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Prepared by the
Institute of Occupational Medicine
for the Health and Safety Executive 2003

RESEARCH REPORT 117

HSE
Health & Safety Executive

Development of a method to assess biologically relevant dermal exposure

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This study has investigated the feasibility of developing a “biologically relevant” dermal sampler for toluene. This prototype Institute of Occupational Medicine (IOM) dermal sampler consists of adsorbent sandwiched between a permeable membrane and an impervious backing. Toluene on the membrane surface diffuses towards the adsorbent. The concentration of toluene on the membrane surface may be estimated from this mass on the adsorbent and the known permeation rate of toluene through the membrane.

Evaluation of the prototype sampler was undertaken in two stages: laboratory performance in controlled exposure situations and two short field evaluations of the sampler, which included simultaneous measurement of inhalation exposure. In all cases we compared the prototype IOM sampler with activated charcoal cloth (ACC). Laboratory trials were split into spray tests, pour tests and immersion tests. The data from these tests suggests that the prototype IOM sampler responds to toluene concentration rather than the mass of toluene on the surface of the sampler. The field study showed that the prototype sampler was suitable for measuring dermal exposure. An association between inhalation and dermal exposure to toluene was observed in the field tests. Throughout the study there were difficulties with the prototype IOM sampler because of the adsorbent becoming saturated. Future development is required to identify a less permeable membrane, which has characteristics closer to that of the human skin. Additionally, a higher capacity adsorbent would be desirable.

The prototype IOM dermal sampler is the first practical dermal exposure sampler to mimic uptake through the skin. The sampler gave sensible, reproducible results in the laboratory and field trials. We believe further development of the concept would provide an opportunity to place dermal exposure sampling on a firm scientific footing. The concept of a “biologically relevant” dermal sampler will enable measurements to reflect the properties of skin and it will provide an appropriate measure to assess health risks from either uptake or local effects on the skin.

This report and the work it describes were funded by the Health and Safety Executive (HSE). Its contents, including any opinions and/or conclusions expressed, are those of the authors alone and do not necessarily reflect HSE policy.

HSE BOOKS

First published 2003

ISBN 0 7176 2223 1

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SUMMARY

Occupational dermal exposure to volatile liquids can cause a variety of skin disease and may be taken up through the skin and contribute to systemic dose. However, the investigation of the health risk from dermal exposure is hampered because of the absence of appropriate exposure measurement methods. We have previously suggested a new way to measure dermal exposure (Cherrie and Robertson, 1995), based on a patch sampler that would collect volatile liquids by diffusion. This report summarises a study to investigate the feasibility of developing a "biologically relevant" dermal sampler for toluene based on this principle.

The design of the proposed IOM dermal sampler was based on an absorbent material sandwiched between a permeable membrane and an impervious backing. Toluene vapour or liquid would come into contact with a membrane and diffuse towards the adsorbent. At the end of the sampling period the toluene would be desorbed and analysed by gas chromatography to determine the total mass adsorbed. By knowing the permeation rate of toluene through the membrane and the duration of exposure it would be possible to calculate the original concentration of toluene solution to which the patch was exposed. In order to realise the concept, the various component parts had to be sought; a suitable diffusive membrane, an adsorbent and a backing material.

The most widely used, cheapest and most effective adsorbent for organic liquids is activated carbon. After a limited amount of evaluation it was decided this would be appropriate for the prototype dermal sampler. Since the sampler was designed to provide a biologically relevant indicator of dermal exposure we judged that it was desirable for the membrane to have similar properties of human skin. A wide range of candidate membrane materials was tested. From the literature review, it was clear that the dermal permeation rate for neat toluene was somewhere between 10 and 1,200 $\mu g/cm^2/hr$, with the likely flux being towards the top of this range. Comparing these data with the information from membrane permeation tests suggested that the most suitable membrane was Pallflex AO1603. However, the permeation rate was considerably higher than we would have really wished (78,000 $\mu g/cm^2/hr$) when compared to the estimated permeation rate through human skin. The most suitable backing material was aluminium foil, since it is impervious, resistant to organic solvents, flexible, robust and has good thermal conductivity properties.

The prototype sampler design comprised the membrane sealed to the backing material with the adsorbent sandwiched between. In addition, a PTFE mesh was placed in between the activated carbon cloth and the membrane to minimise direct wicking of liquid to the adsorbent. The sampler was assembled using a commercial impulse heat sealer.

Evaluation of the prototype IOM dermal sampler was undertaken in two stages. A number of laboratory evaluations were undertaken to determine the basic performance of the sampler in a range of controlled exposure situations. The second stage evaluation comprised two short field tests of the sampler: one in a factory making rubber goods and the second in a plant that printed designs onto metal foil. In both evaluation stages we have compared the prototype dermal sampler with activated carbon cloth (ACC) patches, similar to those proposed by Cohen and Popendorf (1989).

In the laboratory trials, IOM dermal samplers and activated carbon patches were exposed to varying concentrations of toluene over a range of times. These tests were split into spray tests, pour tests and immersion tests. In the field trials, employees were selected and asked to wear an IOM dermal sampler and activated carbon patch side by side on the forearm and chest. They also wore a 3M diffusive badge to measure their inhalation exposure.

