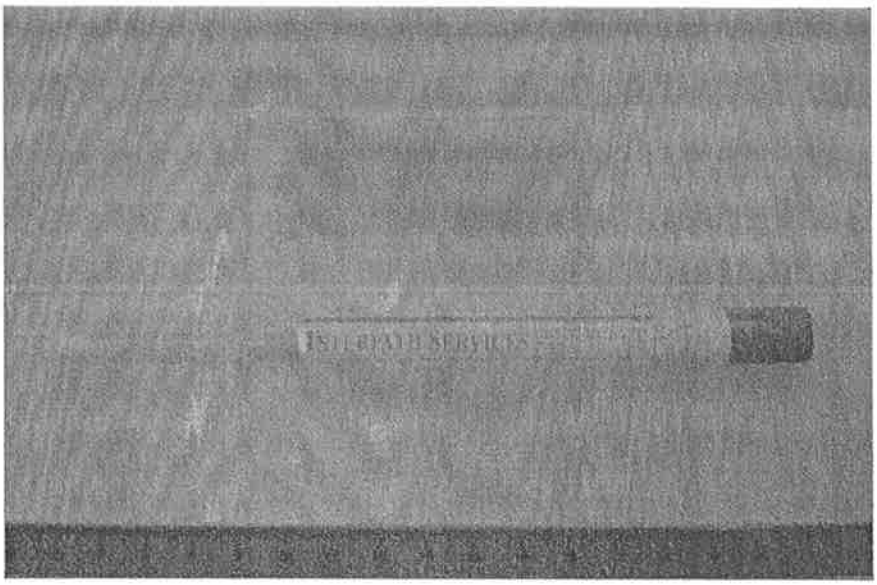


Plate 9: Equipment for Ocular Monitoring

2.3.1.5 Biological monitoring

Urine Sampling

Pre- and 24 hour post-spray urine samples were collected on site during the field simulation. The samples were stored at -20°C prior to laboratory shipment.

Urine samples were sent to an external laboratory (WorkCover NSW) for analysis of alkylphosphate metabolites such as dimethylphosphate (DMP), dimethythiolphosphate (DMTP), dimethyldithiophosphate (DMDTP), diethylphosphate (DEP), diethylthiophosphate (DETP) and diethyldithio-phosphate (DEDTP). See Appendix 4 for an example laboratory report.

Gas chromatography with flame photometric detection (FPD) was used for the analysis of dialkyl phosphates. Creatinine assays were performed by using the Jaffe reaction, and colorimetric measurements were done at 500 nm.

Blood Sampling

Venous blood samples were collected into heparinized tubes by a registered nurse on site before spraying and 24 hours after spraying. Plate 10 illustrates the sampling equipment.

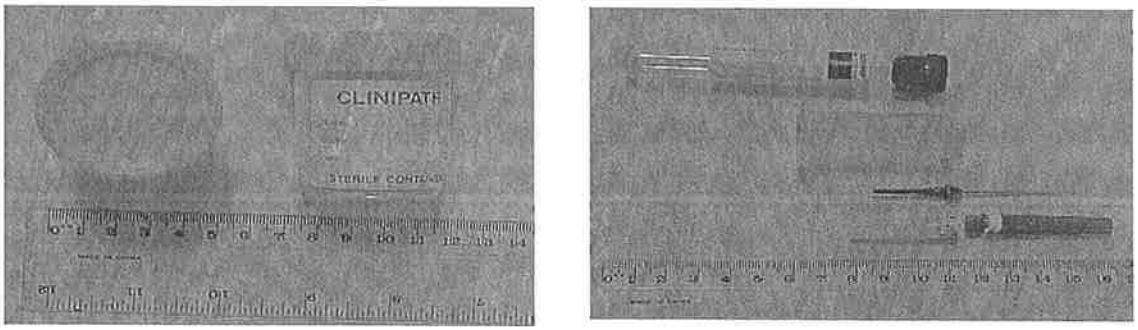


Plate 10: Equipment for Urine and Blood Sampling

Following centrifugation, the red cell pellet was washed twice in Earles BSS, and then was ruptured by freeze/thawing after resuspension in an equal volume of 0.2 M phosphate buffer (pH 8.0).

Serum cholinesterase activity

This was measured by the method of Kalow and Lindsay (1955). Substrate (benzoylcholine) was added at a final concentration of 50 mM to a mixture of 15 µl serum in 3 ml of 133 mM phosphate buffer (pH 7.4) at 30°C. The disappearance of substrate was measured at 240 nm wavelength and was expressed as nmol substrate hydrolyzed/ml serum.

2.3.2 Laboratory Methods

2.3.2.1 Method development

Various laboratory experiments were conducted to (1) assess the pesticide desorption efficiency from the OVS air sampling tube; (2) check on the pesticide degradation rate during storage; and (3) optimize glove permeation testing arrangements.

2.3.2.1.1 OVS tube sampler

Multi-section OVS tubes (13-mm glass fibre filter, XAD-2, 270 mg/140 mg, polyurethane foam separators) were supplied by SKC. Malathion (98%) was purchased from Supelco, and Fenthion (96%) from Sigma Aldrich.

The efficiency of toluene for the extraction of the pesticides (MAL, FEN) from OVS tube components was assessed using known amounts of MAL and FEN spiked onto polyurethane foam separators and XAD-2 porous polymer.

The desorbing solution was 3ml of toluene containing 0.5 μg of lindane/ml as an internal standard. Lindane was purchased from Alltech.

2.3.2.1.2 Degradation experiments

According to the National Institute for Occupational Safety and Health (NIOSH, 1994b), the stability of the OPs in water is at least 30 days at 0°C and 10 days at 25°C.

OVS tubes were spiked wih known amounts of MAL and FEN and degradation was assessed over time, and in two different storage conditions, i.e. room temperature and -20°C.

2.3.2.1.3 Test cell for glove performance assessment

For the determination of the glove permeation resistance to pesticides (MAL, FEN), reference was made to Australian/New Zealand Standard 2161.10.3:2002 (Occupational protective gloves Part 10.3: Protective gloves against chemicals and micro-organisms-Determination of resistance to Permeation by chemicals.

One-inch and two-inch ASTM permeation test cells (Pesce Lab Sales, Inc. USA) were used. For each different test cell, both compartment volume and sampling area were measured: 18.2 ml and 86.2 ml, and 4.91 cm^2 and 19.63 cm^2 respectively. In addition, calibration of the test cell was conducted following AS/NZS 2161.10.3 (2002).

The test cell was divided into two parts. One part was for liquid or gas challenge (Part A) and other part was the liquid or air sampling compartment for the collecting medium (Part B). A piece of glove material was prepared and the thickness of the specimen was measured using a micrometer. The specimen was placed between two

polytetrafluoroethylene (PTFE) gaskets positioned between two aluminum flanges. The outer surface of the glove material sample was toward Part A to contact with test chemical substances (technical grade and working strength pesticide). The two parts were assembled by using three bolts. To Part A, the chemical or diluted solution of interest was added. To Part B, a collecting medium was provided, such as distilled water or isopropyl alcohol mixture with distilled water. A stirrer was put into the inlet part of the Part B and the liquid was stirred gently. A pneumatic drive was used for continuous stirring.

From the Part B sampling compartment, 200 µl of collecting medium was taken out and then refilled with the same amount of the collecting media. High Performance Liquid Chromatography (HPLC) was used for analysis. Figure 7 shows the standard test cell (2") and setup of the equipment for the performance testing of PVC gloves used by the fruit fly control workers. The small air-driven motor stirred the collecting medium inside the test cell. In the water bath, the test cell was covered by water. The thermo mixer circulated water coming from the pump connected to a refrigeration system. This arrangement allowed for both low and high temperature experiments.

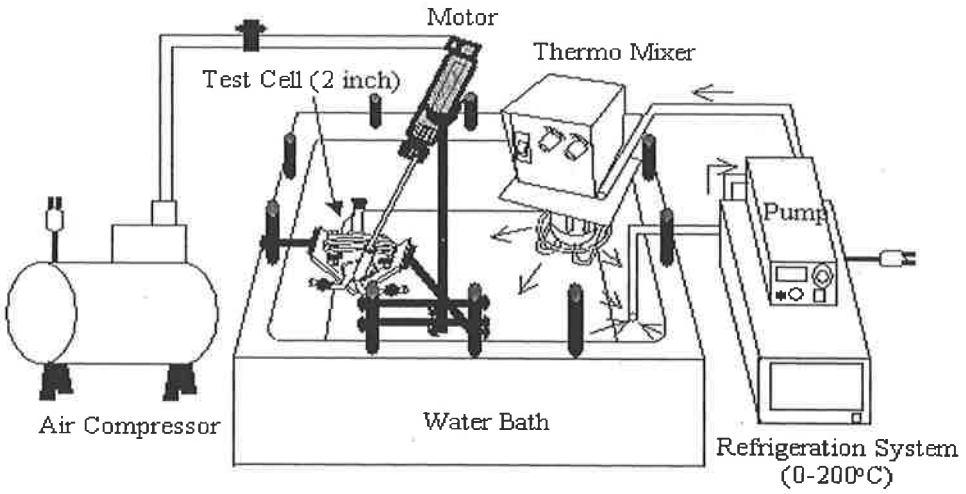


Figure 7: Standard Test Cell and Set Up of Equipment for Glove Permeating Testing

2.3.2.1.4 Preparation of the glove materials

Elbow length Protector Safety PVC gloves were used by spray applicators - Double dipped chemical and oil resistant, 35 cm, Long, Part# IDD14, see Plate 11.

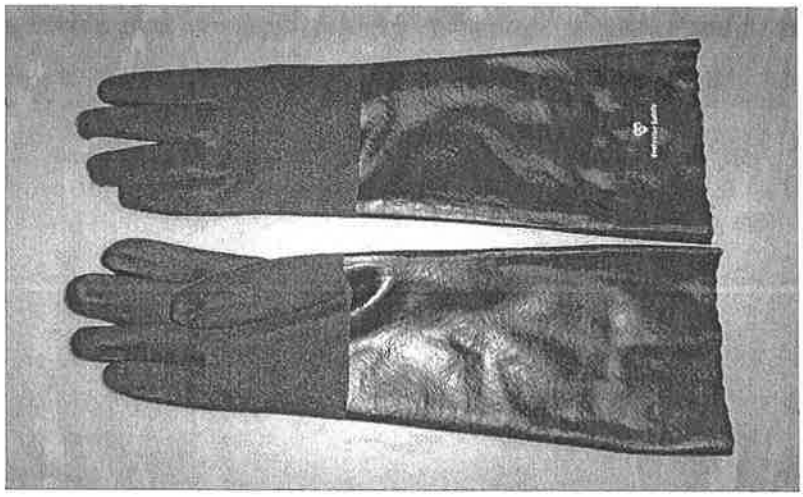


Plate 11: PVC Protector Safety Gloves Used for Fruit Fly Eradication Program

Breakthrough times (BT) and permeation rates (PR) for two parts of the gloves, namely the palm and arm, were determined. Both used and new gloves were tested. Before testing, two pieces (the palm and the arm) were cut out, i.e. 4.5 cm and 7 cm in diameter for the 1'' and 2'' test cells respectively, and then washed and rinsed with distilled water. After rinsing, the glove materials were dried by natural ventilation in a fume cupboard at room temperature.

2.3.2.1.5 Collecting medium

Given the limited solubility of MAL in water, isopropyl alcohol solutions were tested as the collection medium.

Glove performance testing was conducted at different temperatures (23°C, 30°C and 50°C) and with a range of compositions of collecting media. Each collecting medium in the test cell, (isopropyl alcohol:water = 100:0, 15:75, 30:70 and 50:50) was tested with known amounts of technical grade MAL (5 µl of 430.7 µg/ml) and FEN (5 µl of 598.0 µl/ml). The technical grade pesticides were transferred into 20 ml of vials containing 10 ml of different collecting medium.

When the temperature was steady, the samples were left for five to ten minutes to equilibrate, then 200 µl of the solution was collected for analysis by HPLC.

2.3.2.2 Glove testing

2.3.2.2.1 Glove materials

Samples of gloves were supplied by *Protector Safety*. Each was visually inspected prior to use.

2.3.2.2.2 Breakthrough times and permeation rates

Permeation rates (μg/cm^2/minute) were calculated using the equation in AS/NZS 2161.10.3 (2002).

$$P = \frac{(C_i - C_{i-1})(V_t - [i-1]V_s)}{(T_i - T_{i-1})A}$$

Here,

P = Permeation rate, μg/cm^2/minute

A = area of the material specimen in contact in square centimeters (cm^2)

i = an indexing number assigned to each discrete sample, starting with i=1 for the first sample

T_i = the time at which discrete sample i was removed in minutes (minutes)

C_i = the concentration of chemical in collecting medium at time T_i in micrograms per litre (μg/L)

V_t = total volume of the collection medium in litres (L)

V_s = volume of discrete sample removed from the collection medium (L)

Test chemicals were technical grades, and working strengths, such as 1% technical grade MAL (1 g in 100 ml distilled water) and 0.05% of technical grade FEN (0.05 g in 100 ml distilled water).

To calculate the permeation rate of each glove, sample solutions were removed from the collecting medium in Part B of the test cell and were analyzed by HPLC every 20 minutes.

2.3.2.2.3 Thickness measurement

The thickness of each glove was measured at several points by using a Micrometer (Digital 0-1 inch, 97231-61, Cole Palmer Instruments).

2.3.3 Analytical Methods

2.3.3.1 Gas-chromatography

Pure toluene was used to extract samples. Analysis was in accordance with previously published procedures (Pisaniello *et al.*, 2000). For MAL and FEN air samples, tubes were extracted by the addition of 18 ml of desorbing solution, containing 0.5 μg of lindane/ml. Extracted solutions were evaporated to 1 ml, and then transferred into separate vials prior to GC analysis.

PPE samples were extracted in 40ml of toluene. In the case of eye samples, 10 ml of toluene was used.

For OVS tube, forehead wipe, ocular samples and glove samples (Study group 2 only), a GC with 0.33 mm id 25 m, BP5 non-polar fused silica column with electron capture detector was used. Nitrogen was used as the carrier gas (17 psi) and as the make-up gas (flow rate 48.5 ml/minute). Temperatures of column, detector and injector were 175°C, 350 °C and 300 °C respectively. For all other samples, e.g. PPE samples, a GC with TSD (nitrogen, phosphorus detector) was used.

For the GC analysis, lindane was used as an internal standard. Retention times of lindane, MAL and FEN were 2.2 minute, 4.4 minute and 2.4 minute respectively under the GC operating conditions used.

2.3.3.2 High-performance liquid chromatography (Glove permeation tests)

HPLC methods were adapted from those published by Kaur *et al.*, (1997) and Abu-Qare and Abou-Donia (2001). For this experiment, several samples of analytical grade pure MAL were tested by using three different mobile phases in order to decide on an appropriate mobile phase. For the permeation experiments, 20 μl of sample was directly injected into the HPLC column. The HPLC conditions were 25 cm x 46 mm

Spherisorb ODS2 at 30°C, 1.0 ml/minute flow with helium sparging, and 220 nm for Kortec K95 UV detector.

2.3.4 Limits of Detection

With GC-TSD, the limits of detection were 0.14 μg/ml for FEN and 0.29 μg/ml for MAL, and 10 μg/ml was for FEN and MAL with GC-FPD. The detection limits for overalls/PPE were 0.035 $\mu g/cm^2$ for FEN and 0.073 $\mu g/cm^2$ for MAL. In the case of personal/air samples by using GC-ECD, the limits of detection were 0.4 μg/ml for FEN and 0.012 μg/ml for MAL. For the ECD results, the limits of detection for airborne concentration based on a sampling time of 15 minutes. The detection limit for air sampling for FEN and MAL were 17.78 $\mu g/m^3$ and 0.53 $\mu g/m^3$ respectively.

The limits of detection for urinary samples were reported to be; DMP (1.5 μmol/L), DEP (0.7 μmol/L) and DETP, DEDTP, DMTP (0.2 μmol/L).

From the HPLC analysis for glove performance, the retention times of MAL and FEN were 14.5 minutes and around 9.4 minutes respectively. The limits of detection for those chemicals were 0.13 μg/ml (MAL) and 0.005 μg/ml (FEN).

2.4 Results

2.4.1 Work Practices

During MAL bait spraying activities (Study Group 2), it was observed that some of the solution leaked from the knapsack container, and the nozzle of the spray gun. The filler screw cap seal of the knapsack was sometimes faulty, and a rag would occasionally be used around the screw thread to control leaking. However, this was not always effective, resulting in visible shoulder contamination. During the application, it was observed that the workers' back, shoulders, pants, hands and shoes were sometimes wet with the spray solution. In windy conditions, after they had sprayed onto foliage or trees, they were covered by mist of the diluted solution on the body and the face. After finishing the spraying or before taking a break, they took off

protective gloves, safety glasses or goggles and hats by hand. Their hands were washed with water using normal detergent or soap. However, their overalls and boots were still worn when they left to go home. Used spray equipment (knapsacks and spray guns) were not rinsed, and were left for the next day for spraying. All used gloves were stored in a car boot or a small container which may have been contaminated. The inside of the used gloves were washed and dried before spraying was started. Cotton gloves were worn under the PVC gloves by about 70% of the spray applicators.

2.4.2 Survey Results

The questionnaire survey was conduced using two questionnaires, one for the exposed group (Study Group 2) (see Appendix 2.1) and one for the unexposed group (see Appendix 2.3). To obtain further information about gloves, another survey for the pesticides workers was carried out (see Appendix 2.4).

2.4.2.1 Subjects

Personal baseline data are summarized for the exposed group and the unexposed group in Table 3.

Table 3: Baseline Variables for Pesticide Workers and Controls*

Items	Exposed# (n=27)	Controls # (n=91)
Mean age (STD) (years)	40 (±10)	38 (±9)
Current smokers	18 (67%)	43 (47%)
1-5 per day	1 (4%)	7 (8%)
6-10 per day	7 (26%)	7 (8%)
11-15 per day	3 (11%)	7 (8%)
16-20 per day	5 (19%)	12 (13%)
> 20 per day	2 (7%)	10 (11%)
Ex-smokers	5 (9%)	12 (13%)
Suffer from hayfever?	7 (26%)	35 (39%)
Suffer from asthma?	3 (11%)	7 (8%)
Suffer from eczema?	0 (0%)	5 (6%)
More severe reaction than others to insect bites?	5 (19%)	7 (8%)

 # all males
*** The proportions for exposed workers are not statistically different from controls ($p < 0.05$, two-tailed test,) (Fleiss, 1981)**

The average ages were similar. Smoking prevalence was higher among pest control workers, but not statistically significnat. There were no significant differences for hayfever, asthma, eczema, and insect bite sensitivity.

2.4.2.2 Symptom prevalence

Symptom prevalences are given in Table 4.

Table 4: Work-related Symptom Prevalence Data

Symptoms	Exposed (n=27)	Non-exposed (n=91)
Skin symptoms		
Dry cracked skin	8 (30%)	17 (19%)
Skin rash	3 (11%)	5 (6%)
Dermatitis/skin irritation	5 (19%)	4 (4%)
Eye symptoms		
Eye irritation*	1 (4%)	24 (26%)
Itchy eyes*	2 (7%)	26 (29%)
Dry eyes*	0 (0%)	15 (17%)
Conjunctivitis	0 (0%)	2 (2%)
Others	0 (0%)	3 (3%)
Headaches*	3 (11%)	36 (40%)
Blackouts#	0 (0%)	0 (0%)

***Statistically different proportion from controls ($p < 0.05$, two-tailed test,) (Fleiss, 1981)**

#"Blackouts" was a dummy question included to detect positive bias in reporting symptoms

For skin symptoms, there were no significant differences between the exposed group and the unexposed group. The exposed group attributed skin symptoms to chemical handling and hot weather conditions. In the case of the unexposed group, the skin problems were attributed to individual susceptibility.

However, eye symptoms (irritated, itchy and dry) and headaches were statistically more common for the unexposed. These were largely attributed to poor air conditioning and computer work.

2.4.2.3 Accidental exposures

Table 5 gives the results of accidents caused by chemical use. From the exposed group, 7% had a major spill (> 500 ml). All of the exposed group used overalls during

pesticide application. However, due to chemical liquid leakage from equipment or splashes from the application, 41% of the exposed group reported wet overalls during carrying chemical solutions and spraying. Thirty seven percent had a splash in the eyes. In most cases, eye contact occurred for people who did not wear eye protection or who wore sunglasses and safety glasses, rather than those wearing safety goggles. Direct skin contact by splashing with the body occurred for 37% of the exposed group.

Table 5: Accidental Exposures from Chemical Use Among Pesticide Workers

Items	Number (% prevalence) n=27
Major spill (>500ml)	2 (7%)
Wet overalls from liquid leak or splash	11 (41%)
A splash in eyes	10 (37%)
Splashing any other part of the body	10 (37%)
Accident free	12 (44%)

2.4.2.4 Use of personal protective equipment

Table 6 provides data with respect to protective equipment usage.

Table 6: PPE Use and Work Practices Among Pesticide Workers

Items	Number (% prevalence) n=27
PPE usage	
Overalls	27 (100%)
Safety glasses or sunglasses	12 (44%)
Safety goggles	3 (11%)
Protective gloves	25 (93%)
Cotton gloves under gloves	17 (63%)
Foot protection	
Shoes	19 (70%)
Boots	8 (30%)
Replacement of overalls	
Once per week	16 (59%)
Twice per week	7 (26%)
Cleaning PPE	
Shoes	13 (48%)
Overalls	0 (0%)
Respirator	0 (0%)
Gloves	10 (37%)
Remove overalls at lunch break	4 (15%)

During the period of application, all workers wore overalls. Pesticides workers used PVC gloves (93%) with cotton gloves (63%) underneath the PVC gloves. Sports shoes (70%) were often worn rather than safety boots (30%). In the case of eye protection, safety goggles (11%) and safety glasses or sunglasses (44%) were common.

More specific information about glove usage among pesticide workers is given in Table 7. The maximum length of time which the gloves were used was 14 days, because the eradication program ran for 2 weeks. However, only one of the spray bait applicators rinsed his gloves with water before their use every morning.

Table 7: Glove Usage Among Pesticide Workers

Items	Pesticides workers (n=12), % prevalence
Baiting only?	12 (100%)
Cotton undergloves used?	6 (50%)
Full days of usage	
3 days	4 (33%)
7 days	3 (25%)
10 days	1 (8%)
14 days	4 (33%)
Has the glove been rinsed each day?	1 (8%)

2.4.2.5 Knowledge and training

Survey results for knowledge and training were described in Table 8.

Table 8: Training and Education Among Pesticide Workers (Study Group 2)

Items	Pesticides workers (n=27), % prevalence
Formal training in use	25 (93%)
Period of training	
1 day course	17 (63%)
> 2 days course	8 (30%)
Education	
Health effects	8 (30%)
PPE usage	20 (74%)
MSDS	20 (74%)

A high proportion of pesticides workers had formal training program (93%) in the safe use of pesticides. Of those with formal training, 63% attended a 1-day course, and 30% attended a course of 2 or more days. In the case of training about health effects, PPE usage and MSDS, 30%, 74% and 74% of the spray applicators respectively reported positively.

2.4.3 Environmental Measurements

2.4.3.1 Study group 1 (2001)

2.4.3.1.1 Observations

The field was located on a hillside surrounded by hills. During spraying in the field, the wind direction changed frequently. The related humidity was high due to recent rain. The average temperature and wind speed were 14.5°C and 2.7 m/second respectively during FEN cover spraying.

The range of wind speeds was from 0.4 m/second to 6 m/second. The wind speed varied significantly.