It proved difficult to systematically compare results from the prototype IOM dermal sampler with activated carbon cloth patch samplers as these became very rapidly saturated. Our experience with the activated carbon cloth samplers suggested that they are not a practicale solution for measuring dermal exposure to volatile organic compounds in an industrial setting.

In the laboratory spray tests we saw that the relative uptake rate for mixtures of toluene with ethanol, compared with pure toluene, was similar to expected i.e. reducing the concentration of toluene in the mixture resulted in corresponding decreases in uptake rate. These data suggest that the sampler is responding to the concentration rather than the mass of toluene, as expected. However, we suspect that the whole of the surface of the samplers was not covered by the challenge liquid.

In pouring tests, where we were confident that a much greater part of the sampler surface would be covered by toluene, the estimates of the concentration of the mixture used in the tests were much closer to those used, i.e. about half of the toluene concentration in the test liquid. It is possible that the test conditions still did not result in the whole of the sampler being covered or, more likely, this very harsh test saturated, or came close to saturating, the adsorbent in the IOM dermal sampler. The data from the short duration immersion tests were also intended to explore the issue of surface coverage but these were also complicated by saturation of both the ACC sampler and the prototype IOM dermal sampler.

In the field study we found that there was an association between the inhalation exposure level and dermal exposure to toluene measured with the IOM prototype sampler. This in part reflected the considerable difference between the two plants studied, with plant A having much poorer overall controls than plant B. The correlation was greater for the chest samples than for the forearm samples, reflecting the relative contributions of direct contact with contaminated materials to these two sampling locations. In some ways these results are encouraging since it may reflect a general linkage between inhalation and dermal exposures.

However, the combination of the membrane and activated charcoal cloth meant that the sampler was both too permeable and had a low capacity. This resulted in the adsorbent becoming too easily saturated during testing. Any future development will require a much less permeable membrane than the current material so that it is closer in collection characteristics of the skin. Possible routes forward include development of a membrane with collection efficiencies for a range of materials closer to those of skin or even preparing a custom-built biological membrane. In addition, a higher capacity activated carbon cloth would be desirable. A number of varying density cloths are available in a range of forms, these can be investigated and discussed further with the relevant manufacturers.

The prototype IOM dermal sampler is the first practical dermal exposure sampler designed to allow both deposition and transfer to and from its surface as occurs on the skin. The sampler gives sensible, reproducible results in the laboratory and field trials. The concept of a “biologically relevant” dermal sampler, which we have demonstrated in this research, offers a real opportunity to have a dermal exposure sampler that will mimic human skin. We believe that further development of the concept will provide an outstanding opportunity to place dermal exposure sampling on a firm scientific footing. This type of sampler will enable measurements to reflect the properties of skin and it will provide an appropriate measure to assess health risks from either uptake or local effects on the skin.

1. INTRODUCTION

Occupational dermal exposure to hazardous substances is known to cause a variety of diseases, including skin cancer and dermatitis. The prevalence of occupational skin diseases in the UK is not known exactly, but there are probably many tens of thousands of workers affected. In addition, many chemicals (e.g. pesticides, polycyclic aromatic hydrocarbons and some solvents) may pass through unbroken skin and contribute to the systemic dose. The diseases caused by dermal exposure, either alone or along with inhalation exposure, have important social and economic consequences for the country.

There are a variety of mechanisms by which skin may be exposed to hazardous chemicals. Direct contact by liquids from splashes and spills are common and immersion is also possible. Contact of hazardous substances with the skin can be exacerbated when the chemicals soak into clothing. The clothing may then act as a reservoir for the chemical and the skin can remain exposed for a considerable time, when otherwise the substance would probably run off the skin surface. The skin may also be exposed to particulate material such as aerosols or through direct contact e.g. surface attrition. Although it is possible that exposure may occur to gases or vapours, a number of authors, including Loizou and Cocker (1997), have demonstrated that they generally make little contribution.

A recent series of review articles has summarised the range of practical sampling methods available to assess dermal exposure (Brouwer *et al*, 2000; Soutar *et al*, 2000 and Cherrie *et al*, 2000). These fall into three broad categories: hand washing or wiping techniques; patches or suit sampling and fluorescence techniques. Both hand wash and wipe techniques remove residual contamination from the skin. These are most commonly applied to substances with low volatility. These techniques are easy to use and require little capital costs. However, there is little standardisation between researchers using these techniques and only a few investigators report the recovery efficiencies they achieve with their technique. Fenske *et al* (1999) has demonstrated substantial differences in recovery between wiping and washing. Fluorescence techniques, either relying on the natural fluorescence of the hazardous substance being investigated or from an added tracer compound have been used since the 1980's. These use an ultraviolet light source to illuminate the skin and a sensitive camera to capture the resultant fluorescent image. Computer analysis of the image can be used to provide a quantitative estimate of the mass of fluorescent compound on the skin, although such equipment is expensive and time consuming to use. Finally, there are patch and suit based techniques, often called surrogate skin techniques because the aim is to provide a covering "skin" for the body that will collect all of the contaminant that would otherwise have landed on the skin. Patches are often constructed from a 25 cm^2 square of cotton or other textile fabrics with an impervious backing. These can be attached to various parts of the body to provide a measure of the mass of contaminant that has landed at that location. Suit samples have the advantage that they sample the whole body, although the amount of sampling material used presents practical difficulties when it comes to sampling and analysis.

We believe that the investigation of the health risk from dermal exposure is hampered because of the absence of appropriate exposure measurement methods. As we have seen, measurement of dermal exposure is currently carried out using a variety of practical techniques where the mass of the contaminant residing on the skin at a point in time or the total mass of contaminant landing on the skin over a period of time are assessed. However, many studies of the uptake of chemicals through the skin have shown that it is the concentration on the skin, rather than the mass, that is the most relevant descriptor of risk (Fiserova-Bergerova, *et al* 1990; Fiserova-Bergerova, 1993).

Cohen and Popendorf (1989) proposed a method to monitor dermal exposure to volatile chemicals. Their sampler comprised a layered charcoal cloth patch with an impervious backing and a polyester fabric front. When they developed the sampler they had the aim of sampling all of the volatile chemical that landed on the patch and they carefully assessed any losses from the sampler so that they could adjust the measured mass of liquid contaminant to reflect any losses. This approach is directly analogous to that taken for low volatility liquids such as pesticides where an adsorbent cotton or cotton-polyester cloth is used to collect the liquid.

Cherrie and Robertson (1995) highlighted the problems with this type of sampler and suggested an improved way to measure dermal exposure. They proposed a patch sampler that would collect a sample by diffusion. This would comprise an adsorbent sealed into a flat assembly, in which one side comprised a semi-permeable membrane. The dermal contaminant would then diffuse though the membrane towards the adsorbent just as it would diffuse through the outer layers of the skin towards the peripheral blood supply. This type of sampler would be particularly appropriate for liquids, including volatile chemicals that might pass through the skin and for which there are currently no validated sampling systems.

Toluene is one of many volatile chemicals that may pass through the unbroken skin. It is widely used in industry as a solvent for oils, natural and synthetic rubber, coal tar, asphalt, pitch and resins. It is also used as a solvent for cellulose paints, varnishes, adhesives and as a component in photogravure inks. With water it forms azeotropic mixtures that have a depolishing effect. In addition, it is often used as a cleansing agent. Its most important use is as an additive to petrol, which may contain between 4 and 16% by weight of toluene. In commercial products, toluene is usually found with other organic solvents such as xylene, butanol and ethanol. Toluene is used in a wide range of concentrations from 5-10% in paints, to 50 - 60% in some cleaners through to 100% toluene. It is also present in many consumer products, including household aerosols, paints, varnishes, rust inhibitors, thinners and solvent based cleaning agents. Such products typically have an average toluene content of around 10%. Its widespread use and ability to be absorbed through skin highlights the need for a validated dermal sampler.

This report summarises a study to investigate the feasibility of developing a “biologically relevant” dermal sampler to measure personal exposure to toluene. The sampler is based on the principles previously described by Cherrie and Robertson (1995), in order to assess the utility of the technique. The aim of this type of measurement is to make it possible to estimate uptake of toluene through the skin.

2. AIMS AND OBJECTIVES

This project aims to develop a prototype patch sampler capable of measuring a biologically relevant index of dermal exposure.

Specific objectives include:

- design and construct a prototype sampler to measure the concentration of toluene contaminating the skin contamination layer, to provide a biologically relevant indicator of dermal exposure;
- carry out a limited series of laboratory experiments to evaluate the performance of the sampler under controlled conditions;
- carry out studies to investigate the practical use of the sampler in a limited number of workplaces, and finally,
- to identify areas for future development.

3. SYNOPSIS OF THE WORK PROGRAMME

The planned programme of work was divided into two stages: development of the prototype sampler followed by laboratory and field testing. Due to the developmental nature of the project it was not practicable to prepare a detailed protocol for the work in advance and this was carried out progressively throughout the project.

The first stage of the development work was the selection of a suitable adsorbent with a high capacity for organic solvents, especially toluene. The adsorbent also had to be readily available, flexible, inexpensive and permit easy desorption of chemicals. The stability and recovery of the adsorbent at different concentrations of toluene had to be assessed.

A literature review was carried out to collate information on the permeability of human skin and a selection of various materials to a range of organic solvents, in particular toluene. This was followed up by contact with potential suppliers to ascertain the suitability and availability of membranes for the project. Information about the characteristics of the membranes was also obtained. Based on this information a number of materials were sourced and these were then subjected to more detailed laboratory evaluation.

Membrane selection was principally based on permeation. The permeation rate was assessed by exposing each membrane material to liquid toluene in a flow cell and then measuring the rate at which toluene vapour diffused through the membrane into the air behind the membrane. Each test was carried out at least three times. Mean permeation rates were calculated for each material and a matrix of results was constructed. The membrane material selected had to be chemically stable in a wide range of organic solvents, flexible and robust. Ideally, the chosen diffusive membrane should have a permeation rate similar to that of human skin, with similar surface properties.

The backing material for the sampler needed to be chemically stable, impervious, strong and suitable for sealing to any other materials used in the sampler construction, most importantly the membrane material. It also had to be flexible and provide good thermal contact with the skin; allowing simulation of the evaporative effect caused by the warm surface of the skin. Contact was made with a number of material suppliers to locate candidate backing materials.