Each simulation lasted approximately 15 minutes. After this time, workers were required to remain in protective clothing until one hour after the commencement of spraying.

2.4.3.1.2 Air monitoring

Table 9 gives air sampling results for the field simulation.

Table 9: Air Sampling Data (2001)

I.D.	Applied chemical	Total amount (μg)	Sampling time (minute)	Total air volume (m^3)	Airborne conc. ($\mu g/m^3$)
P1	Malathion	<2	15	0.023	< 92
P2	Malathion	<2	15	0.023	< 92
P3	Malathion	<2	15	0.023	< 92
P4	Fenthion	13	15	0.023	565
P5	Fenthion	18	18	0.027	666
P6	Fenthion	8	13	0.020	400

MAL Limit of detection 2 μg

For bait spraying, no MAL was detected for any of the air samples collected.

However, FEN was detected for the workers spraying FEN. The airborne concentration of FEN ranged from 400 to 667 μg/ m^3. Cover spraying generated significant aerosol which was swirling due to weather conditions.

2.4.3.1.3 Overalls

Table 10 gives the detected quantity on the overall samples from MAL bait spraying.

In general, workers held a spray gun with their left hands and operated the piston with the right. Only two samples had detectable MAL. These were on the left forearm, where, based on observation, spray was most likely to deposit.

Table 10: Malathion Spray Workers' Overalls Samples (2001)

I.D.	Applied chemical	Concentration (μg/cm^2)			
		LFF	RFF	LSF	RSF
P1	Malathion	0.32	<0.07	<0.07	<0.07
P2	Malathion	0.11	<0.07	<0.07	<0.07
P3	Malathion	<0.07	<0.07	<0.07	<0.07

Limit of detection 0.07 μg/cm^2

LFF; left forearm front, RFF; right forearm front, LSF; left shoulder front, RSF; right shoulder front,

Table 11 gives the corresponding data for FEN cover spraying. It was observed that workers normally had their left side of their body facing toward the spraying area.

Table 11: Fenthion Spray Workers' Overalls Samples (2001)

I.D.	Applied chemical	Concentration (μg/cm^2)			
		LCF	RCF	LLAF	RLAF
P4	Fenthion	0.21	0.14	0.09	<0.04
P5	Fenthion	<0.04	0.06	<0.04	<0.04
P6	Fenthion	0.10	0.11	0.12	0.2

LCF; left chest front, RCF; right chest front, LLAF; left lower arm front, RLAF; right lower arm front

Limit of detection: <0.04 μg/cm^2

2.4.3.1.4 Other PPE monitoring

The workers' inner cotton gloves, socks and hats were collected and analyzed. Table 12 gives results. Most samples had no detectable pesticide.

For MAL bait spraying, the range of pesticide measured was from 0.09 to 0.69 mg/cm^2. The highest concentration was measured for a hat containing 0.69 mg/cm^2 from P1. However, FEN cover spray samples generally did not have detectable pesticide. Only the left glove of P6 had some pesticide (0.03 mg/cm^2). As the cotton gloves were worn under the PVC protective gloves, it is likely that contamination occurred when removing gloves.

Table 12: Workers PPE Samples (undergloves, socks and hats, 2001)

I.D.	Applied chemical	Concentration (mg/cm^2)				
		LG	RG	LS	RS	Hat
P1	Malathion	0.39	0.51	0.26	0.09	0.69
P2	Malathion	ND	-	ND	-	ND
P3	Malathion	0.37	0.09	ND	ND	ND
P4	Fenthion	ND	ND	ND	-	ND
P5	Fenthion	ND	ND	ND	ND	ND
P6	Fenthion	0.03	ND	-	ND	ND

LG; Left cotton glove, RG; Right cotton glove, LS;Left cotton sock, RS;Right cotton sock

ND; Not detected. Limit of detection: FEN (0.01 mg/cm^2), MAL(0.01 mg/cm^2)

2.4.3.1.5 Ocular monitoring

No detectable pesticide was found.

2.4.3.1.6 Biological monitoring

Dialkyl phosphates were not detectable in any worker urine samples. Similarly, cholinesterase activities were not depressed (see Table 13). Collectively, these demonstrate low uptake of pesticide during the field simulation experiment.

Table 13: Serum Cholinesterase levels pre- and post exposure (2001)

	SChE (μmol/minute/ml serum)	
Subject	Pre-simulation	Post-simulation
M1	12.3	11.3
M2	14.6	14.8
M3	13.5	12.7
F1	14.4	16.1
F2	15.7	16.8
F3	10.8	13.0

2.4.3.2 Study group 2 (2003)

2.4.3.2.1 Observations

The field sampling involved collection of forehead wipe samples and inner cotton gloves for 8 workers. During the baiting, the average temperature was about 30°C and it was sunny weather and dry conditions. There was little or no wind on the sampling day.

2.4.3.2.2 Forehead wipe and PPE monitoring

All the samples including forehead samples were collected as soon as the sprayers finished their work. The samples were transferred to clean bottles and stored in the freezer prior to analysis.

Table 14 gives the results.

Table 14: Malathion in Skin Wipe and Inner Cotton Glove Samples (2003)

I.D.	Concentration (μg/cm^2)		
	FH	RG	LG
S1	0.21	1.34	0.57
S2	0.25	2.97	24.7
S3	0.05	0.23	0.27
S4	0.03	1.60	3.19
S5	0.09	1.51	1.81
S6	0.02	10.8	5.16
S7	0.03	0.92	2.30
S8	0.10	2.77	2.73

FH; Forehead, RG; Right cotton glove, LG; Left cotton glove.

All workers used the right hand or both hands during the baiting onto trees and foliage. Baiting time was nominally around 2 hours for each worker.

2.4.4 Laboratory Analysis

2.4.4.1 Optimized analytical conditions

2.4.4.1.1 Desoprtion efficiency of XAD-2

The OVS tube (see Plate 7) used in this study comprises a glass fibre filter, two polyurethane foam separators and two layers of XAD-2 porous polymer.

Table 15 gives the pesticide recovery rates from XAD-2 and polyurethane foam in the OVS tube with different concentrations of technical grade MAL and FEN. Toluene is the desorbing solvent.

Table 15: Desorption Efficiency of Malathion and Fenthion from OVS Tube Components Using Toluene

Sample	Percent recovery (%)	AM (%)	STD
0.015µg/ml MAL(M-std1)	-	-	-
0.025µg/ml MAL(M-std2)	-		
0.039µg/ml MAL(M-std3)	-		
Foam with M-std1	80	89	9
Foam with M-std2	97		
Foam with M-std3	90		
XAD with M-std1	61	72	16
XAD with M-std2	64		
XAD with M-std3	91		
0.006µg/ml FEN(F-std1)	-	-	-
0.032µg/ml FEN(F-std2)	-		
Foam with F-std1	96	86	14
Foam with F-std2	76		
XAD with F-std1	76	70	8
XAD with F-std2	64		

Known amounts of technical grade MAL (58% purity) and FEN (55%) were spiked on tubes. Recovery rates from polyurethane foam and XAD-2 were 89% and 72% for MAL and 86% and 70% for FEN. According to NIOSH (1994b), the acceptable desorption criteria for OPs is > 75% average recovery with a standard deviation of less than 9%.

It was established that the retention of pesticides on the glass fibre filter of the OVS tube was negligible.

2.4.4.1.2 Storage and analytical limitations

Prior to field work, experiments were done to determine the OVS tube sample stability with storage method, i.e. freezer or room temperature.

The two kinds of samples were labeled as "R" (stored at room temperature) and "F" (stored in a freezer). Table 16 gives the comparison of the two conditions and the recovery percentage with time in storage. The samples stored in the freezer appeared to display more stability within ten days. From these data, it was decided that all samples should be stored in a freezer.

Table 16: Recovery of Malathion and Fenthion from OVS Tubes by Time and Storage Method

Time (Hours)	Percentage recovery (%)	
	Malathion-R	Fenthion-R
0	0	0
26	100	100
99	92	88
195	89	89
240	87	89
AM.±SD	92 ± 6	92 ± 6

Time (Hours)	Percentage recovery (%)	
	Malathion-F	Fenthion-F
0	0	0
26	103	109
76	99	98
195	92	90
240	95	95
AM.±STD	97 ± 4	98 ± 8

Malathion; 4.2 μg/ml, Fenthion; 2.24 μg/ml,

R; Stored at room temperature (25°C), F; Stored in freezer (approx –20°C)

2.4.4.1.3 HPLC mobile phase

HPLC was used for the analysis of MAL and FEN during glove permeation experiments.

Different mobile phases were tested to optimise sensitivity and linearity of response. Table 17 gives the results for MAL.

Table 17: Comparison of Different Mobile Phases to Detect Malathion by HPLC

Malathion conc. (μg/ml)	Area of UV signal (x 10^{-3})		
	63% acetonitrile pH 6.0	50% acetonitrile pH 6.0	50% acetonitrile pH 4.0
0.46	n.d.	3.05	n.d.
4.57	12.5	29.4	22.2
9.14	43	82.6	93.8
45.7	385	408	222
457.0	2914	3271	1865
4570.0	18937	29376	22259
R^2 (linear regression)	*0.997*	*0.9999*	*0.9997*
Approx. Limit of detection (μg/ml)	*1.49*	*0.125*	*1.28*

Data indicated that the second mobile phase (50% acetonitrile:water, pH 6.0) gave the greatest sensitivity.

Table 18 shows the sensitivity of the UV detector for the same mobile phase, in the case of FEN. The extrapolated limit of detection was 0.005 μg/ml.

Table 18: Sensitivity of HPLC UV Detector for Fenthion

Fenthion conc. (μg/ml)	Area of UV signal (x 10^{-3})
	50% acetonitrile pH 6.0
0.07	195
0.23	224
2.25	2013
2.31	2013
2.91	3573
R^{2*}	*0.994*
Approx. Limit of detection (μg/ml)	*0.005*

*** Linear regression**

2.4.4.1.4 Collecting medium

Distilled water and isopropyl alcohol (0, 15, 30 and 50%) were tested as liquid collecting media in the permeation test cell. The reason for selecting isopropyl alcohol as a co-solvent was that it was likely to improve solubility of malathion and there

were no reactions with the tested glove materials (PVC and Nitrile gloves) and no interference on the HPLC.

In initial experiments with the permeation test cell, using technical grade MAL as the challenge material, it was found that there was a difference between pure water and 50% isopropyl alcohol, i.e. lower MAL concentrations for water under the same experimental conditions.

In order to establish a IPA:water mixture that could serve as a suitable collection medium, the following experiment was conducted:

Known amounts (5 µl) of technical grade MAL and FEN were added to different IPA/water mixtures (10 ml). The solutions were shaken and allowed to stand for several minutes.

Samples were injected into the HPLC. The experiment was repeated at 30°C and 50°C. Table 19 gives the MAL concentrations measured and shows that 30% and 15% of isopropyl alcohol in distilled water provided best solubility for MAL and FEN respectively.

Table 19: Solubilities of Malathion and Fenthion in Different Collecting Media

Temp (°C)	Detected concentration of malathion (µg/ml)			
	0% IPA	15% IPA	30% IPA	50% IPA
23	32 %	64 %	97 %	94 %
30	37 %	84 %	97 %	90 %
50	23 %	87 %	96 %	81 %

Temp (°C)	Detected concentration of fenthion (µg/ml)			
	0% IPA	15% IPA	30% IPA	50% IPA
23	81 %	98 %	89 %	89 %
30	82 %	95 %	93 %	97 %
50	75 %	88 %	89 %	95 %

IPA = isopropyl alcohol

However, when solutions were kept at 50°C for several hours, there was significant decomposition of both MAL and FEN. This precluded glove experiments at 50°C for extended periods.

2.4.4.2 Glove testing

2.4.4.2.1 Effect of temperature (30% Isopropyl Alcohol)

The elbow length Protector Safety PVC gloves were tested for permeation resistance against working strength MAL and FEN at different temperatures and using different collecting media. Table 20 gives the observed BTs and PRs of the glove material.

At the ambient temperature, neither MAL and FEN were detected from the palm and lower arm within 24 hours. However, MAL was detected at 37°C. When the palm and the lower arm were compared, the palm had a longer BT and lower PR.

Table 20: Breakthrough Times and Permeation Rates of PVC Glove Material under Various Conditions

Test chemical	Working strength	Collecting media	Glove material location	Temp(°C)[3]	B.T (minute)[4]	P.R.[5] (µg/cm²/minute)
Fenthion	0.05%[1]	water	Palm	22±1	> 1440	N.D
				37±1	> 1440	N.D
			Lower Arm	22±1	> 1440	N.D
				37±1	> 1440	N.D
		15% IPA	Palm	22±1	> 1440	N.D
				37±1	> 1440	N.D
			Lower Arm	22±1	> 1440	N.D
				37±1	> 1440	N.D
Malathion	1%[2]	water	Palm	22±1	> 1440	N.D
				37±1	1428, 1434, 1431	1.2, 1.2, 1.2
			Lower Arm	22±1	> 1440	N.D
				37±1	1381, 1386, 1384	1.3, 1.3, 1.3
		30% IPA	Palm	22±1	> 1440	N.D
				37±1	1151, 1156, 1154	5.3, 5.2, 5.3
			Lower Arm	22±1	> 1440	N.D
				37±1	564, 568, 567	7.7, 7.7, 7.6

Each sample was run three times

1) 0.05% of Technical Grade Fenthion: 0.05g in 100ml distilled water,
2) 1% of Technical Grade Malathion: 1g in 100ml distilled water,
3) Temperature,
4) Breakthrough time,
5) Permeation rate, TG; Technical Grade, IA; Isopropyl alcohol, PVC Pro. Safety; PVC Protector Safety™, ND; Not detected within 24 hours,

The breakthrough times and permeation rates for gloves exposed to full technical strength versus working strength at different temperature are given Table 21. Thirty percent isopropyl alcohol in distilled water was used for MAL. In addition, pure

distilled water was used as a comparison with 30% isopropyl alcohol. Two parts of the glove were selected to test. They were the palm and the arm. Samples were run in triplicate.

Table 21: Breakthrough Times and Permeation Rates of New PVC Gloves with Technical Grade and Working Strength Malathion

(1) Part: Palm

Temp (°C)	Coll. media [1]	Thickness (mm) ±0.02	Challenge. chemical [2]	B.T [3] (minute)	P.R [4] (μg/cm²/minute)
22±1	DW	1.32	Tech. Grade [6]	1335, 1340, 1337	0.01, 0.01, 0.01
	30% IPA [5]	1.33	Tech. Grade	1012, 1005, 1009	0.02, 0.03, 0.03
37±1	DW	1.30	Tech. Grade	1062, 1066, 1064	1.9, 1.6, 1.7
	30% IPA	1.32	Tech. Grade	860, 864, 862	47.3, 46.0, 46.6
22±1	DW	1.34	1% of T.G [7]	> 1440	N.D.
	30% IPA	1.32	1% of T.G	> 1440	N.D.
37±1	DW	1.29	1% of T.G	1428, 1434, 1431	1.2, 1.2, 1.2
	30% IPA	1.28	1% of T.G	1151, 1156, 1154	5.3, 5.2, 5.3

(2) Part: Arm

Temp (°C)	Coll. media [1]	Thickness (mm) ±0.03	Challenge chemical [2]	B.T [3] (minute)	P.R [4] (μg/cm²/minute)
22±1	DW	1.10	Tech. Grade [6]	1306, 1310, 1308	0.01, 0.01, 0.01
	30% IPA [5]	0.96	Tech. Grade	805, 812, 809	0.03, 0.03, 0.03
37±1	DW	1.15	Tech. Grade	928, 917, 923	1.6, 2.4, 1.8
	30% IPA	1.13	Tech. Grade	508, 502, 505	50.0, 58.8, 53.0
22±1	DW	0.99	1% of T.G [7]	> 1440	N.D.
	30% IPA [5]	0.99	1% of T.G	> 1440	N.D.
37±1	DW	1.06	1% of T.G	1381, 1386, 1384	1.3, 1.3, 1.3
	30% IPA	1.02	1% of T.G	564, 568, 567	7.7, 7.7, 7.6

Each sample was run three times

ND; Not detected within 24 hours

1) Collecting media in the collecting cell,
2) Chemical to pass through the glove material,
3) Breakthrough time of malathion,
4) Permeation rate ,
5) 30% of Isopropyl Alcohol in distilled water,
6) Pure Technical Grade malathion used in the field (58% malathion),

7) 1% of technical grade (T.G.) malathion in 100ml of pure water as working strength in the field (0.58% malathion),

Part of the palms of the gloves were coated with extra rubber, i.e. the palms are thicker. With technical grade MAL, the breakthrough time for the palm was slightly longer in distilled water compared with 30% isopropyl alcohol at room temperature. At 37°C, the breakthrough times in distilled water and the 30% isopropyl alcohol were

1064±3 minutes and 862±3 minutes respectively. With working strength solution, there was no detectable breakthrough in distilled water and for 30% isopropyl alcohol at ambient temperature. The test was prolonged for up to 24 hours. However, at 37±1°C, the breakthrough time was detected at around 1431 minutes in distilled water and 1154 minutes in the 30% isopropyl alcohol.

The arm section of the gloves had shorter breakthrough times (1308 ±3 minutes in distilled water, 809 ±5 minutes 30% IPA) and higher permeation rates (0.02±0.01 μg/cm^2/minute in distilled water, 0.03±0.01 μg/cm^2/minute in 30% IPA) compared with the palm. There was no MAL solution breakthrough up to 24 hours with the working strength solution. At 37±1°C, the permeation rate in 30% IPA was about 25 times higher than in water with the technical grade MAL. When the temperature was changed from 22±1°C to 37±1°C, the breakthrough times were decreased by 14.5% (palm) and 37.5% (arm). Under the same conditions, permeation rates were increased by greater than 100% (palm, arm).

2.4.4.2.2 Performance of used PVC gloves

For Study Group 2, new gloves were provided to each worker before commencement of MAL bait spraying on the first day. Two pairs of gloves were then randomly removed from workers at defined periods and tested for permeation resistance in the laboratory.

The palm and the arm were cut out from left and right gloves for testing after the gloves had been used for 3, 7 and 14 days. The used gloves were tested with technical grade MAL in order to determine breakthrough time and permeation rates. This would provide the worst case scenario rather than using working strength MAL solution. Samples were run in triplicate, and two used gloves were tested for each situation. The results are reported in Table 22.

Palm

With the gloves used for three days, breakthrough times of the palm were between 240 minutes and 617 minutes, and permeation rates were between 0.04 μg/cm^2/minute and 0.05 μg/cm^2/minute. Gloves used for seven days had shorter breakthrough time

(101 minutes to 189 minutes) and higher permeation rates (0.04 μg/cm^2/minute to 0.3 μg/cm^2/minute).

In the case of the gloves used for 14 days, the breakthrough time was decreased to a minimum of 33 minutes and the permeation rate was up to 0.8 μg/cm^2/minute. There is some evidence that the palm of the left hand gloves has lower breakthrough times than right hand gloves. The reason for this might be that most of sprayers used their left hand to grip the spray gun and pushed the piston up and down with right hand. In the case of the right palm of the glove used for 7 days, breakthrough times could not be detected. The glove material was already contaminated with high concentrations and MAL that had passed through the glove material before the analysis.

Arm

As the worst case, breakthrough times for the arm dropped down from 562 minutes with gloves used for 3 days to 81 minutes with gloves used for 14 days. The permeation rates were increased from 0.06 μg/cm^2/minute (3 days used glove) to 0.4 μg/cm^2/minute (14 days used glove).

Table 22: Breakthrough Time and Permeation Rate of Used PVC Gloves with Technical Grade Malathion at 22 °C

(1) Part: Palm

Period of Use (days) [1]	Location	Thickness (mm) (AM ±STD)	B.T [2] (minute)	P.R [3] (μg/cm^2/minute)
3	Left	1.31±0.05	400	0.04
		1.31±0.05	240	0.05
	Right	1.30±0.01	617	0.04
		1.27±0.03	402	0.04
7	Left	1.28±0.01	189	0.04
		1.27±0.02	101	0.30
	Right	1.28±0.01	N.A.*	0.19
		1.26±0.03	140	0.35
14	Left	1.25±0.01	33	0.40
		1.24±0.03	73	0.50
	Right	1.18±0.04	86	0.23
		1.20±0.02	49	0.77

(2) Part: Arm

Period of Use (days) [1]	Location	Thickness (mm) (AM±STD)	B.T [2] (minute)	P.R [3] (μg/cm²/minute)
3	Left	0.98±0.02	565	0.06
		0.97±0.03	562	0.06
	Right	0.99±0.07	572	0.06
		0.94±0.04	572	0.06
7	Left	0.97±0.02	484	0.05
		0.95±0.01	191	0.06
	Right	0.95±0.01	541	0.19
		0.94±0.03	308	0.03
14	Left	0.93±0.01	171	0.13
		0.90±0.033	153	0.12
	Right	0.88±0.012	87	0.07
		0.92±0.071	81	0.45

*** Breakthrough occurred immediately. The initial amount in the first minute was estimated to be 1.3 μg/cm2.**

1) Period of the usage of glove (3.5hours per day),
2) Breakthrough time of malathlon,
3) Permeation rate,

2.4.4.2.3. Thickness changes observed during use

Unless gloves were removed, sprayers used the same gloves everyday without replacement over the two week period. In the case of workers whose gloves were removed, a new pair was provided (without further testing).

The thickness of the gloves was measured and reported in Tables 21 and 22. The palm and the arm thicknesses should be compared with new gloves (Table 21). Thicknesses generally decreased with usage time, with corresponding reductions in breakthrough time.

2.5 Discussion

This appears to be the first systematic study of occupational exposure to MAL and FEN during Mediterranean fruit fly eradication activities.

In 2001 a group of 6 pesticide applicators applying MAL and FEN in a field simulation were intensively studied.

In 2003 a group of 27 MAL bait sprayers were investigated using questionnaires and limited dermal exposure assessments were conducted with 8 workers.

In addition, the resistance of PVC gloves towards permeation by MAL and FEN were tested under conditions of variable concentration, temperature and worker use.

With respect to the research questions given in Chapter 1, the following conclusions may be drawn:

- Evaluation of dermal exposures, in total and in respect to particular areas of exposed skin, e.g. hands, and assessment of the opportunities of exposure;

For MAL bait sprayers involved with the field simulation, it appears that the heaviest exposure is on the left front forearm (Table 10). For FEN sprayers, the contamination is more widespread which is consistent with cover spray activities. Glove contamination was detectable in many cases, with some values being high. One worker (P1, Table 12) was observed to transfer contamination from outer gloves to inner gloves and socks upon removal. Indeed, surface contamination transfer by poor work practice and storage may represent a significant means of exposure in these pesticide applications. Skin wipes of the forehead in 2003 yielded relatively low values indicating that aerosol deposition is minor. This is consistent with air sampling data (Table 9). In the case of cover spraying with FEN, the air concentrations would be in excess of the TWA Exposure Standard of 0.2 mg/m^3 if the spraying were done throughout the day. The observations made during the course of both studies indicate that visible liquid contamination of clothing can occur from leaking equipment, poor work practice or skill, or unfavourable wind direction. Opportunities for exposure include

(1) leaking knapsacks or splashes resulting in direct contact;

(2) contamination transfer due to poor storage and removal of PPE; and

(3) aerosol deposition, especially for FEN.

- Evaluation of chemical contamination of the eye surface, arising from the spray application of chemicals;

Pesticide was not detected in the eye during the field simulation, possibly as a result of effective eye protection, but perhaps also due to dilution/decomposition of pesticide on the eye surface prior to ocular sampling. All other factors being equal it is likely that cover spray will result in more ocular exposure than bait spray.

- Prevalence of skin and eye-related symptoms, in absolute terms and in comparison with a control group of unexposed workers;

Skin symptoms were relatively common among the exposed workers, and more prevalent than for controls. However, the difference was not statistically significant. In a study of nurses by Pisaniello *et al.,* (1994), dry cracked skin and rashes affected 39% and 13% respectively. In general terms, skin problems among pest controllers could be considered moderate.

Eye symptoms were, in fact, more common among the controls. The low prevalence of eye irritation is not readily explained, although eye protection was routinely worn by the operators, who mainly worked outdoors.

- Comparison of measured exposures with observed work practice, equipment and control measures;

As previously mentioned, observations of leaking equipment, personal hygiene and poor storage of PPE can be correlated with dermal exposures of the hand and forearm. These results are consistent with other studies. In a study by Pisaniello and coworkers (2000), contamination of foreheads by hand contact was observed. Similarly, smoking of externally contaminated cigarettes facilitated the contamination of the mouth area and inhalational exposure. In the present study, no measurements of vehicle cabin contamination were carried out. However, it is known that eating in contaminated vehicles and touching contaminated steering wheels or gear sticks may contribute to exposure (Cattani *et al.*, 2001). From Table 6, it can be seen that only 15% of workers removed potentially-contaminated overalls during their lunch break.

- Evaluation, where feasible, of uptake using biological monitoring methods and correlation with ambient and dermal measurements;

Serum (plasma) cholinesterase depression and the presence of dialkylphosphates in urine were used for biological monitoring in this study. Whilst there was evidence of skin contact with MAL and FEN, biological monitoring results demonstrate low uptake. Coupled with questionnaire data, these suggest low health risk. There is a paucity of information on the rate of transdermal penetration by MAL and FAN, especially for working strength solutions. Existing data (ATSDR, 2000) suggest inefficient penetration through the intact skin.

The field simulation experiments in 2001 were of limited duration, entailing only about 75 - 100 minutes of contact with potentially contaminated clothing. No BM was conducted during the 2003 fruit fly outbreak. Thus it is possible that partially contaminated and/or absorbant PPE (Garrod *et al.*, 1998) may represent only a small health risk if it is worn for short periods. On the other hand, damaged, hot or occluded skin will increase the likelihood of uptake. Further work is required to clarify the issue under actual field conditions, and preferably in hot weather.

- Assessment of PPE service life, in particular repeated usage of gloves, in actual field use and in simulated laboratory experiments.

This study has shown that the elbow length PVC gloves currently used by PIRSA staff are effective under normal conditions. However, over a period of two weeks of daily usage, a measurable decrease in thickness and permeation resistance occurred, without any obvious change in physical appearance. Furthermore, differential wear is possible, depending, for example, on the technique and handedness of the operator.

Breakthrough times after two weeks usage were approximately one hour for technical grade MAL at room temperature (Table 21). At elevated temperature, resistance would be further decreased (Table 20).

It appears that a marked reduction in performance occurs after one week, and thus it would be desirable to replace gloves after one week of usage.

Limitations

This study is limited by the fact that there was only one small fruit fly outbreak in 2003, and the fieldwork only lasted two weeks. Fenthion cover spray was not evaluated under actual field conditions due to a temporary ban from 2001.

Hence, the sample size of applicators was relatively small for questionnaire purposes. Due to practical/cost limitations, it was not feasible to analyse all available PPE. In the case of cotton overalls, sections were pre-selected for analysis based on visible or observed contamination.

Strengths

This is one of the few studies that has examined service life of gloves (Klingner and Boeniger, 2002). By a combination of thickness and permeation measurements in two sections of gloves it was possible to assess the impact on peformance, arising from repeated use under actual field conditions.

The ability to observe the effect of temperature was also a strength.

Although no residual pesticide was found in the eyes of applicators, this appears to be the first study to specifically look for it.

Careful observation of work practice, coupled with environmental and biological sampling and questionnaires has enabled an assessment of health risk due to the use of MAL and FEN for fruit fly control.

Recommendations

The following recommendations can be made to further reduce exposures;

- Leaking equipment should be replaced or repaired.
- Suitable facilities should be provided in the vehicle for storage of PPE. Gloves, respirators and overalls should be separated to avoid cross contamination.
- Applicators should be given training on proper removal and storage of PPE so as to avoid secondary contamination.

- Hands should be washed prior to eating and smoking, and this should not be in the vehicle cabin.
- Proper chemical resistant footwear should be provided.
- Elbow length PVC gloves should be replaced after approximately a week of use.

2.6 Conclusions

From the simulation study in 2001, questionnaire data in 2003, and discussions with workers and supervisors, it appears that exposure to MAL and FEN under the circumstances of use is insufficient to cause appreciable health problems. However, pesticides were commonly detected in glove samples, on the forehead, and on the forearm, and chest regions. Visible contamination was occasionally observed on the back, forearms and lower leg regions due to leaking equipment. There was also the potential for an accumulation of pesticides on inappropriate footwear and subsequent exposure.

Glove permeation tests, under conditions of variable use, temperature and active ingredient concentration, were conducted. In the case of gloves used for malathion bait spraying, the polyvinyl chloride gloves provided good permeation resistance when new. However, significant reductions in performance were observed after two weeks of usage. In addition, the physical appearance of the gloves did not give any indication of their lowered breakthrough time.

Ocular exposure was not detectable in the circumstances.

CHAPTER 3. DERMAL AND OCULAR EXPOSURE TO HEXAMETHYLENE DIISOCYANATE (HDI) BASED PRODUCTS

3.1 Introduction

An introduction to isocyanates used for spray painting has been given in Section 1.7 of Chapter 1.

The two industries selected for isocyanate exposure assessment were automotive spray painting and furniture manufacturing.

The spray painters from the two industries agreed voluntarily to undergo skin and ocular monitoring after finishing spray painting. However, no biological monitoring was conducted, because of the difficulty of the detection of suitable metabolites. In addition, urinary hexamethlenediamine (HDA) is not likely to be a useful biomarker to monitor HDI exposure.

In order to investigate exposure levels and the prevalence of adverse health symptom prevalence, questionnaire surveys and a range of sampling methods were applied (see Section 3.3). Glove permeaion testing was conducted to determine glove performance. All results are described in Section 3.4.

3.2 Study Populations

In 2003, a number of private automobile repair workshops and two apprentice training schools in SA were investigated. A mobile touch up spray painting situation was also investigated. Spray painters usually applied isocyanate-based (two-pack) paints inside a dedicated spray booth (Plate 12) or enclosure, collectively termed "indoor" spraying. In some cases, spraying was carried out undercover but subject to natural ventilation (termed "outdoor" spraying), e.g. carport.

Either panels or a whole body of a car were sprayed inside the spray booth.

Plate 12: Two-Pack Spray Painting in Crash Repair Shops

In 2004, spraying in a private furniture manufacturing company was also investigated. Spray painting was conducted inside the spray booth (Plate 13).

Plate 13: Two-Pack Spray Painting in The Furniture Industry

3.2.1 Study Group 3 (Crash Repair Shops & Associated Industries, 2003) *

Twenty six spray painters participated in this study. Of these, 21 workers were qualified spray painters in crash repair workshops, and the others were apprentices from a TAFE college (1 worker) and a Motor Trade Association (MTA) training

* Study group 1 and 2 were described and exposures discussed regarding to the pesticides study (Chapter 2)

school (3 workers), and one mobile spray painter. A list of crash repair workshops was provide by the MTA and an introductory letter was sent in advance (see Appendix 5). Nine workshops (50%) agreed to participate. The non-responders did not appear to be different from the responders in terms of workshop size or location.

For vehicle refinishing, a sealer/filler containing isocyanate was often used in order to seal small gaps or holes on the auto body surface. The surface was left for around 12-17 hours, and then rubbed down by using very fine sand paper or a powered sander. The surface was rinsed and dried, and masked up. Before the spray painting, the spray booth was typically heated up to 30°C for 10-15 minutes. The paint ingredients were then mixed, i.e. HDI-based hardener, resin base (clear or colour) and reducer, and poured into the spray gun.

A range of hardeners used in the automobile repair industry, such as PPG (2K MS Normal Hardener 980-35239), Spies Hecker (2K-Acryl-System, Permacron, MS Plus Hardener, Slow 3030, 975-65507) and Sikkens (Autocryl, Hardener MS 10) (Mohanu, 1996).

Either a conventional (high-pressure) or an HVLP (high-volume low-pressure) spray gun was used with between 20 and 70 psi air pressure. After all these procedures, baking was conducted at around 60°C for 45 minutes. The application time was about 20 minutes for a small part of a car. When this process was completed, the small part or car was left for 2-3 hours to completely harden.

Workers usually wore overalls, gloves respiratory protection, and in some cases eye protection.

3.2.2 Study Group 4 (Furniture Industry, 2004)

A large furniture manufacturer in SA agreed to assist with this study. This group included spray painters using isocyanate-based spray paints. Three spray painters and one spray paint mixer were involved in this study.

In this furniture manufacturing company, very low concentrations of isocyanate (0.1 mgNCO/g liquid hardener) were used for 2-pack spray painting. HDI-based hardener (AKZO NOBEL; Fast, No 895002013, Code 310.700) was used.

There was a preliminary sealer for wood panels or small pieces of wood before the application of the 2-pack spray paint in a spray booth. After applying the sealer, the wood panels or small pieces of wood were moved to either of two spray paint booths, an automatic spray booth and a manual spray booth. For the spray painting, the main components of the spray paint were resin:hardener (2:1) and reducer (approx. 10% in total).

The spray paint mixer prepared spray paint for the automatic spray painting system and provided spray paint for the spray painters working in the manual spray booth which had a water curtain system and a small duct system at the ceiling. In general, small articles were sprayed. The application time was about 20 minutes for 2 or 3 pieces. The mixing area was not enclosed.

The two different spray booths shared the same collecting room. After finishing the 2-pack spray painting from both spray booths, all the sprayed wood panels and small articles of wood were stored in the collecting room (average temperature was around 26°C) to dry out for 12-15 hours. Workers wore overalls, respirators and eye protection.

3.3 Methods

3.3.1 Fieldwork Methods

For the isocyanate spray paint applicators, a range of methods were used:

Health and work practice questionnaire, personal air samples, general area air samples away from spraying spots or spray booths, ocular sampling, skin wipes, skin patches and PPE samples (respirators and goggles).

3.3.1.1 Questionnaire survey

3.3.1.1.1 Development and pilot investigation

A cross-sectional study was conducted for the isocyanate (HDI) spray painters similar to that for pesticide workers.

The aim of project was explained to the workers by a member of the research team and an information sheet was supplied to the exposed group (see Appendix 1.2), and

they were interviewed individually. They were given an opportunity to ask questions and then asked if they wished to participate. If they agreed, a consent form was issued (see Appendix 1.3), along with a complaint form (see Appendix 1.4).

The questionnaire based on a previous questionnaire (Pisaniello *et al.*, 2000) for workers implementing isocyanate (HDI) spray painting. The strategy of this questionnaire was the same as for the pesticide workers.

This questionnaire included personal information (name, date of birth, sex, workplace, job title, work experience and educational status), health information (respiratory symptoms, skin symptoms, ocular symptoms, other symptoms and smoking status) and work practices (chemical usage and PPE usage) (see Appendix 2.2).

The control group was the same as for the pesticide workers in Chapter 2.

3.3.1.1.2 Administration and human ethics

Ethics approval was given by the Human Research Ethics Committee of The University of Adelaide. Notification of approval was provided in a letter dated in March, 2003 (see Appendix 3.2).

The author selected volunteer operators who were exclusively using isocyanate (HDI) during the 2-pack spraying painting.

3.3.1.1.3 Data analysis

The same data storage system was used for personal confidential information as for the data from the pesticides workers as well as statistical analysis (see Section 2.3.1.1.3).

3.3.1.2 Worksite observations

In order to observe working environment and conditions, semi-quantitative Dermal Exposure Assessment (DREAM) based on dermal exposure assessment (Van-Wendel-De-Joode *et al.*, 2003) was adopted. A worksite observational sheet was

developed, and used for the inspection of the areas in which isocyanates-based products were used and for examining dermal exposure (see Appendix 6). This sheet includes workplace name (company), workshop size, procedures, environment, ventilation system, chemical used, contamination areas on the body, exposure status, cleaning status and PPE use.

3.3.1.3 Environmental measurements

3.3.1.3.1 Air monitoring

Air monitoring was conducted in order to provide quantitative inhalational exposure data in the workplace. Impregnated glass fibre filters were used following the HSE MDHS 25/3 method (HSE, 1999). For personal air monitoring, an air sampler (cassette type-composed of three parts) was attached within the worker's breathing zone at a flow rate of 1 L/minute controlled using an air sampling pump (Plate 14). The flow rate was checked using a calibrated rotameter prior to and after sampling. In addition (for group 3 only) positional air samples were collected at various distances to determine potential exposure of other employees and how far isocyanate spreads.

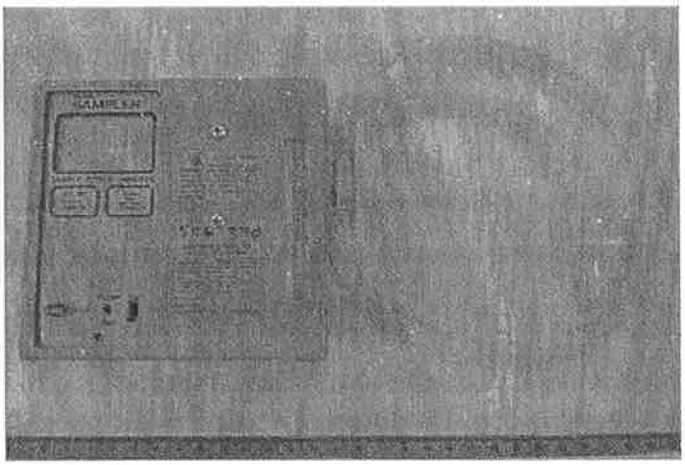


Plate 14: Air Monitoring Apparatus for Isocyanate (HDI)

3.3.1.3.2 Surface monitoring

For surface monitoring, color change was observed from contaminated surfaces using a Paper Tape (Replacement Detection Tape Cassette; Aliphatic Isocyanates, GMD SYSTEMS Inc.) and commercial products (Permea-Tec™ Colorimetric Swype

Indicators, Package of 25 Surface SWYPES™ (Aliphatic. Iso.; J-ISOAL-SUR), Package of 25 Skin SWYPES™ (Aliph. ISO.; J-ISOAL-SKN) and Package of 20 pads (Aliphatic Iso.; J-ISOAL-PERM, Omega Speciality Instrument Company, USA)). Plate 15 shows the Paper Tape and the Permea-Tec™ Pads. The Colorimetric Swype Indicators were recommended by Lawrence (2002).

The selected contaminated areas and PPE were wiped. Before wiping surfaces and observing color changes, pure IPA was sprayed on the surface (see Section 3.4.4.1.4). Table 23 describes sampling items and sampling areas. For surface monitoring, a total area of wiping was 10 cm x 10 cm or the whole area of door handles, cabinet handles or a spray gun handle.

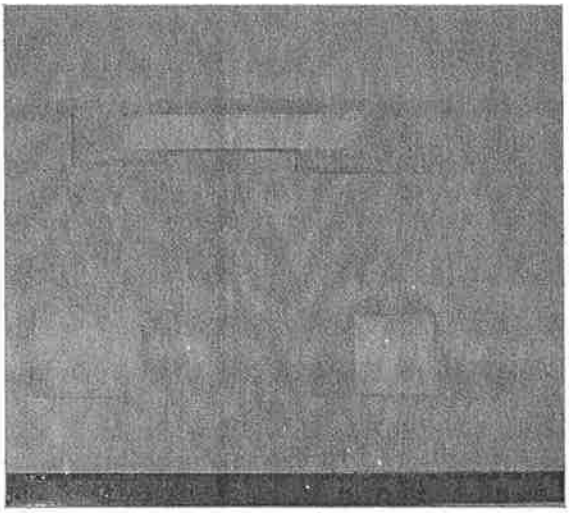


Plate 15: GMD Systems Paper Tape and Permea-Tec™

Table 23: List of Items Used for Surface Wipes and Approximate Areas Wiped

Items	Description
BT	Bench Top (100cm^2)
CB	Chemical Balance (100cm^2)
RHM	Rocker Handle in Mixing Room (66cm^2)
IDHM	Inside Door Handle in Mixing Room (70cm^2)
ODHM	Outside Door Handle in Mixing Room (70cm^2)
IDHB	Inside Door Handle in Booth (98cm^2)
ODHB	Outside Door Handle in Booth (98cm^2)
SIR	Inside Surface of Air Purifying Respirator (60cm^2)
SIAR	Inside Surface of Hood-Airline Respirator (558cm^2)
SOAR	Outside Surface of Hood-Airline Respirator (558cm^2)
SG	Spray Gun (99cm^2)
IG	Inside Goggle (56cm^2)
OG	Outside Goggle (56cm^2)
ST	Sitting Table (100cm^2)

In order to measure exposure levels while using personal protective equipment (PPE), the spray painters provided their respiratory protective equipment, rather than providing overalls or disposable coveralls for assessment. None of the spray painters used cotton gloves underneath the protective gloves. This investigation of PPE contamination was conducted by wiping the inside and outside surface of respiratory protection (a full face-air line mask or a half face respirator) used, after pure IPA was sprayed. The outside surface of the respirator provided potential exposure levels from air contamination and direct skin contact, and the isocyanate level on the inside surface indicated the amount of leakage and facial exposure.

3.3.1.4 Dermal and ocular monitoring

Dermal monitoring was conducted by using Ghost™ Wipe pads purchased from Environmental Express (USA). Pure IPA was sprayed on the skin before the skin was wiped by the Ghost™ Wipe pads (see Section 3.4.4.1.4). For qualitative assessment of skin contamination, commercial products (colorimetric Paper Tape and Swype Pads) were also used. Figure 8 describes dermal monitoring areas for isocyanate (HDI).

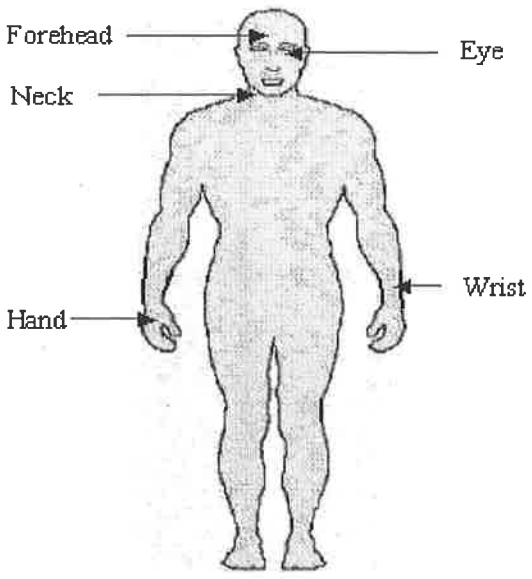


Figure 8: Positions of Dermal Sampling

In particular, the commercial product (Permea-Tec™ Pads) was attached to the fingers and the hands under protective gloves before their application, to check for

isocyanate penetration to the skin through the glove material. Color change would be observed, if there was the presence of isocyanates (e.g. HDI).

No sampling and analytical procedures for ocular monitoring of isocyanates are currently available. However, ocular sampling was conducted using the same eye drops (Allergan "Refresh") (see Section 3.4.4.1.3), which were used for the pesticide workers in 2001 and 2003 (Plate 11). Excess liquid from the corner of each eye was absorbed on a sterile cotton swab. All the samples were collected immediately as soon as the spray painters had finished the spray painting. Eye samples were then put in a small vial containing 10 ml of the derivatizing solution.

3.3.1.5 Biological monitoring

Biological monitoring for isocyanate exposure was considered, in particular HDA, but for practical reasons including the cost associated with development of new method or shipment overseas, it was decided not to proceed. Other researchers have utilized this approach, but the relationship between HDA and inhalational exposure has not been straightforward and there is no biological exposure standard based on urinary HDA at present (Liu *et al.*, 2004).

3.3.2 Laboratory Methods

In order to develop sampling methods and analytical methods, there were a number of optimization experiments carried out for derivatizing solutions and dissolving solutions. For wipe sampling, Ghost™ Wipes, Paper Tape and Permea-Tec™ Colorimetric Swype Indicators were tested for suitability. For testing glove performance, a new test cell was developed for this study.

3.3.2.1 Method development

3.3.2.1.1 HSE method (MDHS-25, UK)

To determine exposure levels of workers handling isocyanate (HDI) products and peripheral surfaces, the basic methodology was to use a derivatizing reagent. The advantages and disadvantages of selected reagents are summarized in Table 24.

Table 24: Reagent Systems for the Quantification of Airborne Isocyanates

Agents	Principle	Advantages	Disadvantages	Reference
Marcali	Acid impinger/ diazotization with nitrous acid and N-2-aminoethyl-1-naphthylamine	On-site colorimetric analysis. Similar response for polymeric isocyanates	Only aromatic isocyanates. Amine interference messy and inconvenient. Reagent potentially carcinogenic.	NLI, 2001
Ethanol	Impinger, forms urethane analyzable by HPLC	Separation of isocyanated (mainly monomers)	Only aromatic isocyanates (UV detection)	NLI, 2001 Skarping *et al.*, 1988
Nitro reagent [N-(4-nitrobenzyl) -n-propylamine]	Impingers/glass wool tube, forms urea analyzable by HPLC	Separation of isocyanates (mainly monomers) Equalsensitivity for Aliphatic and aromatic isocyanates	Less sensityve than ethanol for aromatic isocyanates. Reagent unstable HPLC column degradation.	NLI, 2001 Corbini *et al.*, 1991 Hakes *et al.*, 1986
MAMA [9-(N-methy-aminomethy l) anthracene]	Impinger/filter, forms urea analyzable by HPLC. Isocyanates identified by detector ratio (fluor/UV)	Can quantify polyisocyanates. Near universal UV response factor.	Variable fluorescent yield per NCO.	NLI, 2001 Andersson *et al.*, 1983 Gudehn, 1984
1-2MP [1-(2-methoxyphe nyl)piperazi ne]	Impinger/filter, forms urea analyzable by HPLC. Isocyanates identified by detector ratio (EC/UV)	Can quantify polyisocyanates	Analysis is more complex. EC detector unstable.	NLI, 2001 Schmidtke and Seifert, 1990 Huynh *et al.*, 1992 NIOSH, 1984b
1-2PP [1-(2-pyridyl) piperazine]	Impinger/filter, foams urea analyzable by HPLC.	Separation of isocyanates (mainly monomers) Filter option more convenient.	Polyisocyanates still difficult	NLI, 2001 Ellwood *et al.*, 1981
Tryptamine [2-(2-aminoethyl) indole]	Impinger, forms urea Analyzable by HPLC. Isocyanates identified by detector ratio (fluor/UV)	Can quantify polyisocyanates. More constant fluorescent yield per NCO.	EC detector unstable. Exposure hazard from DMSO.	NLI, 2001 Wu *et al.*, 1990

Table 24: Reagent Systems for The Quantification of Airborne Isocyanates (Continued)

MAP [9-(1-methyl anthracenyl) piperazine]	Impinger/filter, foams urea analyzable by HPLC. Isocyanates identified by detector ratio (fluor/UV)	Can quantify polyisocyanates. Near universal UV response factor/sensitive UV detection. Compatible with Ph gradient elution..	Variablefluorescent yield per NCO. Stability of derivatives uncertain. MAP not commercially available. MAP artifact peaks.	NLI, 2001
DBA [dibutylamine]	Impinger, forms urea analyzable by LC/MS. Isocyanates identified by MS.	Can quantify isocyanates and amines. Faster reaction times.	Non-routine expensive analysis. Quantifying polyisocyanates requires standards.	NLI, 2001
PAC [9-anthracenyl methyl-1-piperazine carboxylate]	Inpinger, forms urea analyzable by HPLC. PAC derivatives can also be cleaved to single product	No chromatographic losses of isocyanate species. Simple chromatogram. No response factor variability between isocyanates.	Impurities may give high blank of cleavage product.	NLI, 2001
Iso-Chek™	Combination of PTFE (post-reacted with 2-MP) and MAMA-doped filter.	Separates vapor and aerosol. Adopted by ASTM.	Short-term sampling (15min). Sample may not react efficiently.	NLI, 2001

The HSE (UK), MDHS-25 method using glass fibre filters impregnated with 1-(2-methoxyphenyl) piperazine was used in conjunction with high performance liquid chromatography (HPLC) with ultraviolet (UV) and electrochemical (EC) detectors (Pisaniello and Muriale, 1989a).