A series of laboratory trials were used to assess the performance of the sampler under controlled conditions. Varying concentrations of toluene solution were produced by mixing with ethanol. Samplers were then exposed to known concentrations of toluene solutions via spraying, pouring and immersion. These test conditions were chosen to represent a range of realistic occupational exposure scenarios. In addition to the IOM dermal sampler we used activated carbon patches for comparison. After the tests the adsorbent section from each sampler was removed, the chemicals desorbed and analysed by gas chromatography.

Limited field testing was carried out at two sites. Testing was carried out over one day for each site and workers were assessed each day over two shifts, eight workers at Plant A and six workers at Plant B. There was no attempt to select these sites at random since the purpose of the trials was to evaluate the prototype sampler. We approached industrial contacts with which we had previously measured toluene and selected suitable sites. During the sampling, activated carbon cloth sampling patches were worn alongside the IOM dermal sampler for comparison. Usability, wearability and robustness of the sampler were also assessed at this stage.

4. SAMPLER DESIGN AND CONSTRUCTION

4.1 PRINCIPLE

The principle of operation of the proposed dermal sampler was simple. Toluene vapour or liquid would come into contact with a diffusive membrane, diffuse across this membrane and be adsorbed onto a suitable adsorbent. At the end of the sampling period the toluene would be desorbed and analysed by gas chromatography to determine the total mass adsorbed. By knowing the permeation rate of toluene through the membrane and the duration of exposure it would be possible to calculate the original concentration of toluene solution to which the patch was exposed. Figure 1, below is a schematic of the original idealised sampler.

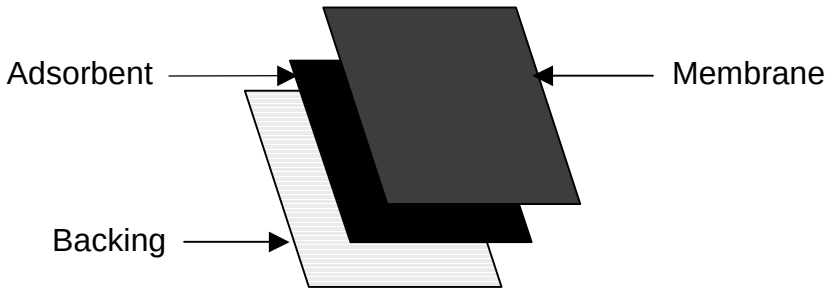


Figure 1 – Idealised prototype IOM dermal sampler

4.2 ADSORBENT SELECTION

4.2.1 Selection Criteria

A literature review was carried out to identify suitable adsorbent materials. This included use of in-house databases, ISI Web of Science service for UK education (Athens), internet (using the Google search engine) and the University of Edinburgh library catalogue. Keywords used were; organic vapour adsorbent, organic vapour sampling methods, collection of organic vapours, organic vapour desorption, activated carbon, activated charcoal, activated charcoal cloth. The adsorbent had to have a high capacity for organic solvents, especially toluene. It also had to be relatively inexpensive, flexible and permit easy desorption of chemicals.

The literature review confirmed that the most widely used, cheapest and most effective adsorbent for organic liquids is activated carbon. This is used in many applications, such as water purification, ventilation and air conditioning systems, air and water pollution, personal protective equipment, industrial waste control, malodorous substance control, solvent/precious metal recovery and many other situations. Activated carbon is produced by the controlled burning of carbon rich materials such as coal, wood or nut shell. It is either steam or chemically activated to further develop its internal pore structure (Chemviron, 2001). Activated carbon is produced in many forms: granular, powdered and woven/knitted cloth.

Granular activated carbon is composed of irregular shaped particles, with sizes ranging from 0.2 to 5 mm. Powder activated carbon is pulverised carbon with sizes predominantly less than 0.18 mm (Chemviron, 2001). Both granular and powdered forms are mainly used in liquid (water treatment) and gas phase applications (flue gas treatment). Activated carbon cloth (ACC) is constructed of bundles of activated carbon filaments in a textile form. These fibres are approximately 20 microns in diameter which results in them having similar adsorption kinetics to very fine powdered activated carbon (Chemviron, 2001). Gases and liquids can flow through the activated carbon fabric with very fast adsorption kinetics. As the adsorption

is faster, it allows the size of the adsorption area to be reduced considerably. This property was essential when considering the proposed size of the dermal sampler, which was planned to fit comfortably on the back of a hand. It was judged to be much more practical to use a single piece or double layer of ACC as the adsorbent, rather than loose fitting granular or powdered forms. Activated carbon cloth can also be impregnated with a range of different chemicals to enhance the adsorption capacity for certain gases/vapours, although this was unnecessary for toluene.

Taking all of these factors into account, it was decided that ACC was a suitable candidate to act as the adsorbent in the dermal sampler. Searches of suitable suppliers of activated carbon cloth lead us to a US company, Calgon Carbon Corporation. They have a subsidiary known as Chemviron Carbon Limited which owns the European operating unit - Charcoal Cloth International, from which samples of activated charcoal cloth were obtained. Five linear metres of ACC grade FM1/250 were obtained. This is a single plain weave product. Charcoal Cloth International produces a range of activated charcoal cloth products in varying weaves, weights and thicknesses.

4.2.2 Absorption capacity

Samples of this ACC were analysed by gas chromatography in order to test the sample for the presence of any contaminants; none were found. The relative adsorbent capacity of the ACC was also determined using an International Standard Organisation method for the determination of the iodine number of carbon black for use in the rubber industry (ISO-CD-1304[E]). In this test a sample of the ACC was dried, weighed and mixed vigorously with a measured volume of standard iodine solution. The mixture was then centrifuged. A measured volume of the clear iodine solution was titrated with a standard solution of sodium thiosulphate. From this titration value and the sample mass, the iodine adsorption number was calculated and the subsequent capacity determined.

The results showed that the total capacity of the ACC was 960 g/kg, i.e. the activated charcoal can hold close to the equivalent of its mass in toluene. Following trials it was evident that this standard method over-estimates the actual capacity of the ACC. The results of the lab trials indicate that the capacity of the ACC is much less than this (see section 5.3).

Ten ACC patches of approximately 4 cm by 7 cm were weighed using a Sartorious microbalance in order to determine the mean mass of each section. These measurements ranged from 0.304 g to 0.357 g, with a mean of 0.333 g (standard deviation 0.016 g). Assuming a 95% uptake, each patch of ACC at this size was judged to have a maximum capacity to adsorb approximately 300 mg toluene.

4.2.3 Recovery Efficiency

ACC patches were added to three bottles (30 ml Amber). The patches were then spiked with 10 µl of neat toluene (8650 µg) using a microsyringe. They were then removed and desorbed in 10 millilitres of carbon disulphide. An aliquot of each sample was analysed by gas chromatography to determine the mass of toluene present on each patch. The recovery efficiency was calculated as a percentage of the mass of toluene recovered from the total mass originally added. These results are shown in Table 1, below.

Table 1 – Toluene recovery efficiency from ACC

Sample	Mass of Toluene Applied (μg)	Mass of Toluene (μg) measured	% Recovery
1	8650	7970	98.5
2	8650	7970	98.4
3	8650	7860	97.0

4.2.4 Stability

The stability of toluene on activated carbon is well reported. Following exposure, the standard technique is adsorption by activated carbon and subsequent desorption, normally using a desorbing compound such as carbon disulphide. Samples are often stored for a number of days before desorption and analysis by gas chromatography (HSE, 1997). Although there is a risk that sample losses may occur due to chemisorption or catalytic action, Saalwechter *et al* (1977) and Rudling *et al* (1986) have proved that there is no sample loss for toluene over an extended period. Rudling *et al* reported that there was less than 5% loss over at least two weeks of 1 μl samples of toluene with (20 μl) or without water present. Samples generated in this project were generally analysed within one or two days. These contained 10 μl (~9 mg toluene) on the first test and 50 μl (~ 43 mg toluene) on the second, these were more in line with actual masses of toluene sampled on both the prototype IOM dermal samplers and plain ACC patches.

4.2.5 The Selected Adsorbent

A single layer of ACC from Chemviron Carbon Limited was selected as the adsorbent for the prototype sampler. The stability and recovery efficiency were satisfactory. The ACC was judged to have sufficient adsorptive capacity for the purposes of this project. However, it was realised that for a versatile sampler to be used in many diverse environments over a full working day the capacity might not be sufficient and an alternative design could be needed.

4.3 MEMBRANE SELECTION

4.3.1 Selection Criteria

The sampler was designed to provide a biologically relevant indicator to dermal exposure. We judged that it was desirable for the membrane to have similar properties of human skin in order to simulate its effects. Although this was not absolutely essential it seemed appropriate for the sampler to have a response time similar to skin. For example, a membrane with a high permeability to toluene would act in a similar way to the more conventional patch samplers, i.e. it would accumulate toluene that landed on the sampler throughout the exposure period. On the other hand, a membrane which had a low permeability to toluene would probably fail to detect transient contacts with toluene containing mixtures. A literature review and internet search using similar methods to those described in section 4.2.1 was carried out in order to establish candidate materials for use as the diffusive membrane and the obtain information about the rate of permeation of toluene through skin. Suppliers of candidate membrane materials were then sourced.

In addition to the above criteria, we considered that suitable membrane materials had to be resistant to organic solvents, flexible, robust and readily available. Resistance to other solvents was necessary since we wished the sampler to work in industrial environments where there may be many different chemicals present. A range of options for membrane materials was considered; from a surrogate skin material used to treat burns victims in Japan to standard fluoropolymer films such as polytetraflouroethylene (PTFE).

There are a small number of studies that have attempted to measure the permeation rate of toluene through human skin, some of these have used human volunteers and others have used *in vitro* tests with excised human skin. We have not extensively reviewed the available literature but rather we have concentrated on a few key references which provide sufficient information for us to make an appropriate selection of the membrane for the prototype sampler.