3.3.2.1.2 Sampling filter

According to the MDHS 25/3 method (HSE, 1999), a glass fibre filter (25 mm) was recommended for isocyanate sampling and should be impregnated before monitoring a contaminated area. When a derivatizing solution was prepared using 1-(2-methoxyphenyl) piperazine (1-2MP), 200 µl of the solution was dispensed on the glass fibre filter - this was then dried out at room temperature under nitrogen.

3.3.2.1.3 Absorbing solution (Derivatizing Solution)

In order to maintain an excess of derivatizing agent in the derivatization of the potentially larger amounts of isocyanate to be found in wipe samples (as distinct from air samples), a higher concentration of 1-2MP (500 μg/ml instead of 50 μg/ml) was required. The HSE method suggests using 1-2MP in dry toluene. However, it was observed that not all 1-2MP readily dissolved at 500 μg/ml. Methylene chloride was tried as an alternative and the derivatising performance of 1-2MP/methylene chloride solutions were compared with 1-2MP/toluene at the lower concentrations (see 3.4.4.1.1 for results).

3.3.2.1.4 Dissolving solutions

In order to improve the efficiency of dissolving the derivatized isocyanate (HDI), methanol was compared with acetonitrile which is recommended by the HSE method. A range of compositions of methanol in acetonitrile were used and analyzed with a known amount of hardener solution (0.15 μgNCO/ml). The hardener solution was transferred into small vials containing 10 ml of the derivative solution and analyzed by using HPLC.

3.3.2.1.5 Ocular sampling solution ("Refresh" eye drops)

The suitability of Allergan "Refresh" eye drops for sampling isocyanate needed to be checked. Technical grade hardener 10 μl (PPG, 2K MS Normal Hardener 980-35239) was placed in "Refresh" eye drops (1.5 ml in a glass bottle). For comparison, the same amount of hardener was applied to 1.5 ml pure toluene. A 10 μl sample from each of the two solutions was taken every minute and mixed with derivatising solution, and processed in the normal way.

Isocyanates react with water, but this experiment would determine whether the reaction rate was sufficiently slow to allow for ocular sampling.

3.3.2.1.6 Ghost™ Wipes

Following OSHA method No. W4002 (1999), 12 cm x 12 cm polyvinyl alcohol Ghost™ Wipes (Lawrence, 2002) were used for surface and skin wipes. (Plate 16)

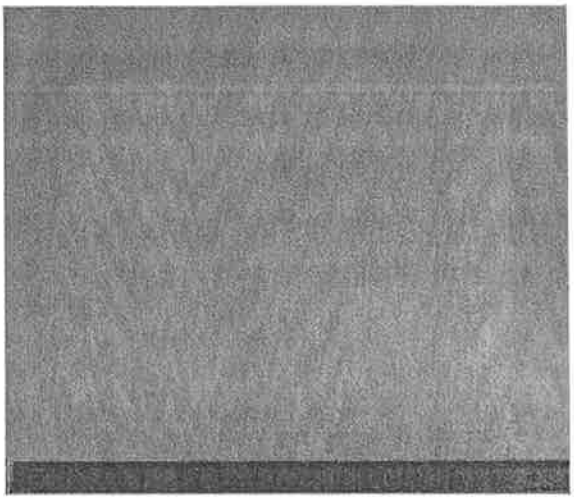


Plate 16: Ghost™ Wipe Pads

Before the Ghost™ Wipe pads were used in the field, their suitability was tested with isopropyl alcohol wetting solutions (pure and 50:50 water).

Known amounts of hardener (30 µl of PPG hardener) were applied to a clean glass plate (10 cm x 10 cm). This pre-contaminated surface was sprayed up to 5 times with IPA wetting solutions and twice wiped over using a dry Ghost™ Wipe pad. Wiping was carried out immediately and after set time intervals (1-3 minutes) before derivatization. For sampling, tweezers were used to wipe across the surface several times after applying IPA. HPLC was used to analyze the samples.

3.3.2.1.7 Test cell for glove performance assessment

There is no standard test method to test isocyanate permeation rates and breakthrough times for glove materials. With this in mind, a simple disposable test cell for glove performance was devised (see Figure 9) in a semi-quantitative methodology. The cell comprised a glass cylinder (2.3 cm i.d.) and a rubber o-ring.

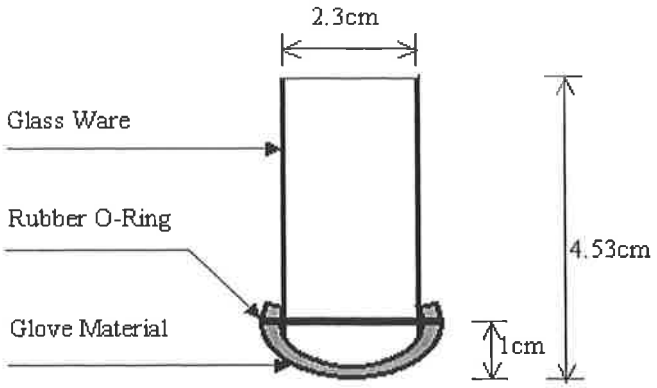


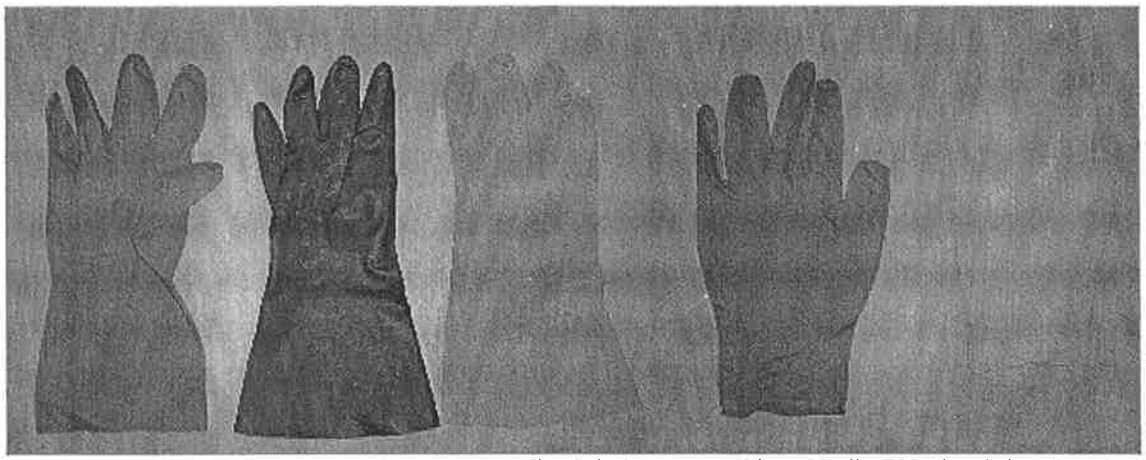
Figure 9: Analytical Test cell

Glove permeation performance with respect to solvents present in the hardeners were also tested using the conventional 1" or 2" ASTM cells (see Chapter 2).

Finally, tests were done on gloves subjected to repeated washing (fatigue).

3.3.2.1.8 Preparation of the glove materials

Several kinds of glove materials were tested with technical grade hardener (PPG 2K MS) and diluted (or working strength) hardener solution. Double layered Latex Examination Gloves, Dermo Plus™ (cotton lined nitrile rubber, Ansell), Neoprene Gloves (cotton lined, 29-865, Ansell) and Nitrosolve Gloves (Code No. 226836) were tested. Plate 17 shows the gloves.



(Nitrile-Dermo Plus) (Neoprene) (NitroSolve) (Dispo. Nitrile-T.N.T.) (Dispo.Latex)

Plate 17: Glove Materials Used for Glove Performance Test

Procedures:

1. For isocyanate permeation tests, the glove materials were cut with > 4 cm diameter. A new analytical test cell was used for each sample.

2. For glove performance with component solvents, breakthrough times and permeation rates were measured from sections of the palms and the arms. Each part was cut into 4.5 cm and 7 cm (diameter) for 1'' and 2'' ATSM test cells respectively. A 1" test cell and a Photo-ionization detector (HNU P1 1010) were used to detect the permeation of the solvent through the glove materials. Figure 10 illustrates of testing procedure for solvents.

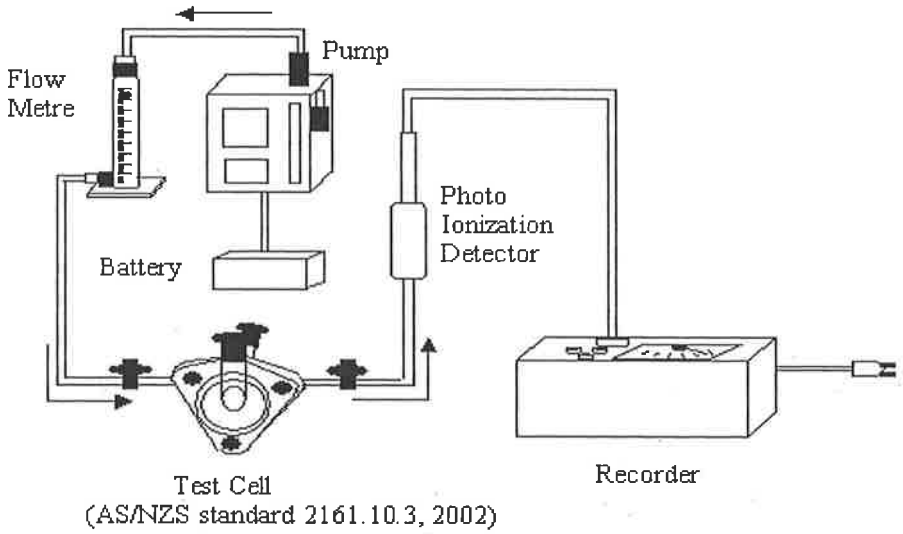


Figure 10: Instrumental Setup for the Detection of Solvent Breakthrough by PID

3. For the fatigue tests, new gloves (Nitrosolve Gloves; Code No. 226836) were put into a washing machine. Warm water (60°C) was poured and then commercial washing detergent (Approx. 110 ml) was added to each pair of gloves. The washing machine was run for 20 minutes, and then rinsed with warm water (60°C). After these procedures, the washed gloves were dried at room temperature for an hour. In order to compare glove performance, four different types of gloves were prepared, such as unwashed gloves and gloves washed between 1 to 3 times. The disposable test cell was used for this test (see Figure 9). See also 3.3.2.2.4.

3.3.2.2 Glove testing

3.3.2.2.1 Glove materials

Samples of the gloves were supplied by MSA (Aust.). Pty. Ltd., and provided by individual industry and autobody shops. Each was visually inspected prior to use.

3.3.2.2.2 Permeation test of the glove materials

Isocyanates

For isocyanate permeation test using the disposable cell the bottom of the cylinder was gently covered by a piece of the glove material without stretching. The challenge hardener was PPG 2K MS Normal Hardener 980-35239 and a 50% solution in xylene.

The outer surface of the glove material was in contact with the test chemical. The palms of the gloves were tested, because most of chemical was in contact with the palm during spray operation rather than other parts. A rubber o-ring held the glove material at 1 cm from the bottom of the test cell.

Colorimetric paper tape detection (GMD systems, aliphatic isocyanates) was used, because it was easier and more economic, and provided more sensitivity than the HPLC analytical method.

At regular time intervals (10 seconds, 1 minute, 5 minutes, 10 minutes and 20 minutes), pure IPA was sprayed onto the bottom of the surface, and then wiped with the paper tape. As soon as the surface of the glove material was wiped, the tape was dried with a hair dryer and the time was recorded. The reason for drying the surface was to speed the colour change.

After the breakthrough times were approximately determined with the paper tape method, subsequent repeat evaluations were with Ghost™ Wipe pads and pure IPA at regular time periods. After wiping, the Ghost™ Wipe pads were saturated with the derivatizing solution, and analyzed by HPLC.

Component solvents

Organic solvents, such as acetone, xylene, isopropanol and toluene, were tested with the selected glove materials.

A fully charged high capacity 6V lead acid battery was connected to a calibrated pump providing constant air flow (100 ml/minute) which was checked using an air flow meter (see Figure 10). The photoionization detector was calibrated for each solvent before use. The test material was prepared, and then put between two compartments in the 1" ASTM test cell. The outer surface of the glove material was exposed to the challenge solvent. Air was supplied from the inlet tube to outlet tube at the back part of the cell, and the contaminated air was run through the outlet tube, which was connected to the photo-ionisation detector which indicate the detection of solvents passes through the glove materials.

3.3.2.2.3 Breakthrough times and permeation rates

Permeation rates were calculated by the following equation based on AS/NZS standard 2161.10.3 (2002).

$$P = \frac{(C_i - C_{i-1})V}{(T_i - T_{i-1})A}$$

Here,

P = Permeation rate ($\mu g/cm^2$/minute)

A = area of the material specimen in contact in square centimeters (cm^2)

i = an indexing number assigned to each discrete sample, starting with i=1 for the first sample

T_i = the time at which discrete sample i was wiped in minutes (minutes)

C_i = the concentration of chemical in collecting medium at time T_i in micrograms per litre ($\mu g/mL$)

V = total volume of dissolving solution (mL)

3.3.2.2.4 Fatigue testing

In order to simulate normal usage, a washing machine was used to provide physical stress to the glove structure.

MSA 226836, Nitrosolve™ gloves, often used by painters for mixing hardeners and cleaning spray guns, were examined. However, disposable gloves (e.g. Touch N Tuff) were used while spraying.

Pure technical grade hardener (PPG; 2K MS Normal Hardener 980-35239) and diluted hardener at a working strength (resin:hardener = 2:1, 5% reducer) were tested with the washed glove materials.

3.3.3 Analytical Methods

For skin and surface wipe sampling, pure IPA was sprayed onto the skin, a target surface or the surface of PPE. The Ghost™ Wipe pads were used for wiping, and then tweezers were used to pick up the pads so as not to contaminate the Ghost™ Wipes. During the sampling, clean disposable Nitrile gloves were worn. Wipes were put directly into a vial containing 10 ml of derivatizing solution (500 μg/ml 1-2MP in methylene chloride). Sampling vials were stored in an icebox to be kept cold until analysis and to be transported safely to the laboratory. After 24 hours, 200 μl of acetic anhydride was added into the vials, and they were left for 30 minutes to ensure the completion of the reaction of the acetic anhydride with 1-2MP. Solutions were then evaporated under nitrogen. The samples were then taken up in 10 ml acetonitrile except in the case of eye samples, where 5 ml was used. For analysis, 20 μl of the solution was injected into the HPLC.

The HPLC operating conditions were based on the HSE method (MDHS, 25/3, 1999) and previously reported (Pisaniello *et al.*, 1989a). An *ICI Instruments* LC 1500 HPLC Pump, TC 1900 HPLC Temperature Controller, *BAS* LC4B/LC17A Amperometric Detector, *Kortec* K95 Variable Wavelength UV/EC Detector, DP 800 Data Interface, and a 25 cm x 4.6 mm *Spherisorb* ODS2 (C18) Column) were used.

The conditions of HPLC were 30°C (oven temperature), 1.5 ml/minute (pump rate), 0.8 V (EC detector) and 242 nm for an UV detector. The mobile phase was 67% acetonitrile, 33% distilled water and pH 6.0 (acetate buffer). Helium gas was bubbled through the mobile phase.

Monomeric and polymeric isocyanate were detected most commonly at 3.08 minutes and 7.8 minutes respectively.

3.3.4 Limits of Detection

The limit of detection was 0.003 μgNCO/ml for the EC detector which is more sensitive than the UV detector (0.008 μgNCO/ml).

The sensitivities of the self-indicating paper tape and Permea-Tec™ *Swype* Pads (approx. 0.002 μgNCO/ml) were greater than that of the HPLC method, and in some cases, dilution was required.

Using a Photo Ionization Detector, the detection limits of acetone, isopropanol and xylene were 1 ppm, and for toluene, the limit of detection was 3 ppm.

3.4 Results

3.4.1 Work Practices

Spray painters in the crash repair workshops somtimes wore disposable latex gloves, full-face airline respirators, disposable coveralls and safety goggles. However, most wore only overalls and half face respirators.

Even though the spray painters wore their PPE during working hours, the PPE was not washed frequently, or did not get washed for a long period of time, in particular full-face airline respirators, helmets and half face respirators. In addition, the respirators were not stored in an airtight containers to protect the charcoal filters from other organic solvents in the air.

It was observed that clothing was occasionally contaminated, and skin/eyes were sometimes contaminated by deposited spray mist. Whenever they were mixing or spraying, several workers folded their sleeves up to the elbows, and the front of their overalls were open. The workers had potential exposure via deposition on their skin or clothing, such as the head, neck, face, eyes, hands and arms from handling hardener during spraying, mixing and cleaning. When they finished the spray painting, they touched contaminated surfaces (e.g., full face/half mask, overalls, mixing table and spray gun) with their hands without wearing protective gloves.

After the spray application, spray guns were somtimes rinsed with acetone. During the rinse process, there was no dermal, eye or respiratory protection worn. In the mixing room, bench tops and floors were frequently not cleaned after mixing hardener, even though it was obvious that there was hardener spilled.

In the furniture industry, the spray painters, including a spray paint mixer, wore disposable nitrile gloves (Touch N Tuff^{TM}), disposable overalls (spray painters only) and half face respirators (spray painters only) during working hours. However, they did not wear appropriate eye protection, and wore normal sports shoes as foot protection. Their lower arms, head, neck and chest were not protected by any PPE. Even though the spray painters used a respirator, the mask was stored or put in a contaminated area without cleaning after the spray painting. Sometimes, their disposable nitrile gloves were physically damaged, and a small hole was observed, because they touched or handled wood panels or small pieces of wood.

The spray paint mixer handled hardener containers and solvent containers. He also used acetone to rinse or clean the top of the automatic spray gun with the index and middle fingers being swollen by solvent contact. In the mixing room, spills of solvents and hardeners were observed.

The spray painters were exposed to isocyanate vapors and mists in the spray booth, even though the isocyanate concentration of hardener was lower than in the vehicle crash repair shops. In the manual spray booth, the spray painters sprayed about 2 m away from the extraction vent.

In the storage room, the ventilation system appeared to be poor as significant solvent odors could be detected.

3.4.2 Survey Results

3.4.2.1 Subjects

Table 25 shows personal baseline data and the prevalence of previous health symptoms from the exposed group and the unexposed group. For the two groups, the average age and smoking prevalence were similar.

Table 25: Baseline Variables for HDI Spray Painters and Controls[#]

	Exposed (n=33)*	Controls (n=91)
Mean Age (STD) (years)	28 (±12)	38 (±9)
Current smokers	15 (46%)	43 (47%)
1-5 per day	1 (3%)	7 (8%)
6-10 per day	3 (9%)	7 (8%)
11-15 per day	2 (6%)	7 (8%)
16-20 per day	3 (9%)	12 (13%)
> 20 per day	6 (18%)	10 (11%)
Ex-smokers	5 (15%)	12 (13%)
Ever had hayfever?	11 (33%)	35 (39%)
Ever had asthma?	7 (21%)	7 (8%)
Ever had eczema?	2 (6%)	5 (6%)
More severe reaction than others to insect bites	2 (6%)	7 (8%)

 # All males, Study Group 3 only

No statistically significant difference in proportions between exposed workers and controls ($p < 0.05$, two-tailed test,) (Fleiss, 1981)

There were no statistically significant differences for hayfever (33% vs 39%), asthma (21% vs 8%), eczma (6% vs 6%), dermatitis (24% vs 12%) and more severe reactions than others to insect bites (6% vs 8%).

Information on hardener usage and application among HDI spray painters is described in Table 26. The average usage of HDI based paint was 0.8 L for 2.2 hours per day. During working hours, 46% of spray painters reported that they had sprayed outside a spray booth. Out of hours (hobby) spraying was reported by 24% of workers.

Table 26: Chemical Usage and Application Among HDI Spray Painters

	Spray painters (n=33, males)
Use amount of chemical (average)	0.8 L/day
Application hours (average)	2.2 hours/day
Outdoor spraying during working hours?	15 (46%)
Spraying outside of regular working hours?	8 (24%)

3.4.2.2 Symptom prevalence

Table 27 gives the symptom prevalence data derived from the questionnaire survey.

Table 27: Work-related Symptom Prevalence Data (HDI Spray Painters)

Symptoms	Exposed (n=33) #	Non-exposed (n=91) #
Skin symptoms		
Dry cracked skin	20 (61%)*	17 (19%)
Skin rash	4 (12%)	5 (6%)
Dermatitis/skin irritation	11 (33%)*	4 (4%)
Pulmonary symptoms		
Cough	13 (39%)	21 (23%)
Morning	6 (18%)	13 (14%)
Day	6 (18%)	3 (3%)
Night	1 (3%)	5 (6%)
Phlegm	16 (49%)*	24 (26%)
Morning	13 (39%)	22 (24%)
Day	0 (0%)	0 (0%)
Night	3 (9%)	2 (2%)
Increased cough/phlegm	5 (15%)	14 (15%)
Shortness of breath with wheezing	10 (30%)	21 (23%)
Chest tight/breathing become difficult	10 (30%)	18 (20%)
Eye symptoms		
Eye irritation	3 (9%)*	24 (26%)
Itchy eyes	4 (12%)*	26 (29%)
Dry eyes	4 (12%)	15 (17%)
Conjunctivitis	2 (6%)	2 (2%)
Others	1 (3%)	3 (3%)
Headaches	16 (49%)	36 (40%)
Blackouts	1 (3%)	0 (0%)

*** Statistically different proportions from controls ($p < 0.05$, two-tailed test,) were indicated (Fleiss, 1981)**

 # All males

The main adverse symptoms were the skin symptoms, pulmonary symptoms and headaches.

Of the 16 people with phlegm problems, 13 people reported that they had more symptoms in the morning.

Among the exposed, pulmonary symptoms were often attribributed to smoking, asthma, hayfever and chemical mists and vapors from spraying.

Eye symptoms, except for conjunctivitis, were relatively uncommon among spray painters. Only four of the exposed group reported itchy eyes, but of these three were apprentices.

A greater prevalence of headaches was reported from the exposed group (49%), compared with the unexposed group (40%). There was no reason given for the causes of the headaches for the exposed group, although it is possible solvent or thinner exposure may have been a factor.

The question on "Blackouts" was used to check on over-reporting of symptoms by the interviewee. As in the pesticide study, over-reporting of symptoms did not appear to be an issue.