Interpretation of these studies is not straightforward as the exposure circumstances vary. If the solvent is left on the skin uncovered then most of the liquid will evaporate and be lost to the surrounding air rather than contribute to dermal uptake. Wilkinson and Williams (2001), from the Skin Research Group at the University of Newcastle-upon-Tyne, reported the results of an extensive *in vitro* study of absorption of volatile liquids funded by the Health and Safety Executive. Their experiments with toluene were carried out with small quantities (10 µl) of neat solvent or saturated aqueous solutions of toluene with 330 µm thick human breast skin. Their flow cell had a charcoal filter above the test liquid and so it was possible for the toluene to evaporate and in the experiments with neat toluene there was insufficient liquid to maintain coverage of the skin throughout the tests. This was not the case for the aqueous solution where there was sufficient liquid to maintain coverage. These authors found that the average flux through the skin was 12 µg/cm^2/hr (neat toluene) and 1.7 µg/cm^2/hr (aqueous toluene). The difference in flux reflects the lower toluene concentration in the water, although the calculated permeability coefficient was about 6,000 times higher for the water solution compared with the neat toluene, which the authors attribute to differences in the time that toluene was in contact with the skin during the experiment, which lasted 24 hours. However, it is possible that during the tests with neat toluene the test liquid may have evaporated into the airspace above the skin and the measured permeation rate may partly reflect absorption from the saturated vapour phase rather than the liquid toluene.

Bowman and Maibach (2000) also report the results of *in vitro* assessments of dermal permeation for toluene. Their test system was similar to the Newcastle group with the main exception that they used much larger quantities of solvent in their system (200 or 300 µl) and

they sealed the apparatus to reduce evaporation of the test liquid. These authors found that their system reached steady state diffusion after two hours and they show that then approximately 0.08% of the applied dose was then absorbed per hour. Unfortunately, they do not quote the mass flux through the skin and do not unambiguously specify the original volume of toluene used in the test. However, from the information available in the paper we have estimated that the flux was either 140 or 220 $\mu g/cm^2/hr$. This is much higher than Wilkinson and Williams found, but is probably more appropriate for our purposes because it represents permeation from an unlimited liquid toluene reservoir.

Kežić *et al* (2001) exposed volunteers to a range of solvents over a 27 cm^2 area on the forearm for three minutes. They carefully controlled the experimental conditions so that it was not possible to inhale toluene during the test. Toluene was then measured in expired air for about an hour after exposure. The dermal toluene flux was calculated from comparative data for the exhaled toluene concentrations resulting from inhalation exposure, with the assumption that regardless of the route of exposure for the same mass uptake the concentration in expired air would be the same. The permeation rate of toluene averaged over the exposure period was approximately 1,200 $\mu g/cm^2/hr$. It is unclear whether the results from such a short exposure period are truly representative of steady state diffusion conditions and so may be higher than would occur in a longer exposure scenario.

4.3.2 Testing of Candidate Membranes

A summary of the materials selected for testing is shown below in Table 2, with the complete list in Appendix 1. These materials ranged from simple films of various thicknesses, with or without pores, through to complex composite membranes. Some of the membranes that were supplied for testing were currently under development and we were not privy to the composition.

Sixteen of these membranes were supplied by the Pall Corporation, four by DuPont, two by ICI and the remainder by a variety of other manufacturers.

Table 2 – Summary of Materials Tested for use as Diffusive Membranes

Material	Pore size (μm)	Brief description
Anodisc	0.02 μm	Aluminium Oxide
Biydyne	0.45 and 5 μm	Nylon 66
Emflon	0.02 to 0.45 μm	ePTFE supported with non-woven polyester
Melinex	125 μm film	Polyethylene terephthalate
Pallflex® 40	-	Hemp fibre base with glass fibre matrix, EVA binder and hydrophobic/olephobic fluoropolymer formulation
Pallflex® 8E	-	Manila cellulose paper with glass fibre matrix, VA latex binder & Fluorochemical oil
Pallflex® AO1603	Submicron (<0.1 μm)	Unique composition of solvent compatible aramid fibres with EVCL-PVA thermoplastic proprietary binder. "Organophobic", flexible membrane with good vapour transmission property
Pallflex® KO1601K	-	Development Material – not specified
Pallflex® PO1618	-	Development Material – not specified
Pallflex® RO1569J	-	Development Material – not specified
Pelnac	Bilayer	Collagen sponge base with silicon top layer
PTFE	12.5 to 500 μm	Polytetrafluoroethylene
Purple Nitrile Glove	-	Purple Nitrile. 100% nitrile, synthetic co-polymer
TS6	-	Randomly distributed glass microfibres reinforced with woven glass fabric. Saturated with PTFE and silicon formulation.
TV2	-	Randomly distributed glass microfibres reinforced with woven glass fabric. Saturated with PTFE and silicon formulation.
TX4	-	PTFE, glass microfibre & fine glass cloth
Versapor® 1200	1.2 μm	Modified acrylic copolymer cast on non-woven nylon support.
Versapor® R 1200	1.2 μm	Modified acrylic copolymer cast on non-woven nylon support. Treated with FluoRepel for hydrophobic/Olephobic surface properties

The permeation rate of each material was measured using a modification of EN 374-3 – Protective gloves against chemicals and micro-organisms – Part 3: Determination of resistance to permeation by chemicals. Figures 2 and 3, below, illustrate the experimental set up for this stage of the research. A Thermo Electron Instruments (TEI) Toxic Vapour Analyser (TVA 1000B) was used to measure the concentration of toluene in the system. The TVA 1000B had a small probe which was connected to the main unit via an 'umbilical' cord. Readings were logged in the main unit's memory and downloaded after each test. The TVA 1000B contains a flame ionisation detector (FID) which measured the concentration of organic vapours over a dynamic range (0 – 50,000 ppm).