3.4.2.3 Accidental exposures

Table 28 gives the accidents caused by chemical use, and it can be seen that 42% had an experience of a major spill (> 500 ml). Eighty five percent had experienced a splash on the body, due to chemical liquid leakage from spray guns, chemical spillage from mixing, chemical splash from washing/cleaning equipment etc. While 72% reported using eye protection, 42% had experienced a splash in the eye. People who reported wearing safety goggles or full face-airline respirator (see below) did not suffer from a splash to the eyes.

Table 28: Accidents from Chemical Use Among HDI Spray Painters

	Spray painters (n=33, males)
Major spill (>500 ml)	14 (42%)
A splash in eyes	14 (42%)
Splashing any other part of the body	28 (85%)
Accident free from spill and splash	2 (6%)

3.4.2.4 Use of personal protective equipment

Table 29 gives information on PPE usage. The main PPE used were full-face airline respirators (33%), half face-airline respirators (18%), hood or helmet-airline respirators (18%), half face cartridge respirators (73%), overalls (67%), disposable

coveralls (49%), safety glasses including prescription lenses (12%), safety goggles (9%) and protective gloves (46%).

Table 29: Use of Personal Protective Equipment Among HDI Spray Painters

Items	Spray painters (n=33, males), % prevalence
PPE usage	
Full face-airline respirator	11 (33%)
Half face-airline respirator	6 (18%)
Hood or helmet-airline respirator	6 (18%)
Air purifying cartridge respirator	24 (73%)
Overalls	22 (67%)
Disposable coveralls	16 (49%)
Glasses (prescription lenses)	4 (12%)
Goggles	3 (9%)
Face shield	0 (0%)
Protective gloves	15 (46%)
Protective Gloves [1)]	
Type of gloves	
Cotton	0 (0%)
Disposable latex examination	9 (27%)
Disposable rubber	0 (0%)
Disposable nitrile	3 (9%)
Disposable vinyl	3 (9%)
Leather	0 (0%)
Neoprene	18 (55%)
Nitrile	0 (0%)
Nitrosolve	0 (0%)
PVC	0 (0%)
Replacement of gloves	
Every time	11 (33%)
Every day	2 (6%)
1/Week	3 (6%)
Foot protection	
Shoes	7 (21%)
Boots	25 (76%)
Cleaning	
Shoes	5 (15%)
Overalls	14 (42%)
Respirator	21 (64%)
Remove overalls at lunch break	15 (46%)
Remove overalls before going home	26 (79%)

1) More than one glove were used by subjects

Of the protective gloves, the main types of gloves used were disposable latex (27%), disposable nitrile (9%), disposable vinyl (9%) and neoprene (55%). However, for spray painting, disposable latex examination gloves were mostly used in the crash repair shops. Neoprene gloves were used for cleaning spray guns after the spraying painting. In the case of disposable gloves, the gloves were replaced every time (within 20 minutes as maximum). Several workers used more than one type of glove for different purposes on the same day, such as spraying paints and cleaning or washing equipment.

For foot protection, of the exposed group, 21% used sports shoes and 76% used safety boots during working hours. However, since they were provided with safety boots or they had bought a new pair of safety boots, they used the same safety boots without cleaning or replacement. In the case of sports shoes, overalls and respirator, the percentages of use were 15%, 42% and 64% respectively. Sports shoes and overalls were cleaned once a week or two weeks. The respirator was often kept in contaminated areas, such as bench tops or the floor. Not everyone cleaned their respirator every time or daily.

At lunch breaks, 46% removed overalls. Seventy nine percent of the exposed group removed contaminated overalls before going home.

3.4.2.5 Knowledge and training

Table 30 gives the survey results for knowledge and training among the exposed group.

Table 30: Training and Education among HDI Spray Workers

	Spray painters (n=33), % prevalence
Formal training in use	28 (85%)
Period of training	
1 day course	0 (0%)
> 2 days course	28 (85%)
Education	
Health effects	27 (82%)
PPE usage	29 (88%)
MSDS	24 (73%)

A high proportion of the spray painters had attended formal training program (85%) about using isocyanates (e.g. HDI). Of the 33 spray painters, 28 (85%) had more than a 2-day training course. In the case of education about health effects, PPE usage and MSDS, 82%, 88% and 73% were reported respectively to have had such training.

3.4.3 Environmental Measurements

3.4.3.1 Study group 3

3.4.3.1.1 Observations

The spray painting was normally conducted inside a downdraught or lateral flow spray booth.

3.4.3.1.2 Air monitoring

Air monitoring was conducted for the spray painters performing the 2-pack spray painting to determine air contamination levels inside and outside spray booths. Impregnated glass fibre filters were attached within the breathing zone of the operators during the spray painting.

3.4.3.1.2.1 Spraying in a booth

The spray painting was carried out inside the spray booth with the temperature controlled by an auto heating system at about 30°C. Table 31 gives the personal air monitoring results of the spray painters during the spray painting conducted inside the spray booth.

The maximum sampling time was 20 minutes. In general, a small part of a vehicle needed to be sprayed and the application time of the 2-pack spray was 15 minutes. A high volume low pressure (HVLP) spray gun was mostly used for the spraying inside the booth. The level of air contamination was usually lower than the STEL (0.07 $mgNCO/m^3$ in 15 minutes), except for S5 and S8. In the case of study subjects S5 and S8, S5 placed his head next to the area being painted in order to check the surface during the spraying and S8 was close to the area being sprayed.

Without an extraction system, the lowest and the highest levels of air contamination were 0.55 mgNCO/m^3 (S18) and 2.4 mgNCO/m^3 (S19) respectively. These are much higher than the STEL.

Table 31: Personal Isocyanate Exposure Concentrations of Spray Painters Inside Spray Booths within Breathing Zone in Study Group 3

I.D.	Extraction system (Yes/No)	Total isocyanate (μgNCO)	Sampling time (minute)	Total air volume (L)	Isocyanate conc. (mgNCO/m^3)
S3@	Yes	0.12	2	2	0.06
S4@	Yes	0.06	3	3	0.02
S5@	Yes	3.42	4	4	0.9
S6@	Yes	< 0.03	4	4	< 0.008
S8@	Yes	0.62	7	7	0.09
S10@	Yes	0.17	15	15	0.01
S16@	Yes	0.14	18	18	0.008
S17@	Yes	0.06	20	20	0.003
AM ± STD (GM)					0.14 ± 0.3 (0.024)
S18#	No	1.09	2	2	0.55
S19#	No	7.23	3	3	2.4
S20#	No	3.42	4	4	0.86
AM ± STD (GM)					1.3 ± 1.0 (1.04)

All subjects were touch up spray painters, GM: geometric mean

<0.03 μgNCO; limit of detection, Exposure limits (STEL): 0.07 mgNCO/m^3

@ Sprayed in a dedicated spray booth with an extraction system

 # They were not in a dedicated spray booth, but a ventilated room. Extraction system was not turned on.

3.4.3.1.2.2 Spraying outside of the booth

Personal and fixed position air samples were collected from outside spray booths or in the general area near touch spraying that was not conducted in a dedicated booth.

Workshop employees in the general area were fitted with personal monitors and measurements were taken when spraying was conducted in the booth by another worker.

Table 32 shows undetectable levels of isocyanate in various situations. This indicates that isocyanate leakage from the booth is negligible.

Table 32: Personal and Fixed Position Isocyanate Concentrations Outside Spray Booths in Study Group 3

I.D.	Total isocyanate (μgNCO)	Sampling time (minute)	Total air volume (L)	Isocyanate conc. (μgNCO/m^3)
S21[a]	< 0.03	2	2	< 15.00
S22[a]	< 0.03	4	4	< 8.00
S23[a]	< 0.03	20	20	< 2.00
S24[a]	< 0.03	30	30	< 1.00
S25[a]	< 0.03	50	50	< 1.00
S26[a]	< 0.03	60	60	< 1.00
G1[b]	< 0.03	2	2	< 15.00
G2[c]	< 0.03	60	60	< 1.00

<0.03 μgNCO; limit of detection ,

a: Personal measurements for workshop employees, when spraying was conducted in the dedicated booth
b: Mobile spray painter (Sampling at 3-4 m away from the spray spot),
c: Mobile spray painter (Sampling at 4-5 m away from the spray spot).

3.4.3.1.3 Dermal and surface monitoring

The Ghost™ Wipe pads were used for skin sampling and either the paper tape or Permea-Tec™ pads were used for surface monitoring. Pure IPA was sprayed on a target area and then the area was wiped with the Ghost™ Wipe pads for both indoor and outdoor spray painting. Several parts of the painters' body were wiped after the spray application, such as the neck, hands, wrists and forehead. Spray application time was between 1- 20 minutes. For surface monitoring, a wide range of surfaces were selected, such as chemical balances, bench tops, door handles and spray guns.

3.4.3.1.3.1 Indoor spraying

Skin wipe samples were collected as soon as they had finished the spray application inside the dedicated spray booth. Table 33 gives the results of skin surface monitoring with Ghost™ Wipes.

Table 33: Isocyanate Dermal Monitoring of Indoor Spray Painters in Study Group 3

I.D.	Samp. time (minute)	Total isocyanate (μgNCO)							
		N	FH	LBH	RBH	LP	RP	LW	RW
S2	1	< 0.03 [c]	< 0.03 [c]	< 0.03 [b]	< 0.03 [b]	< 0.03 [b]	< 0.03 [b]	< 0.03 [f]	< 0.03 [f]
S3	2	< 0.03 [c]	< 0.03 [c]	0.06 [a]	< 0.03 [a]	0.08 [a]	< 0.03 [a]	< 0.03 [c]	< 0.03 [c]
S4	3	0.08 [c]	0.09 [c]	0.17 [c]	< 0.03 [c]	0.08 [c]	0.11 [c]	1.95 [c]	< 0.03 [c]
S5	4	< 0.03 [c]	< 0.03 [c]	0.05 [c]	0.04 [c]	2.03 [c]	0.11 [c]	0.14 [c]	0.06 [c]
S6	4	0.09 [g]	0.11 [g]	< 0.03 [c]	< 0.03 [c]	< 0.03 [c]	< 0.03 [c]	< 0.03 [c]	< 0.03 [c]
S8	7	< 0.03 [e]	< 0.03 [e]	< 0.03 [a]	< 0.03 [a]	0.05 [a]	0.04 [a]	0.04 [c]	< 0.03 [c]
S9	9	0.31 [g]	< 0.03 [g]	< 0.03 [a]	0.19 [a]	0.18 [a]	< 0.03 [a]	0.06 [c]	0.08 [c]
S10	15	0.13 [c]	0.30 [c]	0.08 [c]	0.05 [c]	0.07 [c]	0.15 [c]	0.12 [c]	0.27 [c]
AM±STD		0.08 ±0.10	0.07 ±0.10	0.05 ±0.05	0.04 ±0.06	0.32 ±0.69	0.06 ±0.06	0.29 ±0.67	0.06 ±0.09
S1*	1	< 0.03 [e]	< 0.03 [e]	0.25 [c]	0.18 [c]	1.23 [c]	0.72 [c]	< 0.03 [e]	< 0.03 [e]
S7*	5.3	0.79 [e]	0.11 [e]	0.15 [a]	0.1 [a]	0.42 [a]	0.39 [a]	0.5 [c]	0.17 [c]
S11*	25	0.2 [c]	< 0.03 [d]	< 0.03 [a]	0.48 [a]	0.1 [a]	0.48 [a]	0.43 [c]	3.05 [c]
S12*	30	1.53 [c]	2.46 [c]	2.53 [c]	2.62 [c]	1.69 [c]	2.16 [c]	2.72 [c]	2.13 [c]
AM±STD		0.63 ±0.68	0.65 ±1.21	0.14 ±0.12	0.85 ±1.19	0.86 ±0.73	0.94 ±0.83	0.92 ±1.22	1.34 ±1.49

***S1, S7, S11, S12: Apprentices from MTA and training school (TAFE)**

<0.03 μgNCO; limit of detection,

N;Neck, LBH: Left back hand, RBH: Right back hand, LP: Left palm, RP: Right palm, FH: Forehead, LW: Left wrist, RW: Right wrist,

a: Wore disposable latex gloves,
b: Wore disposable nitrile gloves,
c: No protection,
d: Wore full face-air lined mask,
e: Wore disposable coverall,
f: Covered by disposable overall,
g: Touched by contaminated hands

When the spray application time was greater, more isocyanate was detected on the skin, as is the case for S12 who incidentally did not wear personal protective equipment. Not surprisingly therefore, S12 gave the highest quantities of isocyanate. In general, the apprentices had higher exposure levels than the experienced spray painters, and painters who wore body protection and gloves had lower exposures.

Several spray painters (S3, S7, S8, S9 and S11) used disposable latex gloves giving exposure levels up to LBH (S7-0.15 μgNCO), RBH (S11-0.48 μg/NCO), LP (S7-0.42

μgNCO) and RP(S11-0.48 μgNCO). Screening with skin SWYPES™, underneath the disposable latex, yieled a color change.

After the spraying, the behaviors of workers were observed. S6 and S9 had contaminated hands after finishing the spraying and transfer occurred, thus the exposure levels of the neck and the forehead were 0.31 μgNCO (S9) and 0.11 μgNCO (S6) respectively. S6 had low levels of exposure, except for his neck and forehead, because he used a lower concentration of hardener (3% of isocyanate) for the 2-pack spray painting than the normal 2-pack spray painting (30% of isocyanate in liquid hardener).

3.4.3.1.3.2 Outdoor and mobile spraying

For the outdoor and mobile spray painters, skin exposure levels were measured after they finished the spray application. Table 34 gives the results of dermal monitoring.

Table 34: Isocyanate Dermal Monitoring of Outdoor/Mobile Spray Painters in Study Group 3

I.D.	Samp. time (minute)	Total isocyanate (μgNCO)							
		N	FH	LBH	RBH	LP	RP	LW	RW
S13 [a]	2.4	0.54 [d]	0.19 [d]	< 0.03 [c]	< 0.03 [c]	< 0.03 [c]	< 0.03 [c]	< 0.03 [d]	0.06 [d]
S14 [a]	7.3	0.35 [d]	0.54 [d]	0.80 [d]	1.08 [d]	1.83 [d]	2.58 [d]	< 0.03 [d]	< 0.03 [d]
S15 [b]	31	< 0.03 [d]	< 0.03 [d]	0.08 [d]	0.07 [d]	0.06 [d]	< 0.03 [d]	< 0.03 [d]	< 0.03 [d]
AM±STD		0.30 ±0.27	0.25 ±0.27	0.30 ±0.44	0.39 ±0.60	0.64 ±1.04	0.88 ±1.48	0.02 ±0.00	0.03 ±0.00

All subjects were doing touch up spray painting except S15.

<0.03 μgNCO; limit of detection,
N;Neck, LBH: Left back hand, RBH: Right back hand, LP: Left palm, RP: Right palm, FH: Fore head, LW: Left wrist, RW: Right wrist,

a: Outdoor sprayer,
b: Mobile sprayer,
c: Wore disposable nitrile gloves,
d: No protection

S14 had the highest skin exposure. He was significantly closer to the spray surface, spray mist was visible and there did not appear to be sufficient air movement.

3.4.3.1.3.3 Surface monitoring

Qualitative (Permea-Tec™) and semi-quantitative (Ghost™ Wipe) surface monitoring were conducted. Table 35 gives the monitoring results, and suggests that many of the surfaces were contaminated, including the door handles.

Table 35: Quantity of Isocyanate on Surface Samples in Spray and Mixing Areas in Study Group 3

I.D.	Isocyanate conc. (μgNCO/cm²)		Total isocyanate (μgNCO)					
	CB	BT	RHM	IDHM	ODHM	IDHB	ODHB	SG[c]
B1[a]	0.05	< 0.03	< 0.03	< 0.03	< 0.03	41.7	< 0.03	21.1[d]
B2[a]	< 0.03	-	-	< 0.03	< 0.03	-	-	-
B3[a]	-	-	-	0.1	1.2	-	-	0.4[e]
B4[a]	< 0.03	< 0.03	-	< 0.03	< 0.03	1.6	0.5	10.5[f]
B5[a]	< 0.03	-	-	0.04	< 0.03	-	-	0.2[g]
B6[a]	0.12	-	-	0.04	0.04	-	-	0.3[h]
B7[a]	< 0.03	< 0.03	-	< 0.03	< 0.03	0.3	0.1	< 0.03[i]
B8[b]	< 0.03	< 0.03	-	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03[j]
B9[a]	-	0.05	-	0.9	-	-	-	4.6[k]
AM±STD	0.04 ±0.04	0.02 ±0.02	0.02 ±0.00	0.13 ±0.29	0.17 ±0.42	10.9 ±20.54	0.16 ±0.23	4.64 ±7.60

<0.03 μgNCO/cm² & <0.03 μgNCO; limit of detection,

CB: Chemical balance, BT: Bench top, RHM: Rocker handle in mixing room, IDHM: Inside door handle in mixing room, ODHM: Outside door handle in mixing room, IDHB: Inside door handle in spray booth, ODHB: Outside door handle in spray booth, SG: Spray gun,

a: Containing high level of hardener (~300 g/L),
b: Containing lowest level of hardener (~28 g/L),
c: Wiped after spray application each time.,
d: During 25min,
e: During 1min,
f: During 15min,
g; During 4min,
h: During 2min,
i: During 7min,
j: During 4min,
k: During 7.3min.

Two kinds of different hardeners were used for this monitoring. The high level hardener contained around 30% of isocyanate and the lower level of hardener contained around 3% of isocyanate at B8. B8 used the lower level hardener and no isocyanate (HDI) could be detected in any of the samples.

In the case of spray guns, B1 had the highest level of exposure (21.1 μgNCO) after 25 minutes. In the case of B4, the spray painter cleaned the surface of the chemical balance in the mixing room after each use resulting in no detectable isocyanate.

Table 36 gives the surface results, when using qualitative colorimetric tape or Swype. The results were described as positive and negative. If there was isocyanate, a positive (P) result was recorded, otherwise a negative (N) result was recorded. Even though there were positive results from the surface monitoring (B1-BT, IDHM, ODHM and ODHB, B2-CB, IDHM and ODHM, B4-BT and B7-IDHM), they were mostly under the limit of analytical HPLC detection.

Table 36: Isocyanate Indicator Paper Testing of Surfaces at Automobile Shops by Using Paper Tape or Permea-Tec™ Pads in Study Group 3

I.D.	Color reaction (P:positive, N:negative)					
	CB	BT	IDHM	ODHM	IDHB	ODHB
B1	P	P	P	P	P	P
B2	P	P	P	P	-	-
B3	P	-	P	P	P	P
B4	N [a]	P	P	P	-	-
B5	P	P	P	N [b]	-	-
B6	P	P	P	P	-	-
B7	P	P	P	N [b]	-	-
B8	P	P	N [b]	N [b]	-	-
B9	P	P	P	P	P	P

CB: Chemical balance, BT: Bench top, IDHM: Inside door handle in mixing room, ODHM: Outside door handle in mixing room, SIRM: Surface of inside respiratory mask, IDHB: Inside door handle in spray booth, ODHB: Outside door handle in spray booth, SG: Spray gun,

a: Clean after use,
b: Open all the time without touching.

3.4.3.1.4 PPE monitoring

PPE monitoring was carried out to detect possible contamination in terms of work practices. For this monitoring, the same sampling procedures were used as for surface monitoring.

3.4.3.1.4.1 Indoor spraying

The indoor spray painters used either a full-face air line respirator or a half face respirator for organic solvents and isocyanate. The respiratory protective equipment was tested after the spray application. Table 37 gives the monitoring results for PPE after the indoor spraying.

Table 37: Isocyanate Contamination Levels of Personal Protective Equipment (PPE) for Indoor Spray Painters in Study Group 3

I.D.	Total isocyanate (µgNCO)		
	SIAR	SOAR	SIR
S2	2.8 [a]	21.8	-
S3	-	-	2.60 [a]
S4	-	-	0.08 [b]
S5	-	-	< 0.03 [b]
S6	-	-	< 0.03 [b]
S8	-	-	0.07 [a]
S9	-	-	0.86 [a]
S10	< 0.03 [b]	< 0.03	-
AM±STD			0.61 ± 1.0
S1*	0.44 [a]	9.0	-
S7*	1.61 [c]	9.0	-
S12*	< 0.03	< 0.03	-
AM±STD	0.69 ± 0.83	6.0 ± 5.2	-

<0.03 µgNCO; limit of detection,
***S1, S7, S12: Apprentices from MTA and training school (TAFE),**

SIAR: Inside surface of full face air line respirator, SOAR: Outside surface of full face air line respirator, SIR: Inside surface of air purifying respirator

a: Not cleaned before and after use, and stored in contaminated area
b: Poor facial fit, due to beard and different size,
c: Touched by contaminated hands, and stored in contaminated area

The highest levels of HDI inside and outside full-face air line respirator were 2.8 µgNCO and 21.8 µgNCO respectively. From the inside the half face respiratory mask, the highest level detected was 2.6 µgNCO (S3). In the case of S2 and S3, they stored the respirator in a contaminated area and the respirator were kept in a container with no appropriate isolation from solvents.

It was found that the inside of the respiratory protective devices were contaminated by isocyanate in most cases. From S4, S5 and S6, it was observed that the fit of the respiratory mask was poor, due to facial hair. In the case of S7, 1.61 μgNCO was detected from the inside respirator. During and after spray painting, the sprayer (S7) touched the inside the respirator with contaminated hands while donning and taking off the respirator. In general, it was shown that the exposure levels on the outside of the respirator were over ten times higher than the inside levels.

3.4.3.1.4.2 Outdoor and mobile spraying

Spray painters using safety goggles and respirators were tested. The inside of the goggles and respirators were wiped. The results were described in Table 38.

Table 38: Isocyanate Exposure from Personal Protective Equipment (PPE) for Outdoor/Mobile Spray Painters in Study Group 3

I.D.#	Total isocyanate (μgNCO)		
	IG	OG	SIR
S13	0.14 [a]	0.97	0.53 [a]
S14	-	-	1.17 [a]
S15	0.07 [a]	< 0.03	< 0.03 [a]
AM±STD			0.57 ± 0.58

 # All subjects were touch up spray painters

<0.03 μgNCO; limit of detection

IG: Inside safety goggle, OG: Outside safety goggle, SIR: Inside surface of half mask air puifying respirator

a: Not cleaned before and after use, and stored at contaminated area without storing in evacuated container

All goggles and masks were stored in contaminated areas and not cleaned before or after spray painting. The inside of the safety goggles gave up to 0.14 μgNCO, and 1.17 μgNCO was detected inside the respirator. The mobile spray painter used a half face respirator.

3.4.3.1.5 Ocular monitoring

Ocular monitoring was conducted to examine whether potential eye problems could occur. The left eye and right eye were measured separately, and eye protection was also checked. Application times for the spray painting ranged were between 1-20 minutes.

3.4.3.1.5.1 Indoor spraying

Ocular sampling results are given in Table 39. The results are divided into two parts, i.e. one group wearing no eye protection (S1-S5) and the other group wearing eye protection (S6-S12).

Table 39: Isocyanate Ocular Exposure for Indoor Spray Painters in Study Group 3

I.D.	Eye protection	Total isocyanate (μgNCO)	
		Left eye	Right eye
S2	None	0.02	0.03
S3	None	N.D.	N.D.
S4	None	N.D.	N.D.
S5	None	N.D.	N.D.
S6	Full face air line mask	N.D.	N.D.
S8	Full face air line mask	N.D.	N.D.
S9	Full face air line mask	N.D.	N.D.
S1*	None	0.05	0.25
S7*	Full face air line mask	N.D.	N.D.
S11*	Full face air line mask	0.1	N.D.
S12*	Full face air line mask	N.D.	0.18

*** S1, S7, S11, S12: Apprentices from MTA and training school (TAFE),**

N.D.: Not detected; <0.02 μgNCO; limit of detection

In the case of S1 (an apprentice), the right eye had 0.25 μgNCO. From the group wearing eye protection, there was no detectable isocyanate except for S11 and S12, observed to be due to touching of their eyes with contaminated hands after the spray painting.

3.4.3.1.5.2 Outdoor and mobile spraying

Ocular isocyanate exposure was measured for outdoor and mobile spray painters and given in Table 40.

Table 40: Isocyanate Ocular Exposure for Outdoor/Mobile Spray Painters in Study Group 3

I.D.#	Total isocyanate (μgNCO)	
	Left eye	Right eye
S13 [a]	0.05	0.02
S14 [b]	N.D.	N.D.
S15 [b]	N.D.	N.D.

#All subjects were touch up spray painters

N.D. <0.02 μgNCO; limit of detection

a: No protection, b: Wore safety goggle

S13 did not wear any eye protection . There was no significant exposure for S14 and S15 who wore safety goggles.

3.4.3.2 Study group 4 (Furniture spray painters)

3.4.3.2.1 Observations

When the door of the manual spray booth was closed, the extraction system on the ceiling did not appear to be working properly. The air flow rates at 1 m from the extraction system were between 0.1-0.2 m/second using a hot-wire anemometer, but at 2 m away from the extraction system, no air movement was observed using a smoke tube.

3.4.3.2.2 Air monitoring

Personal monitoring of spray painters and a spray paint mixer was carried out. They used hardener with less than 2% isocyanate.

Table 41 gives personal air monitoring results indicating insignificant exposure.

Table 41: Personal Isocyanate Exposure Concentrations of Spray Painters Inside Spray Booth in Study Group 4

I.D.#	Total isocyanate (μgNCO)	Sampling time (minute)	Total air volume (L)	Isocyanate conc. (μgNCO/m^3)
F1 [a]	< 0.03	18	20	< 2.00
F3 [a]	< 0.03	200	200	< 1.00
F2 [b]	< 0.03	156	160	< 1.00
F2 [b]	< 0.03	390	390	< 1.00

#All subjects were touch up spray painters (i.e. re-spraying imperfections in the manual booth)

<0.03 μgNCO; limit of detection,

a: Spray painter working inside the booth
b: Spray paint mixer working in mixing area.

Table 42 gives isocyanate results for fixed positions which were away from the spray booth. Monitoring locations were beside the spray booth (the mixing area) and the middle of the work area located over 10 m away from the spray booth. No isocyanate was detected.

Table 42: Isocyanate Exposure Concentrations in General Area in Study Group 4

I.D.	Total isocyanate (μgNCO)	Sampling time (minute)	Total air volume (L)	Isocyanate conc. (μgNCO/m^3)
A1 [a]	< 0.03	440	440	< 1.00
A2 [b]	< 0.03	445	445	< 1.00
A3 [b]	< 0.03	445	445	< 1.00

<0.03 μgNCO; limit of detection,

a: Sampling at collecting room beside the spray booth,
b: Sampling outside the spray booth.

3.4.3.2.3 Dermal and surface monitoring

There were several types of monitoring, i.e skin monitoring, surface monitoring and qualitative hand monitoring.

Table 43 gives the skin monitoring results for the spray painters and mixer. No isocyanate could be detected on the skin, probably due to the low isocyanate concentration in the hardener.

Table 43: Isocyanate Dermal Monitoring of Spray Painters in Study Group 4

I.D.#	Samp. time (min)	Total isocyanate (μgNCO)							
		N	FH	LBH	RBH	LP	RP	LW	RW
F1	4	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03
F2	240	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03
F3	525	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03	< 0.03

#All subjects were touch up spray painters (i.e. re-spraying imperfections)

<0.03 μgNCO; limit of detection,

N;Neck, LBH: Left back hand, RBH: Right back hand, LP: Left palm, RP: Right palm, FH: Forehead, LW: Left wrist, RW: Right wrist

Table 44 gives the monitoring results of surface samples. Door handles of the spray booth did not show any contamination of isocyanate (HDI), and no isocyanate was detected on the spray gun, which was wiped as soon as spray painting was finished.

Table 44: Quantity of Isocyanate on Surface Samples at Spray and Mixing Areas in Study Group 4

I.D.#	Total isocyanate (μgNCO)		
	SG	IDHSB	ODHSB
F1	< 0.03	< 0.03	< 0.03
F2	< 0.03	-	-

#Monitoring relates to touch up spray painters (i.e. re-spraying imperfections)

<0.03μgNCO; limit of detection,

SG: Spray gun, IDHSB: Inside door handle at spray booth, ODHSB: Outside door handle at spray booth

Table 45 gives the monitoring results of isocyanate permeation through the disposable nitrile gloves (Touch N Tuff).

The Permea-Tec™ Pads were attached on the palms and index fingers. There was no isocyanate penetration through the gloves after 240 minutes, in the case of the spray painting only. However, when the gloves either had a small hole(s) or was torn after moving sprayed wood panels to the collecting room, there was a positive result. Therefore, F4 had positive indication of isocyanate on the fingers. The reasons for the positive result are that F4 touched a hardener container, and the hands of the sprayer were contacted by thinners and acetone used to clean the spray gun and to prepare the

spray paint. After 220 minutes, a positive result for HDI was obtained for the fingers, due to physical damage on the gloves.

Table 45: Use of Permea-Tec™ Pads for Hand Monitoring of Spray Painters Wearing Protective Gloves (Disposable Nitrile Glove-TNT) - Group 4

I.D.#	Sampling time (minute)	Color reaction (P:positive, N:negative)			
		Left palm	Right palm	Left index	Right index
F1 [a]	7	N	N	N	N
F2 [b]	95	N	N	N	N
F3 [a]	180	N	N	N	P [d]
F2 [b]	200	N	N	P [e]	P [e]
F4 [c]	220	N	N	P [f]	P [g]
F1 [a]	240	N	N	N	N

#Monitoring relates to touch up spray painters (i.e. re-spraying imperfections)

Det. Conc.: Detected concentration, Samp. Time: Sampling time,

a: Spray painter,
b: Spray paint mixer,
c: Spray painter, paint mixer and sander,
d: A hole was observed,
e: Touched the fingers with thinner and acetone,
f: Damaged glove surface by sanding,
g: A hole and damaged glove surface were observed.

3.4.3.2.4 PPE monitoring

PPE monitoring of the spray painters was conducted by wiping the respirator (NORTON N7500 Series, Part No-022330, particulate and gas filter). No detectable isocyanate (HDI) was found from the inside of the respirator wiped after 4 minutes and 240 minutes.

3.4.3.2.5 Ocular monitoring

Ocular monitoring was conducted for one spray painter and the spray painter mixer after finishing spray painting. Table 46 gives the results of the ocular monitoring. No isocyanate was detected.

Table 46: Isocyanate Ocular Monitoring of Spray Painters in Furniture Industry in Study Group 4

I.D.	Total isocyanate (μgNCO)	
	Left eye	Right eye
F1	< 0.015	< 0.015
F1 [a]	< 0.015	< 0.015
F3	< 0.015	< 0.015

All subjects were touch up spray painters

<0.015 μgNCO; limit of detection

LD; limit of detection,

a: No protection

3.4.4 Laboratory Analysis

3.4.4.1 Optimized analytical conditions

3.4.4.1.1 Absorbing solution (Derivatizing Solution)

Toluene and methylene chloride were compared, with regard to their use as a solvent for 1-2MP (see section 3.3.2.1.4). Toluene was used in the HSE method (1999). Different concentrations of 1-2MP in toluene and methylene chloride were used. A known amount of hardener solution (6 μl of 0.04 μgNCO/ml) was transferred in small vials containing 10 ml of two different derivative solutions. For this analysis, HPLC was used.

Table 47 gives the comparison of both chemical solutions in order to determine isocyanate derivatization. It can be seen that methylene chloride and toluene give similar results.

Table 47: Comparison Between Toluene and Methylene Chloride for Derivatizing Solution

Sample	Recovery rate (%)	Mean (%)	STD
R-T	97.3	97.1	0.77
	96.2		
	97.7		
R-MC	97.8	97.5	0.25
	97.3		
	97.4		

R-T; Reference sample of Hardener in the derivatizing solution of 1-2MP in Toluene,
R-MC; Reference sample of Hardener in the derivatizing solution of 1-2MP in Methylene Chloride

3.4.4.1.2 Dissolving solutions

Acetontrile is the solvent recommended by UK HSE for uptake of derivatised isocyanate, although methanol has also been used to dissolve the urea (Pisaniello and Muriale, 1989a). Table 48 gives the results of a comparison of different acetonitrile and methanol mixtures. As can be seen, results are similar. The 90% methanol mix appeared to be optimal in terms of urea dissolution.

Table 48: Isocyanate Extraction Efficiency of Different Acetonitrile:Methanol Mixtures

Sample	Detected concentration (μgNCO/ml)	Recovery rate (%)
R-Hard	0.15	100
H100M	0.16	105
H90M	0.18	123*
H50M	0.14	96
H10M	0.14	91

R-Hard; Reference hardener sample dissolved in 100% acetonitrile (0.15 μg NCO/ml)
H100M: Hardener sample extracted by 100% methanol,
H90M: Hardener sample extracted by a mixture with 90% methanol and 10% acetonitrile
H50M: Hardener sample extracted by a mixture with 50% methanol and 50% acetonitrile
H10M: Hardener sample extracted by a mixture with 10% methanol and 90% acetonitrile
*** The result could not be explained.**

3.4.4.1.3 Ocular sampling solution ("Refresh" eye drops)

The rate of decomposition of isocyanate (technical grade hardener: PPG, 2K MS Normal, 980-35239) in "Refresh" eye drops was evaluated. Table 49 gives the results.

Table 49: Rate of Decomposition of HDI-based Hardener in Ocular Sampling Solution

Sample	Sampling time (minute)	Total amount (µg NCO)#	Recovery efficiency (AM: %)
Reference*	-	0.49	100
Ocular sampling solution "Refresh" eye drops	1	0.07, 0.05, 0.06	12
	2	0.03, 0.03, 0.02	5
	3	0.02, 0.02, 0.02	4
	4	0.01, 0.01, 0.01	2
	5	< 0.01	< 2

 # Each sample was run three times using HSE (25/3) HPLC method.

*** Technical grade hardener (2K MS PPG Hardener) dissolved in pure toluene**

Although significant isocyanate degradation was found, it is not instantaneous and it appears feasible to recover a small proportion of the original isocyanate, if the ocular sampling (and derivatization) is conducted immediately after spraying.

3.4.4.1.4 Ghost™ Wipes

Isopropyl alcohol was ultimately used to wet surfaces prior to using dry Ghost™ Wipes. However, two IPA compositions (50% in water and 100%) were tested under different isocyanate loading conditions and delay times prior to derivatisation.

Table 50 gives the results.

On the basis of these data, it was decided that the most versatile wetting procedure was 2 sprays of 100% IPA.

Table 50: Efficiency of Isopropyl Alcohol as a Surface Wetting Agent

Wetting Agent*	No. of spray applications #	Time before placing in derivatizing solution (min) @	Average recovery for isocyanate (%)
50% IPA	1	Immediately (zero)	86
50% IPA	2	Immediately (zero)	83
50% IPA	5	Immediately (zero)	91
50% IPA	1	3	82
50% IPA	2	3	75
50% IPA	5	3	82
100% IPA	1	Immediately (zero)	70
100% IPA	2	Immediately (zero)	92
100% IPA	5	Immediately (zero)	88
100% IPA	1	3	88
100% IPA	2	3	81
100% IPA	5	3	80

Each sample was run three times, and there were two wipes with Ghost™ Wipe

30 µl technical grade hardener (PPG) was applied on a smooth glass surface prior to wiping

*** Wetting solution sprayed on pre-contaminated glass surface using a sprayer, 50% IPA is 50% isopropanol in distilled water, 100% IPA: Pure isopropanol**

 # Number of sprays from a dispenser of IPA solutions

@ After spraying wetting solution on glass surface, delay time of keeping Ghost™ Wipe pads before derivatization.

3.4.4.2 Glove testing

3.4.4.2.1 Effect of solvents on selected gloves

In the crash repair shops, the spray workers used hardeners and thinners containing xylene, toluene and cleaning agent (acetone). It was necessary to test the permeation resistance of gloves against these component solvents.

Table 51 gives results with different solvents and glove materials tested. In this table, it can be seen that the selected solvents passed through most of the glove materials quickly. Disposable Latex Examination gloves gave the worst results with acetone, xylene and toluene. Even when double thickness, BTs were considerably quicker than others.

Nitrosolve gloves appear to have the best permeatin resistance, and were often used for mixing paint and cleaning guns.

Table 51: Breakthrough Times of Glove Materials with Diverse Solvents

Chemical Substance	Glove material	Thickness (mm) (AM ± STD)	B.T [4] (minute)
100% Acetone	29-865 Ansell Neoprene	0.42 ± 0.02	10.2, 10.2, 10.2
	Latex Examination [1]	0.12 ± 0.01	< 1.00
	Dermo Plus [2]	0.28 ± 0.04	1.10, 1.15, 1.12
	Nitrile Touch N Tuff™ [3]	0.11 ± 0.00	< 1.00
	226836 Nitrosolve MSA™	0.38 ± 0.01	5.03, 5.03, 4.50
100% Xylene	29-865 Ansell Neoprene	0.42 ± 0.02	7.45, 7.47, 7.48
	Latex Examination	0.14 ± 0.01	< 1.00
	Dermo Plus	0.28 ± 0.02	8.14, 8.30, 8.40
	Nitrile Touch N Tuff™	0.12 ± 0.01	2.47, 2.50, 2.45
	226836 Nitrosolve MSA™	0.37 ± 0.02	69.5, 78.5, 74.2
100% Toluene	29-865 Ansell Neoprene	0.42 ± 0.03	4.38, 4.36, 4.40
	Latex Examination	0.12 ± 0.01	< 1.00
	Dermo Plus	0.28 ± 0.05	6.10, 6.01, 6.16
	Nitrile Touch N Tuff™	0.12 ± 0.00	0.58, 1.02, 1.05
	226836 Nitrosolve MSA™	0.38 ± 0.01	21.1, 22.3, 21.5

Each sample was run three times

1) Disposable latex Examination Glove,
2) Dermo Plus as a commercial product for kitchen,
3) Disposable nitrile Touch N Tuff,
4) Breakthrough time,

3.4.4.2.2 Effect of hardener strength on isocyanate permeation

Gloves were tested aginst pure PPG hardener (980-35239) and 50% in xylene, using the disposable permeation test cell.

Table 52 gives the results. Technical grade hardener was found to permeate more slowly than the 50% solution. It can be seen that xylene appeared to encourage the isocyanate to pass through the glove materials.

Disposable Latex Examination Gloves gave the shortest BTs compared with other materials. It appears that these gloves should not be used for isocyanate spray painting and the cleaning of tools, such as the spray gun and container. However, Nitrosolve (226836) gloves appeared to be the best glove material for isocyanate protection, as there was no detectable isocyanate after 8 hours.

Table 52: Breakthrough Times and Permeation Rates of Selected Glove Materials with Different Composition of Hardeners

Glove material	Application	Thickness (mm) (AM ±STD)	BT [6] (min)	PR [7] (μg/cm²/min)
Latex Exam[1]	Pure[4]	0.12 ± 0.01	1.50, 1.50, 1.40	0.15, 0.17, 0.17
	50%[5]	0.13 ± 0.01	<1.00	0.16, 0.17, 0.16
Dermo Plus[2]	Pure	0.29 ± 0.02	53.2, 53.2, 53.5	3.48, 3.56, 3.55
	50%	0.29 ± 0.02	31.3, 31.4, 31.3	2.26, 2.32, 2.16
29-865 Neoprene glove	Pure	0.41 ± 0.02	8.0, 8.10, 8.0	2.46, 2.69, 2.13
	50%	0.42 ± 0.02	5.2, 5.3, 5.15	1.37, 1.36, 1.40
T N T™ [3]	Pure	0.12 ± 0.01	31.2, 31.2, 31.2	1.06, 1.04, 1.14
	50%	0.11 ± 0.001	18.1, 18.1, 18.1	0.25, 0.29, 0.25
226836 Nitrosolve	Pure	0.40 ± 0.01	ND[8]	ND
	50%	0.36 ± 0.01	ND	ND

Each sample was run three times

1) Latex Examination Glove,
2) Dermo Plus as a commercial product for kitchens
3) Disposable nitrile Touch N Tuff,
4) Pure technical grade hardener,
5) 50% technical grade hardener in xylene,
6) Breakthrough time,
7) Permeation rate,
8) Not detected within 8 hours

3.4.4.2.3 Fatigue test

Nitrosolve (226836) gloves were subjected to repeated washing in a washing machine at 60°C. Permeation testing with the undiluted hardener (PPG; 2K MS Normal Hardener 980-35239) in the disposable test cell was conducted. No isocyanate breakthrough was evident after 8 hours even when gloves had been washed three times.

There was also no significant difference in thickness between the unwashed new gloves and the washed gloves.

3.5 Discussion

Evidence from animal studies (Zissu *et al*, 1998) suggests that dermal exposure to isocyanates may contribute to the development of respiratory sensitization. However, many questions remain about what form of exposure is most harmful, and the biological mechanism of this harm (Sparer *et al*, 2004). Despite the attention given to the control of inhalational exposure in the last 20 years, spray painters using isocyanates are still over-represented in occupational asthma statistics in most

countries. It is possible that lack of control of dermal exposure to isocyanates may be partly responsible for the ongoing problem.

Studies of isocyanate exposure have been previously conducted in South Australia (Pisaniello and Muriale, 1989a; Mohanu, 1996) but dermal and ocular exposures were not assessed. This study sought to address this gap with a wide variety of methods.

Isocyanate spray painting in a sample of automobile repair workshops, training workshops and a furniture manufacturer was investigated.

Laboratory tests of glove permeation resistance were carried out, and simple disposable permeation cell was developed.

With respect to the research questions given in Chapter 1, the following conclusions may be drawn:

- Evaluation of dermal exposures, in total and in respect to particular areas of exposed skin, e.g. hands, and assessment of the opportunities of exposure;

Dermal exposure was evident when wipe samples were taken of the neck, forehead, wrist and hands (Tables 33 and 34). Isocyanate (HDI) was detectable under thin latex examination gloves, used during spray painting. Contamination of exposed skin areas could occur even with relatively brief spraying periods.

Hand exposure could occur at all stages, e.g. mixing, spraying and cleanup.

Liu and coworkers (2000) found similar results, including facial contamination and the poor performance of latex gloves. They argue that while hand contamination may come from both direct contact, e.g. with work surfaces, and aerosol deposition, arm and face contamination is more likely to result from vapour/aerosol deposition during painting.

Significant dermal exposure was observed for outdoor and mobile spraying, due to inappropriate PPE and uncontrolled ventilation.

It is important to note that hardeners with a much lower isocyanate content were used in the furniture situation. No detectable isocyanate was found in the air or in eye, and it was uncommon to find isocyanate on surfaces.

In this study, the overall airborne geometric mean isocyanate concentration in crash repair workshops was 24 μgNCO/m^3, which is marginally lower than other studies (Liu *et al.*, 2004; Sparer *et al.,* 2004), probably due to different sampling and analytical methods and the more widespread use of HVLP spray guns. In an earlier study Pisaniello and Muriale (1989a) found an overall GM of 68 μgNCO/m^3, but HVLP guns were not used. Without an extraction system, high airborne exposure levels (0.55-2.4 mgNCO/m^3) were observed, due to use of low pressure spray guns and low air velocities inside the spray booth. Cooper et al. (1993) considered not to eliminate or minimize air contamination.. This issue has been discussed from both theoretical (Carlton and Flynn, 1997) and empirical perspectives (Woskie *et al*, 2004).

Table 53 indicates the proportion of positive results for skin wipe samples taken over various regions of the body. Approximately 50% or more of the results were positive. The OSHA Technical Manual (OSHA, 1999) suggests skin sampling in regions likely to be exposed. However, neck and forehead regions are not mentioned. The data in Table 53 would suggest that the neck and forehead are likely to yield positive results, and should be included.

Table 53: Proportion of Detectable Dermal Isocyanate Exposures by Body Region

Body region	**Total number of samples**	**Number of positive results#**	**% positive**
Neck	15	9	60
Forehead	15	7	47
Left back hand	15	9	60
Right back hand	15	9	60
Left palm	15	12	80
Right palm	15	10	67
Left wrist	13	8	53
Right wrist	13	7	47

 # Positive results over limits of detection.

- Evaluation of chemical contamination of the eye surface, arising from the spray application of chemicals;

Although isocyanates decompose in aqueous solutuion, the ocular sampling approach described in this study was applicable as a semi-quantitative measure if the sampling was done immediately after spraying. Tables 39 and 40 indicate that eye exposure is

measurable when eye protection is not worn. Even if eye protection is worn, there is potential for exposure via transfer from contaminated surfaces.

This appears to be the first study measuring eye exposure to isocyanates, and the results point to the need for eye protection and good work practice.

- Prevalence of skin and eye-related symptoms, in absolute terms and in comparison with a control group of unexposed workers;

Table 27 indicates that skin and respiratory symptoms are common among these spray painters. This has been noted by others (Pisaniello and Muriale 1989b; Karol, 1986; Belin *et al* 1981). Dry cracked skin, dermatitis/skin irritation and phlegm were significantly more prevalent among exposed workers. In this study, skin symptoms were likely to be from the accidental splashes on the body (the face, head, forehead, lower arms and legs) during mixing, spraying and cleaning/washing equipment, or perhaps spray painting at home, even though 85% of the exposed group had formal training and education including in relation to health effects, PPE usage and MSDS.

Interestingly, eye irritation is less common, and this was also observed in a previous study (Pisaniello and Muriale, 1989a). On the other hand, Randolph and coworkers (1997) reported a greater extent of eye irritation. Conjunctivitis, a more severe eye problem, was more common amongst the exposed (Hardy and Devine, 1979).

- Comparison of measured exposures with observed work practice, equipment and control measures;

This study (Table 26) shows that 46% of painters spray outside of the dedicated booth, compared with 59% in 1988 (Pisaniello and Muriale, 1989) and 25% in 1995 (Mohanu, 1996). The variation in percentages may reflect changing awareness or levels of business activity relative to booth availability, but it is clear that such spraying is common (Cullen *et al.*, 1996). Bystander exposure may be significant (Williams *et al.*, 1999; Liu *et al.*, 2004).

Isocyanate contamination was noted on peripheral surfaces (i.e. door handles, bench tops and chemical balances), respirators and working tools (i.e. spray guns). However, when the peripheral surfaces (i.e. chemical balance and door handles) were cleaned

after use, a negative result was reported – as in Table 36 (B4). In particular, isocyanate contamination was detected on the inside and outside of PPE (i.e. full face air line respirator, half face respirators and safety goggles). The extent of contamination inside the respiratory protection might provide an indication of the potential for ocular exposure. More work is required to assess this.

Spray guns had obvious contamination after the spray painting was finished. PPE was often selected or maintained inappropriately.

Before and after the spray painting, the spray painters put on the respiratory protection or eye protection in contaminated areas and/or did not store them in an proper container after cleaning. Cushmac *et al.,* (1997) reported similar observations.

Two different kinds of disposable gloves were often used for spraying, i.e. disposable latex examination gloves and disposable nitrile gloves. When the disposable latex gloves were worn, hand exposure to isocyanate was evident. Even though hands could be protected by wearing appropriate hand protection (disposable nitrile gloves), significant glove damages (pinholes, abrasion etc.) were observed, particularly for the furniture painters, e.g. as a result moving wood panels.