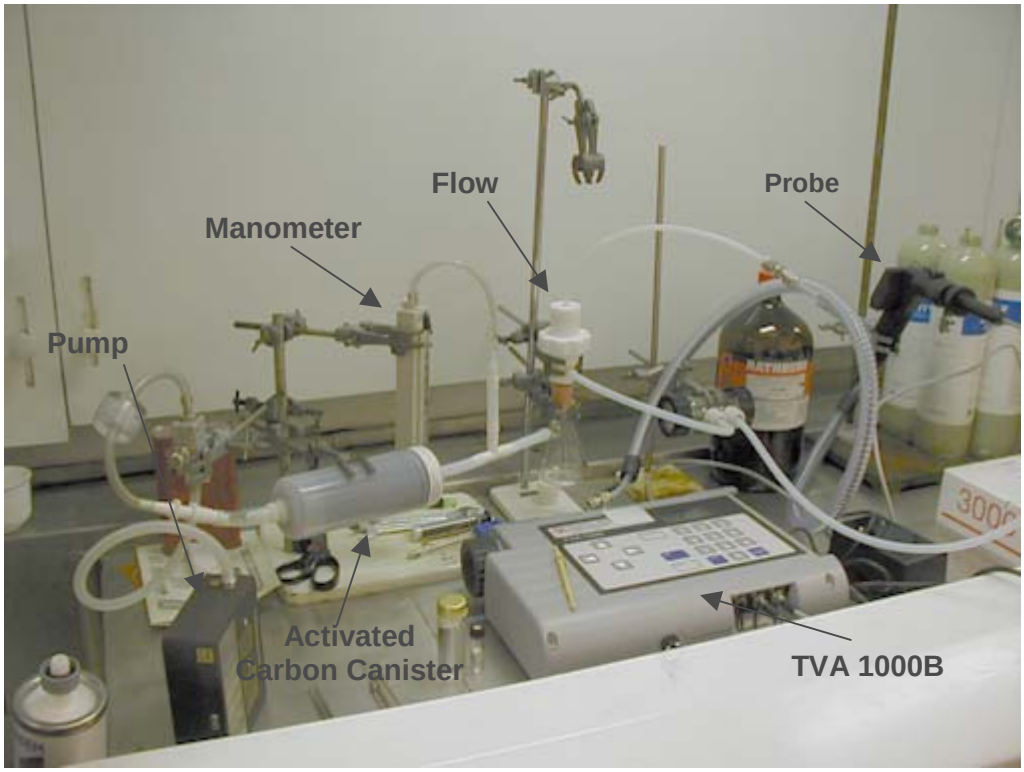


Figure 2 - Experimental set up for permeation testing of membranes

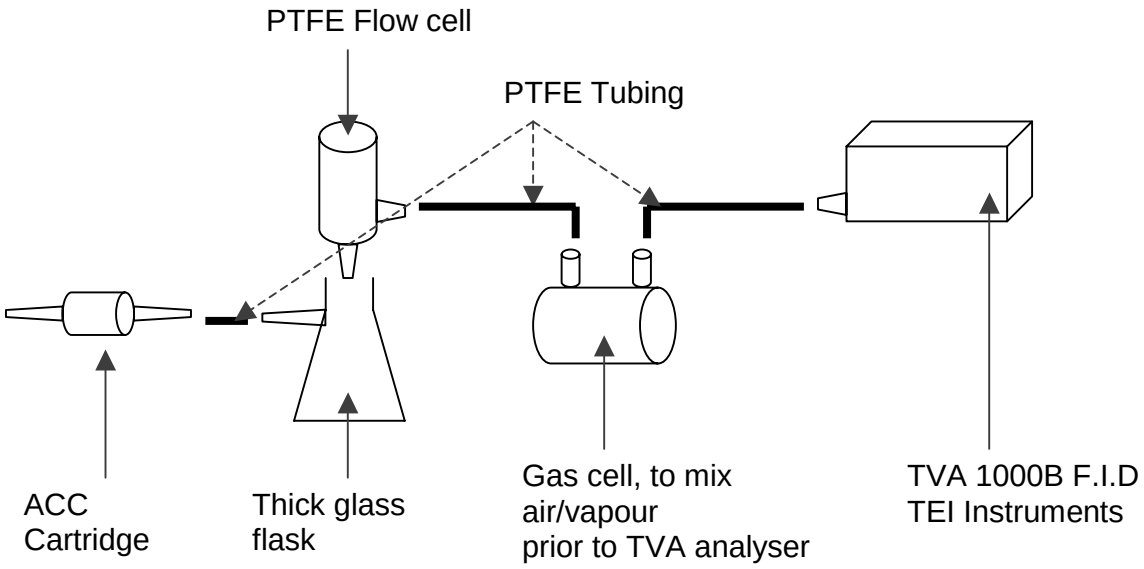


Figure 3 – Schematic diagram illustrating equipment use per permeation testing of membranes