Finally, it appears the apprentices may be experiencing greater isocyanate exposure, possibly due to poor work practice or less experience.

- Evaluation, where feasible, of uptake using biological monitoring methods and correlation with ambient and dermal measurements;

As previously mentioned, there is presently no valid biological monitoring method suitable for the quantitative assessment of isocyanate exposure when spraying HDI-based paints (Liu *et al*, 2004).

- Assessment of PPE service life, in particular repeated usage of gloves, in actual field use and in simulated laboratory experiments.

The permeation of isocyanates through gloves may be facilitated by the presence of solvents such as xylene, commonly found in the paints. Table 51 shows that xylene permeates more slowly through Nitrosolve gloves than Ansell neoprene gloves, even though the gloves are of similar thickness (0.4 mm). Table 52 shows the same trend

for pure hardener and a 50% solution in xylene. Breakthrough of xylene occurs at 7 minutes for the neoprene, and breakthrough of isocyanate occurs at about the same time for this glove. On the other hand, isocyanate breakthrough was not detected for Nitrosolve gloves, and is clearly much slower (53 and 31 min) than xylene breakthrough (8 min) for Dermo Plus gloves. In general, however, the thicker the glove material, the longer the BT.

When disposable gloves were tested in this study, monomeric HDI appeared to be detectable in the HPLC chromatogram, soon after breakthrough occurred.

Higher molecular weight HDI oligomers occurred more commonly later. This observation might be expected on the basis of molecular diffusion in the glove material, and may have implications for worker health, if HDI monomer is more toxic than the oligomers. Further work is warranted.

It appears that latex examination gloves are inferior to nitrile Touch N Tuff disposable gloves, and the latter should be worn during spraying. Other researchers have noted that disposable latex examination gloves failed to protect the hands (Mäkel *et al.*,2003b). Abrasion and tearing of the gloves are also an important issue, particularly in the furniture industry.

Limitations

Although intensive monitoring was carried out, this study was limited in respect of worker and workplace sample size. The Motor Trade Association facilitated access to workplaces but only 50% agreed to participate. Skin and ocular sampling were deemed to be more intrusive that air sampling.

Surface wipe sampling of irregular or porous surfaces is not straightforward and there are uncertainties about transfer efficiency (Liu *et al*, 2000). This, coupled with the reactivity of isocyanates, means that surface wipe results can only be regarded as semi-quantitative.

The standard ASTM permeation test cell could not be used for isocyanates, due to the chemical reaction with plastics and other surfaces. This prompted the development of a disposable cell. Variable temperature, and usage experiments were not conducted, athough a fatigue test was conducted with the Nitrosolve glove.

Strengths

This study has provided a wealth of information about surface contamination in workshops, and the data are generally consistent with those recently reported elsewhere (Liu *et al.*, 2000; Sparer *et al.*, 2004). It has measured ocular exposure for the first time, and has looked at the furniture industry where hardeners of lower isocyanate content are used. Exposures experienced by workers operating a franchised mobile spray painting service were also investigated.

The use of HPLC methods in glove permeation testing has given an insight into the relative permeation characteristics of oligomeric isocyanates.

Finally a simple low cost permeation testing system was developed.

Recommendations

The following recommendations can be made.

- Hardeners containing low levels of isocyanate should be used wherever possible.
- HVLP guns should be used.
- All spray paining work should be conducted in a dedicated spray booth.
- Disposable Touch N Tuff gloves should be used in preference to latex gloves for spraying. Nitrosolve gloves should be used for mixing and cleaning up.
- Gloves and other PPE should be selected and stored appropriately, avoiding cross-contamination.
- Any spills of hardener on surfaces should be immediately wiped up.

3.6 Conclusions

Exposure assessment for the spray painters using isocyanates included air monitoring, surface and skin wiping, dermal exposure patches and eye fluid sample analysis. Worksite observation, health and work practice questionnaire and glove performance tests were also conducted.

In this study, the availability of local exhaust ventilation and a high volume low pressure (HVLP) spray gun correlated with lower airborne concentrations resulting in the reduction of airborne and dermal exposure. Apprentice spray painters appeared to have higher skin exposures, associated with poorer work practice. Similarly, outdoor spraying was associated with greater skin contamination.

A high proportion of isocyanate wipe samples from crash repair shops were positive. For instance, dermal exposure was detected on the neck, forehead, back hands, palms and wrists. Surface contamination was obvious in workplaces.

Eye contamination is an issue, unless either a full face air line mask or safety goggles are worn during the spraying.

However, in the furniture factory, no detectable isocyanate was found in air, skin, eye and surfaces samples, probably due to the low concentration of isocyanate in the liquid hardener.

Isocyanate exposed painters experienced more skin and respiratory symptoms than the controls. Eye irritation was uncommon.

For hand protection, gloves made of nitrile provided good protection unless there was either physical damage or pre-contamination inside the gloves.

Isocyanate breakthrough was detected in a variety of disposable gloves. Where this occurred, monomeric HDI was likely to be disproportionately more common than oligomeric HDI, probably due to more facile diffusion of lower molecular weight species. However, there was no detection of monomeric HDI after breakthrough times. Thin latex gloves were commonly used but were found to provide little resistance to permeation, according to the colorimetric observation using PermeaTec^{TM} pads underneath the gloves during working hours.

CHAPTER 4. GENERAL DISCUSSION

4.1 Dermal and Ocular Exposure during Spraying Processes

Spraying processes, as exemplified in the fruit fly, crash repair and furniture manufacturing industries, pose considerable potential for inhalational, dermal and ocular exposure.

Inhalational exposure can be exacerbated by work in unventilated or uncontrolled ventilation situations. Ocular exposure and dermal exposure to the face and arms arises primarily from aerosol deposition. Even in controlled spray booth situations, poor work practice and the wrong choice of PPE and spray equipment may result in appreciable exposure.

The two studies described in Chapters 2 and 3 indicate that dermal exposure can occur by direct contact (splash, leakage etc), secondary contamination (via contaminated surfaces) or aerosol deposition. Measurements can be highly variable, but exposures were determined around the neck, forehead, hands, wrists, forearms and chest. Contamination of the shoulders and leg areas was visually observed.

These data are consistent with other studies that have looked a spraying processes (Brouwer *et al*, 2000b).

Predictive models exist for inhalational exposure during spraying (Carlton and Flynn, 1997), with important factors being the orientation of the body relative to booth air flow (freestream), use of HVLP spray guns, size and shape of the object, temporal characteristics of spraying, variable spray gun to target distance etc. There is the potential for interaction amongst factors, such that HVLP may not always yield lower exposures (Carlton and Flynn, 1997). Ocular exposures may be predictable from inhalational exposures given the proximity of the eye to the nose and mouth.

At present, it is not feasible to use these models effectively in real world situations.

Dermal exposure is even more complex, and much data, as well as professional judgement, are required for semi-empirical approaches such as DREAM.

Visualization studies and whole body dosimetry methods provide direct answers but are laborious and not always practicable.

With regard to ocular exposure, research presented here provides *prima facie* evidence, at least in the case of isocyanates. However, such exposure could also be inferred from forehead wipes, PPE contamination and air samples.

The data point to the need for appropriate eye protection. Surprisingly, eye irritation does not figure prominently among reported symptoms, and the explanation is not clear. One possibility is that the extent of eye exposure is minimal and the natural ocular defences, e.g. production of tears, are sufficient.

Health questionnaires were used in both studies, with mixed success. Skin and respiratory problems were identified among spray painters, in keeping with previous research. Questionnaire approaches are valuable in that correlations between symptoms and work practices can be investigated. However, such a cross sectional approach is subject to survivor bias, such that those who experience problems are more likely to leave the industry.

Splashes and other chemical accidents were common in both studies, and have been noted elsewhere (Cattani *et al*, 2001).

Biological monitoring was only used in the fruit fly study, and the only conclusion to be drawn is that body uptake is low. In general, however, biological monitoring has a potentially important role in spraying situations where there is likely to be dermal exposure, and a heavy reliance on PPE.

There is evidence from the study of crash repair workshops that HVLP spray guns and proper spray booth ventilation do result in overall lower expsosures. However, engineering controls do not completely remove the hazard of high aerosol concentrations. Good work practices, personal hygiene and training, in the avoidance of exposure, are equally important.

In both the fruit fly and spray painting situations, a common observation was inappropriate storage of PPE and equipment, such that cross contamination is possible. Eating and smoking whilst wearing contaminated PPE was also observed. This can lead to eye and skin contamination, as well the possibility of ingestion. It can reduce the effectiveness of respiratory protection, even if the correct cartridges are used.

Foot protection was also seen as inadequate. Some of the workers wore shoes which had the potential to accumulate contaminants and provide ongoing exposure, e.g. through persistent permeation. This issue requires further investigation.

Glove performance testing was a feature of this study, and it is clear that performance depends on the glove type, usage pattern and temperature. The research supports the arguments presented by Klingner and Boeniger (2002) in favour of greater attention to in service testing. Key issues include the potential for differential wear, temperature, mixed chemical exposures and physical pressures. It appears that employers and workers are not aware of these issues.

In the case of the relatively thick PVC gloves used in fruit fly control, performace deteriorated with no obvious change in appearance. Even when these is visible evidence of damage, it appears that workers continue to use gloves.

The research highlights the need for a better understanding of the performance of PPE in actual use. The research findings needs to be translated into guidance material for users and distributors.

4.2 Further Studies

Dermal and ocular exposure to chemicals is a relatively new area, and further studies are required. The work presented here would suggest the following:

Further *in vitro* or *in vivo* studies of chemical permeation through the skin should be conducted. There is a need to better understand transdermal penetration, including the influence of temperature, skin wetness, the presence of an overlying glove material and chemical mixtures. This information would greatly assist in assessing health risks in situations where there is visible contamination of PPE, hot conditions etc.

There should be more widespread testing of gloves used with isocyanates. The disposable test cell has yield useful information, but there are many gloves in use with many different isocyanate/solvent mixtures. In this respect, it is heartening to note that funding has recently been allocated for such work in the USA (Utrecht University X2004 Conference, 2004).

Ocular sampling methodologies should be further developed. There is a need to better understand the significance of the ocular route, and the influence of wearing contact lenses. Sampling protocols for dermal exposure should include neck and forehead areas.

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APPENDICES

Appendix 1. Information Sheets, Consent and Complaint Forms

Appendix 1.1 Information sheet for fruit fly eradication workers

The University of Adelaide, Department of Public Health

INFORMATION SHEET FOR WORKERS

Study of Dermal and Ocular Exposure to Fruit Fly Pesticides

The University of Adelaide is carrying out a study of chemicals used for fruit fly eradication. This study will focus on exposure monitoring for fenthion and malathion, two organophosphorus pesticides approved by the government.

One set of measurements will be of the concentrations of pesticides available to be breathed in, deposited on the skin or eye. The skin assessment will entail a wipe of exposed skin with a wiper, similar to a tissue. To assess whether or not traces of chemical are in your eye, we will ask you to put a couple of eye drops in your eye, and then we will soak up the excess liquid from the corner of your eye with a sterile swab.

The other set of measurements will be one blood and two urine tests, collected at your workplace by a nurse. We will also invite you to participate in a questionnaire survey, which will take around 5-10 minutes.

The blood testing involves drawing blood from a vein which is the same procedure as when blood is collected for any other blood test recommended by a medical practitioner.

If you want to find out the results of the tests, these results will be made available to you. When the final report is published no information will be released which will enable individuals to be identified.

The main purposes of the study are to clarify the extent of human exposure and to monitor effects which may occur following fruit fly treatment in the field with fenthion and malathion according to standard procedures. There is very limited information about exposures, that is how much is taken up by the body, and it is important to be able to monitor the effects of the pesticide once absorbed into the body. It is most unlikely that any significant health effects will be observed in any situations, but we will be using a questionnaire and very sensitive tests to pick up small changes.
The results of this research should assist in developing policies on the sampling for hazardous chemicals. It should also assist in setting exposure standards and in formulating health surveillance programs and control measures for pesticide-exposed workers.

If you would like further information or need assistance, please contact: Dr Dino Pisaniello, Senior Lecturer, Dept. of Public Health, University of Adelaide Ph: 8303 3571

An independent complaints procedure form will also be given to you, if you would like to lodge a complaint about the conduct of the research.

Appendix 1.2 Information sheet for HDI-exposed workers

The University of Adelaide, Department of Public Health

INFORMATION SHEET FOR WORKERS

Study of Dermal and Ocular Exposure to Isocyanates

The University of Adelaide is carrying out a study of chemicals used in the automobile and furniture industries. This study will focus on exposures to isocyanates, used in two pack paints.

In this study we will be measuring concentrations of isocyanates available to be breathed in, deposited on the skin or eye. The skin assessment will entail a wipe of exposed skin with a wiper, similar to a tissue. To assess whether or not traces of chemical are in your eye, we will ask you to put a couple of eye drops in your eye, and then we will soak up the excess liquid from the corner of your eye with a sterile swab.

We will also ask you to participate in a questionnaire survey, which will take around 5-10 minutes.

If you want to find out the results of the tests, these results will be made available to you. When the final report is published no information will be released which will enable individuals to be identified.

The main purposes of the study are to clarify the extent of human exposure and to monitor effects which may occur following the use of isocyanates according to standard procedures. There is very limited information about exposures, that is how much is taken up by the body, and it is important to be able to monitor the effects of the isocyanate once absorbed into the body. It is most unlikely that any significant health effects will be observed in any situations, but we will be using a questionnaire and very sensitive tests to pick up small changes.

The results of this research should assist in developing policies on the sampling for hazardous chemicals. It should also assist in setting exposure standards and in formulating health surveillance programs and control measures for isocyanate-exposed workers.

If you would like further information or need assistance, please contact:

Dr Dino Pisaniello, Senior Lecturer Dept. of Public Health, University of Adelaide Ph: 8303 3571

An independent complaints procedure form will also be given to you, if you would like to lodge a complaint about the conduct of the research.

Appendix 1.3 **Consent form for fruit fly eradication workers and HDI-exposed workers**

CONSENT FORM

The University of Adelaide

See also Information Sheet attached.

1. I _____ (please print)

   hereby consent to take part in the research project entitled:

   Evaluation of dermal and ocular exposure to chemicals in South Australian workplaces

2. I acknowledge that I have read the Information Sheet.
3. I have had the project, so far as it affects me, fully explained to my satisfaction by the research worker. My consent is given freely.
4. I have been given the opportunity to have a member of my family or a friend present while the project was explained to me.
5. I have been informed that, while information gained during the study may be published, I will not be identified and my personal results will not be divulged.
6. I understand that I am free to withdraw from the project at any time.
7. I am aware that I should retain a copy of this Consent Form, when completed, and the relevant Information Sheet.

SIGNED .....DATE .....

NAME OF WITNESS ..... SIGNED .....

DATE .....

I, ... have described to

the nature of the procedures to be carried out. In my opinion, she/he understood the explanation.

SIGNED .....DATE .....

STATUS IN PROJECT .....

Appendix 1.4 Complaint form

INDEPENDENT **COMPLAINTS FORM**

THE UNIVERSITY OF ADELAIDE
HUMAN RESEARCH ETHICS COMMITTEE

Document for people who are subjects in a research project

CONTACTS FOR INFORMATION ON PROJECT AND INDEPENDENT COMPLAINTS PROCEDURE

The Human Research Ethics Committee is obliged to monitor approved research projects. In conjunction with other forms of monitoring it is necessary to provide an independent and confidential reporting mechanism to assure quality assurance of the institutional ethics committee system. This is done by providing research subjects with an additional avenue for raising concerns regarding the conduct of any research in which they are involved.

The following study has been reviewed and approved by the University of Adelaide Human Research Ethics Committee:

Project title:

Evaluation of dermal and ocular exposure to chemicals in South Australian workplaces

1. If you have questions or problems associated with the practical aspects of your participation in the project, or wish to raise a concern or complaint about the project, then you should consult the project co-ordinator:

   Name: **Dr Dino Pisaniello, Department of Public Health, University of Adelaide**
   Telephone: **8303 3571**

2. If you wish to discuss with an independent person matters related to
   - making a complaint, or
   - raising concerns on the conduct of the project, or
   - the University policy on research involving human subjects, or
   - your rights as a participant

   contact the Human Research Ethics Committee's Secretary on phone (08) 8303 4014

Appendix 2. Questionnaire

Appendix 2.1 Questionnaire for fruit fly eradication workers

Department of Public Health

Site Code ☐☐☐

Worker Code ☐☐☐

Date ☐☐ ☐☐ ☐☐

Fruit Fly Pesticide Users Questionnaire

The following questionnaire is a part of a research project addressing occupational health hazards in the pest control industry where malathion and fenthion are used. The University of Adelaide is carrying out this research with the assistance of Primary Industries and Resources SA (PIRSA).

This questionnaire will obtain personal details, health effects and work practices. It will be used to assist in evaluating dermal and ocular exposure. All information will be strictly confidential and only be available to members of the University research team and the individual concerned. No person will be identified and the results will be reported anonymously.

The research will provide a broad picture of the industry and will allow us to make specific recommendations that will lead to improved health and safety.

PART A: Personal Information

Please tick the appropriate box or write

1. Name _____ (Optional)

2. Date of birth

☐☐ Day ☐☐ Month ☐☐☐☐ Year

3. Sex

☐ Female ☐ Male

4. Are you right or left handed?

_____

5. Name of workplace _____

6. Job title (more than one option possible)

☐ Team Leader ☐ Baiting ☐ Knocking Doors ☐ Others _____.

7. Have you been using pesticides professionally before baiting work?

☐ Yes ☐ No

If yes,

How many years have you been using pesticides?

_____

8. Have you had formal training in the use and application of pesticides?

☐ Yes ☐ No

If yes,

☐ One day

☐ More than one day

PART B: Health Information

Please tick the appropriate box or write

9. Do you currently suffer from

☐ Hayfever

☐ Asthma

☐ Eczema

☐ Any other skin problems

9(a). Did you suffer from asthma as a child?

☐ Yes ☐ No

9(b). Do you get a more severe reaction than others to insect bites?

☐ Yes ☐ No

10. Have you experienced dry cracked skin since starting baiting?

☐ Yes ☐ No

11. Have you experienced skin rash since starting baiting?

☐ Yes ☐ No

12. Have you had dermatitis or skin irritation since starting baiting?

☐ Yes ☐ No

If yes, how frequently?

_____

13. Have you had any eye problems since starting baiting?

☐ Eye irritation

☐ Itchy eyes

☐ Dry eyes

☐ Conjunctivitis

☐ Any other eye problems

_____

13(a) Have you experienced headaches during or after baiting?

☐ Yes ☐ No

13(b) Have you had any unusual symptoms during or after baiting?

(e.g. tingling, weak muscles, loss of sensation)

_____

14. Do you wear contact lenses?

☐ Yes ☐ No

15. Are you exposed to any pesticides outside of your regular working hours?

☐ Yes ☐ No

16. Do you suffer from blackouts at work?

☐ Yes ☐ No

17. Are you a smoker?

☐ Current smoker ☐ Ex-smoker ☐ Never smoked

17(a). How many cigarettes do you smoke per day?

☐ 1-5 ☐ 6-10 ☐ 11-15 ☐ 16-20 ☐ more than 20

PART C: Work Practices

Please tick the appropriate box or write

18. How much pesticide do you use? _____ litre per day

19. How many hours do you spend spraying pesticides?

☐ ☐ Min ☐ ☐ Hour per day

20. Apart from one day course, have you had any education and training about?

☐ Health effects of pesticides

☐ PPE

☐ MSDSs

21. Have you had a major spill of pesticide product (500 mls or more)?

☐ Yes ☐ No

If yes,

☐ Concentrate

☐ Dilute

22. Have you had wet overalls from pesticide liquid leak or splash since started in this week?

☐ Yes ☐ No

23. Have you had an accident involving a splash in your eye?

☐ Yes ☐ No

If yes, how did it happen?

_____

24. Have you had an accident splashing any other part of the body?

☐ Yes ☐ No

If yes, how did it happen?

_____

25. What kinds of personal protective equipment do you wear regularly when spraying pesticide?

- ☐ Gas and particulate respirator-cartridge type
- ☐ Particulate respirator-canister type
- ☐ Overalls
- ☐ Disposable Coveralls
- ☐ Glasses (prescription lenses)
- ☐ Goggles
- ☐ Face shield
- ☐ Gloves

26. Do you wear cotton under gloves?

- ☐ Yes
- ☐ No

If yes,

Do you always wear under gloves when baiting?

- ☐ Yes
- ☐ No

27. What type of footwear do you use?

- ☐ Shoes
- ☐ Boots

27(a). Are they your own?

☐ Yes

☐ No

28. Is all your other PPE supplied by your employer?

☐ Yes ☐ No

If yes, what ?

_____

29. How frequently do you change your overalls?

_____ days

30. Do you clean/wash any of PPE yourself?

☐ Shoes

☐ Overalls

☐ Respirator

☐ Gloves

31. Do you completely remove your overalls (or other protective clothing) at lunch break?

☐ Yes ☐ No

The end.

Appendix 2.2 Questionnaire for isocyanate spray painters

Department of Public Health

Site Code ☐☐☐

Worker Code ☐☐☐

Date ☐☐ ☐☐ ☐☐

Isocyanate Users Questionnaire

The following questionnaire is a part of a research project addressing occupational health hazards in the automotive and furniture industries where isocyanate-based products are used. The University of Adelaide is carrying out this research with the assistance of the Motor Trade Association.

This questionnaire will obtain information on personal details, health effects and work practices. It will assist in evaluating dermal and ocular exposure. All information will be strictly confidential and only be available to members of the University research team and the individuals concerned. No person will be identified and the results will be reported anonymously.

The research will provide a broad picture of the industry and will allow us to make specific recommendations that will lead to improved health and safety.

PART A: Personal Information

Please tick the appropriate box or write

1. Name _____ (Optional)

2. Date of birth

☐☐ Day ☐☐ Month ☐☐☐☐ Year

3. Sex

☐ Female ☐ Male

4. Are you right or left handed?

_____

5. Name of workplace _____

6. Job title _____

7. How long have you been working in your current job?_____

8. How many years have you been using isocyanates as part of your current job?

_____

Or, previous job? _____

9. Have you had formal training in the use of isocyanates based paints?

_____

PART B: Health Information

Please tick the appropriate box or write

10. Do you suffer from

☐ Hayfever

☐ Asthma

☐ Eczema

☐ Any other skin problems

10(a). Did you suffer from asthma as a child?

☐ Yes ☐ No

10(b). Do you get a more severe reaction than others to insect bites?

☐ Yes ☐ No

11. Have you experienced dry cracked skin at work in the last 12 months?

☐ Yes ☐ No

12. Have you experienced skin rash at work in the last 12 months?

☐ Yes ☐ No

13. During the past 12 months have you had dermatitis or skin irritation due to your work?

☐ Yes ☐ No

If yes, how frequently?

_____

14. Do you usually cough during the day or night?

☐ In the morning ☐ During the day ☐ At night

If so, is there any particular activity or job which appears to make you cough?

_____

15. Do you usually bring up any phlegm?

☐ In the morning ☐ During the day ☐ At night

If so, is there any particular activity or job which makes you phlegm?

_____

15(a) In the past 12 months, have you had a period of (increased) cough and phlegm lasting for three weeks or more?

☐ Yes ☐ No

If yes, why?

_____

16. Have you ever had attacks of shortness of breath with wheezing?

☐ Yes ☐ No

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

☐ Yes ☐ No

18. Have you had any eye problems in the last 12 months?

☐ Eye irritation

☐ Itchy eyes

☐ Dry eyes

☐ Conjunctivitis

☐ Any other eye problems

_____

19. Do you wear contact lenses?

☐ Yes ☐ No

20. Have you experienced any work-related headaches in the last 12 months?

_____

21. Do you suffer from blackouts at work?

☐ Yes ☐ No

22. Are you a smoker?

☐ Current smoker ☐ Ex-smoker ☐ Never smoked

22(a). How many cigarettes do you smoke per day?

☐ 1-5 ☐ 6-10 ☐ 11-15 ☐ 16-20 ☐ more than 20

PART C: Work Practices

Please tick the appropriate box or write

23. What specific tasks do you carry out involving isocyanates?

- ☐ Mixing
- ☐ Spraying
- ☐ Cleaning up
- ☐ Other (Specify the description): _____

24. How much of hardener do you use? _____ litre per day

25. How many hours do you spend for applying isocyanate-based paints?

☐☐ Min ☐☐ Hour per day

26. Do you spray outside the booth with isocyanates paints?

☐ Yes ☐ No

If yes, how often do you do?

_____

26(a). Are you exposed to isocyanates paints outside of your regular working hours?

☐ Yes ☐ No

27. Have you had any specific education and training about isocyanatess with respect to?

- ☐ Health effects
- ☐ PPE
- ☐ MSDSs

28. Are there work instructions/ procedures for isocyanates sprayers?

☐ Yes ☐ No

29. Have you had a major spill of isocyanates product (500 mls or more) ?

☐ Yes ☐ No

30. Have you had an accident involving a splash of isocyanate-containing products in your eyes?

☐ Yes ☐ No If yes, how did it happen?

_____

31. Have you had an accident involving splashing any other part of the body?

☐ Yes ☐ No If yes, how did it happen?

_____

32. What kind of personal protective equipment do you wear regularly when spraying isocyanates or handling?

☐ Full face-airline respirator

☐ Half face-airline respirator

☐ Hood or helmet-airline respirator

☐ Air purifying cartridge respirator

☐ Overalls

☐ Disposable Coveralls

☐ Glasses (prescription lenses)

☐ Goggles

☐ Face shield

33. Do you wear gloves when spraying car?

☐ Yes ☐ No

If yes, what type of gloves do you use?

_____

34. How often do you replace gloves?

☐ Every time ☐ Everyday ☐ Every two days ☐ Every three days

☐ Every four days ☐ Every five days ☐ Every six days ☐ Once a week

35. What type of footwear do you use?

☐ Shoes

☐ Boots

36. What type of spray gun do you use?

1) Type :_____

2) Pressure: _____

37. Is all your PPE supplied by the employer?

☐ Yes ☐ No If yes, what ?

_____

38. Do you clean/wash any of PPE by yourself?

☐ Shoes

☐ Overalls

☐ Respirator

☐ Gloves

39. Do you remove your overalls (or other protective clothing) at lunch breaks?

☐ Yes ☐ No

40. Do you remove your overalls at the end of a day before going home?

☐ Yes ☐ No

The end.

Appendix 2.3 Questionnaire for unexposed workers (Controls)

Department of Public Health

Site Code ☐☐☐

Worker Code ☐☐☐

Date ☐☐ ☐☐ ☐☐

Control Group Questionnaire

The following questionnaire is part of a research project addressing the use of certain hazardous chemicals in industry. We are particularly interested in skin and eye exposure which may potentially lead to symptoms or more serious health effects. In order to assess the significance of symptoms reported by workers in industry, we need to use a reference group of workers who are not using the chemicals being studied.

You are part of this reference group. As a result of the study we should be able to provide better advice on the safe use of chemicals at work.

All information that you give will be strictly confidential and only available to members of the University research team and the individuals concerned. No person will be identified and any results will be reported anonymously.

Now I am going to ask you questions mainly about health, but also about your own use of chemicals.

PART A: Personal Information

Please tick the appropriate box or write

1. Name _____ (Optional)

2. Year of birth

☐☐☐☐ Year

3. Job title _____

4. Section of work _____

5. Major duties _____

_____

6. Are you a full time or part time employee?

☐ Full time

☐ Part time

7. How many years have you been working with your current employer?

_____ year(s)

8. What percentage of time do you spend outsides during working hours?

_____ %

PART B: Health Information

Please tick the appropriate box or write

9. Do you currently suffer from:

- ☐ Hayfever
- ☐ Asthma
- ☐ Eczema
- ☐ Any other skin problems

10. Did you suffer from asthma as a child?

☐ Yes ☐ No

If YES, was it diagnosed by a doctor?

☐ Yes ☐ No

10(a). Do you get a more severe reaction than others to insect bites?

☐ Yes ☐ No

Skin Symptoms

11. Have you got any of the following symptoms now on your finger, hand, wrist or forearm?

11(a). Dry cracked skin due to work

☐ Yes ☐ No

If no, have you had this symptom in the last 12 months?

☐ Yes ☐ No

11(b). Skin rash due to work

☐ Yes ☐ No

If no, have you had this symptom in the last 12 months?

☐ Yes ☐ No

11(c). Itchy red skin

☐ Yes ☐ No

If no, have you had this symptom in the last 12 months?

☐ Yes ☐ No

11(d). Inflamed (or swollen) skin

☐ Yes ☐ No

If no, have you had this symptom in the last 12 months?

☐ Yes ☐ No

11(e). Any other skin symptoms?

☐ Yes ☐ No

If no skin problems, go to next section (respiratory symptoms)

12. How long have you had your skin problem?

☐ 1-11 months ☐ 1-2 years ☐ 3-5 years ☐ > 5 years

13. In the last 12 months, did you have any medical treatment of your skin problems?

☐ Yes ☐ No

If yes, what was the medical diagnosis?

☐ Irritant contact dermatitis

☐ Allergic contact dermatitis

☐ Others _____

☐ Don't know or can't remember

14. In the last 12 months, did you lose any working days because of your skin problems?

☐ Yes ☐ No

If yes, how many days/weeks in the last year have you been?

_____

15. What do you think caused your skin problem?

_____

Respiratory Symptoms

16. Do you usually cough during the day or night?

☐ Yes ☐ No

If YES

☐ In the morning ☐ During the day ☐ At night

If so, is there any particular activity or job which appears to make you cough?

_____

17. Do you usually bring up any phlegm?

☐ Yes ☐ No

If YES

☐ In the morning ☐ During the day ☐ At night

If so, is there any particular activity or job which gives you phlegm?

_____

17(a). In the past 12 months, have you had a period of (increased) cough and phlegm lasting for three weeks or more?

☐ Yes ☐ No

18. Do you ever have attacks of shortness of breath with wheezing?

☐ Yes ☐ No

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

☐ Yes ☐ No

If YES to any of the above questions:

20. What do you think caused your respiratory problems?

_____

Eye Symptoms

21. Have you experienced the following eye problems 3 or more times in the last 12 months?

- ☐ Eye irritation
- ☐ Sore eyes
- ☐ Itchy eyes
- ☐ Watery eyes
- ☐ Dry eyes
- ☐ Burning eyes
- ☐ Conjunctivitis
- ☐ Any other eye problems _____

If YES to any of the above:

22. What do you think caused your eye problem?

_____

23. Do you wear contact lenses?

☐ Yes ☐ No

Other symptoms

24. Have you experienced headaches 3 or more times at work in the last 12 months?

_____

25. Do you suffer from blackouts at work?

☐ Yes ☐ No

26. Have you had any unusual symptoms from your work?

(e.g. tingling, weak muscles, loss of sensation)

Smoking

27. Are you a smoker?

☐ Current smoker ☐ Ex-smoker ☐ Never smoked

27(a). How many cigarettes do you smoke per day?

☐ 1-5 ☐ 6-10 ☐ 11-15 ☐ 16-20 ☐ more than 20

PART C: Chemical usage and work practices

Please tick the appropriate box or write

Hobbies

28. Do you have any hobbies that entail significant use of chemical(s)?

☐ Yes ☐ No

If YES, describe the hobby(ies). _____

Chemicals at work

29. Do you use any chemical(s) as part of your work?

☐ Yes ☐ No

If NO to both questions then END.
If yes to either, answer the following questions.

29(a). What type of the chemical(s)?

- ☐ Solvent/Thinner/Petrol
- ☐ Corrosive Chemical(s)
- ☐ Pesticides
- ☐ Paints
- ☐ Adhesives
- ☐ Cleaning agents
- ☐ Any other chemicals

_____

29(b). How much of the chemical(s) do you use?

_____ litre/kg per week

29(c). How many hours per week on average do you use the chemical(s)?

_____

29(d). How many days per week do you use the chemical(s)?

_____ days per week

29(e). For many years have you used the chemical?

_____

30. Have you had a major spill of the chemical product (500 mls or more) ?

☐ Yes ☐ No

31. Have you had an accident involving a splash in your eyes?

☐ Yes ☐ No

If yes, how did it happen?

_____

32. Have you had an accident involving splashing any other part of the body?

☐ Yes ☐ No

If yes, how did it happen?

_____

33. Do you wear personal protective equipment when handling the chemical(s)?

☐ Yes ☐ No

If yes, what kind of personal protective equipment do you wear?

_____

If NO, END
If gloves indicated, then:

34. What type of gloves do you use?

_____

35. How often do you replace gloves?

☐ Every time ☐ Everyday ☐ Every two days ☐ Every three days
☐ Every four days ☐ Every five days ☐ Every six days ☐ Once a week

The end.

Appendix 2.4 Glove usage questionnaire for fruit fly eradication workers

The University of Adelaide, Department of Public Health

Fruit Fly Pesticide Exposure

STUDY OF GLOVES

Usage

Baiting only?	YES	NO
Mixing of concentrate?	YES	NO
Liners used?	YES	NO
Full days of usage	.....	days
Has the glove been rinsed each day?	YES	NO

Appendix 3. Ethics Approval

Appendix 3.1 Flinders clinical research ethics committee (69/02)

Flinders Medical Centre
Bedford Park South Australia 5042
Telephone (08) 8204 5511
International 618 8204 5511

Flinders Clinical Research Ethics Committee
Telephone (08) 8204 4507
Facsimile (08) 8204 4006
email: Carol.Hakof@fmc.sa.gov.au

13 July 2001

MEMORANDUM

TO: Dr. J. Edwards, Occupational & Environmental Health

FROM: Ms. C. Hakof, Executive Officer, Flinders Clinical Research Ethics Committee

TOPIC: **Research Application 69/01**

I am pleased to advise that the Flinders Clinical Research Ethics Committee has approved your research application in accordance with the following extract from the Minutes of its meeting held on 9 July 2001.

5089.31 Research Application 69/01 – Dr. J. Edwards
Monitoring changes in cholinesterase enzyme activities in pest control workers with potential exposure to cholinesterase-inhibiting pesticides.
Reviewer: Dr. R. Gibson

This application, as amended, was approved.

If conditional *('subject to' or 'in principle')* approval is granted, research involving human subjects **may proceed only after written acceptance of the conditions of approval** (including a copy of the modifications) has been received by the Committee.

This approval is for a period of one year. Application for re-approval must be made annually. Please note that if this trial involves normal volunteers it will be necessary for you to keep a record of their names and you may be required to supply this list with your annual report. ***A copy of the signed consent form is to be filed in the subject's medical record.***

You are reminded that the Flinders Clinical Research Ethics Committee must approve the content and placement of advertisements for the recruitment of volunteers.

The Committee must be notified and approve any changes (e.g. additional procedures, modification of drug dosage, changes to inclusion or withdrawal criteria, changes in mode and content of advertising) in the investigational plan particularly if these changes involve human subjects.

The safe and ethical conduct of a trial is entirely the responsibility of the investigators. While the Flinders Clinical Research Ethics Committee takes care to review and give advice on the conduct of trials, approval by the Committee is not an absolute confirmation of safety, nor does approval alter in any way the obligations and responsibilities of investigators.

It is the duty of the chief investigator to give prompt notification to the Flinders Clinical Research Ethics Committee of matters which might affect continued ethical acceptability of the project, including:

1. Adverse effects of the project on subjects, including the total number of subjects recruited, and of steps taken to deal with these adverse effects.
2. Other unforeseen events.
3. A change in the base for a decision made by the Committee, e.g. new scientific information that may invalidate the ethical integrity of the study.

If patients are involved the chief investigator is also responsible for the process of notification, seeking approval or permission of Departments, Divisions or individual consultants.

C. Hakof

The Flinders Clinical Research Ethics Committee is constituted and operates in accordance with the National Health and Medical Research Council's National Statement on Ethical Conduct in Research Involving Humans (June 1999).

Appendix 3.2 The human research ethics committee at the University of Adelaide

THE UNIVERSITY OF ADELAIDE
AUSTRALIA

OFFICE OF THE DEPUTY VICE-CHANCELLOR (RESEARCH)

HELEN MALBY
SECRETARY
HUMAN RESEARCH ETHICS COMMITTEE
THE UNIVERSITY OF ADELAIDE
SA 5005
AUSTRALIA

TELEPHONE +61 8 8303 4014
FACSIMILE +61 8 8303 3417
email: helen.malby@adelaide.edu.au
CRICOS Provider Number 00123M

13 March 2003

Dr DL Pisaniello
Public Health

Dear Dr Pisaniello

PROJECT NO: *Evaluation of dermal and ocular exposure to chemicals in South Australian*
H-68-2002 *workplaces*

I write to advise you that the Human Research Ethics Committee has approved the above project. Please refer to the enclosed endorsement sheet for further details and conditions that may be applicable to this approval.

Approval is current for one year. The expiry date for this project is: 31 March 2004

Where possible, subjects taking part in the study should be given a copy of the Information Sheet and the signed Consent Form to retain.

Please note that any changes to the project which might affect its continued ethical acceptability will invalidate the project's approval. In such cases an amended protocol must be submitted to the Committee for further approval. It is a condition of approval that you immediately report anything which might warrant review of ethical approval including (a) serious or unexpected adverse effects on participants (b) proposed changes in the protocol; and (c) unforseseen events that might affect continued ethical acceptability of the project. It is also a condition of approval that you inform the Committee, giving reasons, if the project is discontinued before the expected date of completion.

A standard annual renewal and progress report form is available from the Committee's website. Please submit this prior to the above expiry date.

Yours sincerely

MACE MORTENSEN
Convenor
Human Research Ethics Committee

THE UNIVERSITY OF ADELAIDE
AUSTRALIA

OFFICE OF THE DEPUTY VICE-CHANCELLOR (RESEARCH)

HELEN MALBY
SECRETARY
HUMAN RESEARCH ETHICS COMMITTEE
THE UNIVERSITY OF ADELAIDE
SA 5005
AUSTRALIA

TELEPHONE +61 8 8303 4014
FACSIMILE +61 8 8303 3417
email: helen.malby@adelaide.edu.au
CRICOS Provider Number 00123M

Applicant: Dr DL Plsaniello

Department: Public Health

Project Title: *Evaluation of dermal and ocular exposure to chemicals in South Australian workplaces*

THE UNIVERSITY OF ADELAIDE HUMAN RESEARCH ETHICS COMMITTEE

Project No: **H-68-2002** RM No: 0000005293

APPROVED for the period until: 31 March 2004

on the basis of the supplementary information, amended information sheets and the Committee's contacts/complaints document received on 17.2.03.

Refer also to the accompanying letter setting out requirements applying to approval.

C.

Professor CE Mortensen
Convenor

Date: 13 MAR 2003

Appendix 4. Cover Sheet of Laboratory Report from WorkCover New South Wales

WorkCover New South Wales, 5A Pioneer Avenue, Thornleigh NSW 2120 Tel: (02) 9484 6655 Fax: (02) 9980 6849

WORKCOVER NEW SOUTH WALES

LABORATORY SERVICES UNIT

Dr J W Edwards
Environmental Health
School of Medicine
Flinders University
GPO Box 2100
ADELAIDE SA 5001

Lab. Reference: 2001-2432-A

Your Reference:

REPORT OF ANALYSIS

EMPLOYEE'S NAME: D'SYLVIA, Peter
NAME OF EMPLOYER: Not Stated
TYPE OF SAMPLE: Pre Shift Urine

DATE OF BIRTH: Not Stated
DATE OF COLLECTION: 30/10/01
DATE OF RECEIPT: 22/11/01

Samples Analysed as Received.

ORGANOPHOSPHATE PESTICIDE EXPOSURE

Organophosphate Metabolites in Urine Scr	Result	Uncertainty	BOEL	Units
DMP	ND	± NA		µmol/mol creatinine
DMTP	ND	± NA		µmol/mol creatinine
DMDTP	ND	± NA		µmol/mol creatinine
DEP	ND	± NA		µmol/mol creatinine
DETP	ND	± NA		µmol/mol creatinine
DEDTP	ND	± NA		µmol/mol creatinine

Urinary Creatinine	Result	Uncertainty	Units
Creatinine	1.43	± 0.38	g/L
Creatinine (SI Units)	0.0126	± 0.0033	mol/L

BOEL: Biological Occupational Exposure Limit (Where a BOEL is not stated it is pending)
ND: Not Detected
NA: Not Applicable

For additional advice concerning the interpretation of the above result(s) contact one of our Occupational Physicians at WorkCover NSW (Tel: (02) 9370 5000)

See page 2 for additional information about the above test(s).

Appendix 5. Supporting Letter from Motor Trade Association

17-SEP-2003 11:02 FROM MTA INDUSTRIAL TO 82234075 P.01/01

THE MOTOR TRADE ASSOCIATION OF SOUTH AUSTRALIA INCORPORATED
AUTOMOTIVE CENTRE OF EXCELLENCE, 3 FREDERICK ROAD, ROYAL PARK SA 5014
PO BOX 440, PORT ADELAIDE 5015
TELEPHONE: (08) 8241 1066
FACSIMILE: (08) 8241 1055
INTERNET: http://www.mta-sa.asn.au
EMAIL: mta@mta-sa.asn.au
INDUSTRIAL FACSIMILE: (08) 8241 1062

11 September 2003

«Name»
«Company»

Dear «Sal»

REQUEST FOR YOUR HELP – NEW RESEARCH INTO ISOCYANATE ABSORPTION THROUGH SKIN/EYE CONTACT ---PRELIMINARY TESTING AT MTA-GTS, FURTHER INDUSTRY WORK NEEDED.

The University of Adelaide has been working with the MTA on occupational health and safety issues for many years. In the past there was a focus on the health risks associated with breathing in aerosols and vapours when using or spraying 2-pack paints and annual lung function testing.

However, in the last year or so, there has been an increasing evidence around the world that skin and eye contact with isocyanates may play a role in the development of respiratory disease, as well as causing skin and eye problems, i.e. just preventing breathing in isocyanates may not be sufficient.

Recent University tests at MTA GTS found, (obviously) that gloves perished on contact with isocyanate, air wash hoods (mandatory at MTA GTS) should be worn with air fed respirators to avoid any skin exposure, etc.

With this in mind, the University would like to visit a representative sample of collision repair workshops and focus on possible exposures through the skin. This may help in many was including changes to the way gloves, etc. are manufactured.

As in the earlier study, the survey would involve a short questionnaire. In addition the team would be looking at work practices, protective clothing and carrying out some wipe sampling of surfaces. Finally, some samples of new and old gloves will be tested in the laboratory for their performance against 2-pack paints.

A report will be prepared and will have recommendations on the control of skin and eye exposure. Individual workshops and workers will not be identified in the Report. It will be in anonymous summary form. If you have any concerns, please phone either myself or Brad Dawson (some of you helped David Leng and myself back in 1988 when the last study was done). If I have not heard from you within 10 days, I will give your contact details to Dino*.

This is an important piece of research which will be of benefit to the industry and aims to safeguard the health of all concerned.

There will be practical advice to workshops, suppliers and those involved with training.

The team comprises Dr Michael Tkazcuk, Dr Dino Pisaniello* and Mr SuGil Lee.

Paul Eblen
Manager, Industrial, Legal, OH&S and Environmental Services.

W:\common\INDUST\Oh&s & Environmental Issues\Projects\Uni SA letter re collision Repairers.doc

Appendix 6. Worksite Observation Form

Department of Public Health

Site Code ☐☐☐

Worker Code ☐☐☐

Date ☐☐ ☐☐ ☐☐

Work Site Observation Sheet

Company: _____
Job Task: _____
Job Location: _____

1. Workshop size? Small (1-5 people) Medium (6-20 people) Large (Over 21 people)

2. Work Procedures?

3. Working environment and workers behaviour?

4. Spray gun
   1) Manufacturer?
   2) Type?
   3) Pressure? (Kpa)

5. Ventilation system? Yes (Good, Good-fair, Fair, Fair-poor, Poor) No

6. Chemical source present? Yes No

7. What kind of chemical agent used? Pesticide (malathion, fenthion), Isocyanate (HDI). Any Solvent?

8. Contamination? Surface Air Clothing Skin Eyes

9. Expected body part for contamination? Head, Neck, Ear, Eyes, Upper arm, Lower arm, Forearm, Hands, Wrist, Waist, Upper leg, Lower leg, Ankle, Feet

10. Exposure route? Emission Deposition Transfer

11. In the preparation and handling of a chemical source, emission to

1)	Clothing ?	U	O	R	A
2)	Uncovered skin?	U	O	R	A
3)	Eye?	U	O	R	A

*** U: Unlikely (<1% of task duration)** **O: Occasionally (<10% of task duration)**
R: Repeatedly (10-50% of task duration) **A: Almost constantly (>50% of task duration)**

12. Visually estimated amount of emission? Small Medium Large

13. Deposition of spray mist to

1)	Clothing?	U	O	R	A
2)	Uncovered skin?	U	O	R	A
3)	Eye?	U	O	R	A

*** U: Unlikely (<1% of task duration)** **O: Occasionally (<10% of task duration)**
R: Repeatedly (10-50% of task duration) **A: Almost constantly (>50% of task duration)**

14. Observational amount of deposition? Small Medium Large

15. Transfer to

1)	Clothing?	U	O	R	A
2)	Uncovered skin?	U	O	R	A
3)	Eye?	U	O	R	A

*** U: Unlikely (<1% of task duration)** **O: Occasionally (<10% of task duration)**
R: Repeatedly (10-50% of task duration) **A: Almost constantly (>50% of task duration)**

16. Estimated amount of transfer? Small Medium Large

17. Chemical properties? Solid Liquid Vapour mist

18. Concentration of the used chemical? Low Medium High

19. Barrier cream used? Yes or NO

20. Cleaning after work completion? Worktable, Floor, Machines, Working tools,

21. What kind of PPE worn during
    1) Preparation?
    2) Application?
    3) Clean up?

22. Used PPE worn properly to reduce exposure? Yes No

- **Emission**: Mass transport of substances by direct release from a source onto skin or clothing, such as exposure by splashes, immersion of hands into a liquid or powder (droplets and powder particles have an aerodynamic diameter of 100um).
- **Deposition on skin or clothing**: Mass transport from air. In this case, the contamination mass (e.g. small particles with an aerodynamic diameter of <100 um, such as vapours, mist) is first released into the air and subsequently deposited on skin or clothing.
- **Transfer**: The transfer of mass from contaminated surfaces onto skin or clothing, e.g. skin contact with surfaces or working tools that have been previously contaminated with an agent.

*Source: van-Wendel-de-joode B., Brouwer D.H., Vermeulen R., van Hemmen J.J., Heederik D., and Kromhout H., *DREAM: A Method for Semi-quantitative Dermal Exposure Assessment*, Ann. Occup. Hyg., Vol. 47, No. 1, pp71-87, 2003.