Air was pushed into the system from one end using a small air pump and drawn through the system from the opposite end using the internal pump of the TVA 1000B. This was to ensure that the air pressure was equalised across the material being tested to ensure that vapour permeated the material through the process of diffusion, rather than being actively drawn through the material or forced in the opposite direction by pressure effects. Fresh air was drawn through a large canister filter, containing granular activated carbon. This was to ensure that air entering the system was cleaned of any contaminants prior to mixing with vapour in the permeation flow cell. Air passed through the glass flask, into the lower section of the permeation flow cell where it mixed with toluene vapour that had diffused through the material being tested. This air/vapour mixture was drawn out of the side of the permeation flow cell and into a cylindrical chamber. This was used to promote turbulence in the air steam and facilitate good mixing of the air/toluene vapour before passing into the FID within the TVA 1000B.

The permeation flow cell (Figure 4, below) was composed of polytetrafluoroethylene (PTFE) and comprised two main cylindrical chambers. The base of the upper chamber was cylindrical, with a wider lip at the base. The lower chamber was the same except inverted, so both lips meet when joined. Small square sections of each material were placed on the upper side of the lower chamber and then the upper chamber was then placed on top of this. Both sections were secured together using a threaded PTFE collar ring which secured them together, firmly clamping the material being tested in between. Aluminium tubes were built into the base and the side of the lower chamber which permitted air through-flow. Any toluene that diffused through the test material was collected in the air stream and drawn into the FID.

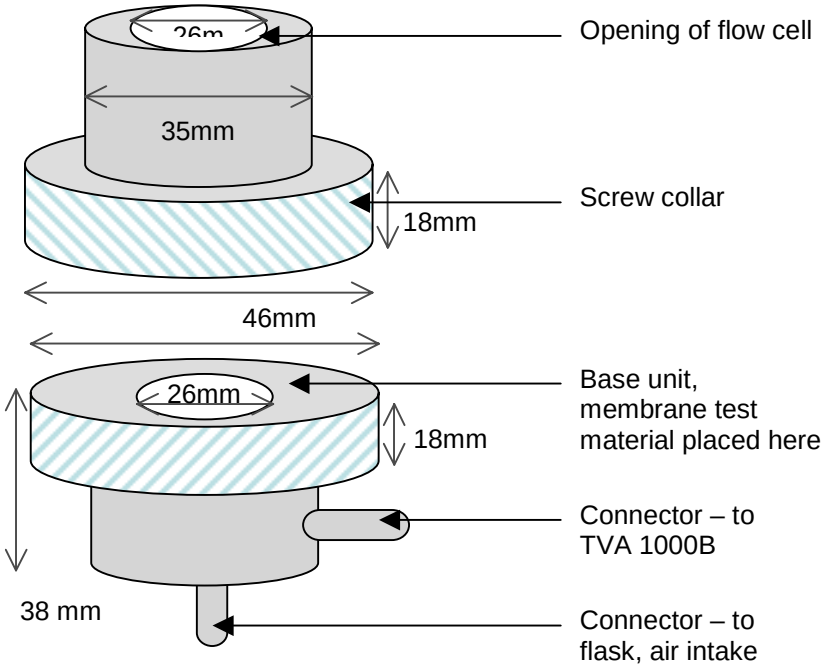


Figure 4 – Schematic diagram of PTFE flow cell used in permeation testing

For each sample, 200 µl of toluene was injected in to the upper section of the permeation flow cell so that it completely covered the test membrane. The open end of the flow cell was covered with aluminium foil to enclose the flow cell and reduce evaporation of toluene from the surface of the material. The TVA 1000B was set to log every second and record these data within its onboard memory. Each sample run lasted one hour and the data was downloaded from the memory after each sample run. The data was corrected using a calibration factor and plotted as concentration of toluene against time. Each material was tested on at least three occasions, in most cases four. The permeation rate was calculated for each run and then a mean permeation rate calculated for each material.

The TVA 1000B was regularly calibrated using zero air, 499 ppm methane and 10,000 ppm methane. As the TVA measured total volatile organic compound concentration (VOC) it was necessary to adjust all the recorded data to correct for toluene. A range of Tedlar bags each containing five litres of air were injected with known volumes of toluene. The toluene concentration within each Tedlar bag was calculated. A series of Tedlar bags were made for lower concentrations and a series for higher concentrations, as the response of the TVA 1000B was non-linear at high concentrations. Data from these were then plotted and the appropriate calibration factors were calculated, one at low concentrations (0 – 5000 ppm) and one at high concentrations (5000 – 50,000 ppm). These were used to adjust data accordingly.

Data from the calibration is shown in Appendix 2.

4.3.3 Results from the Membrane Testing

The results of the permeation test for each material tested are shown below. The full data set is reproduced in Appendix 3.

Table 3 - Summary of permeation tests for membrane selection

		permeation rate		
Pelnac	Bilayer	Membrane unstable	n/a	
Pallflex® RO1569J	n/a	No steady-state diffusion	n/a	
Pallflex® KO1601K	n/a	No steady-state diffusion	n/a	
PTFE	12.5 to 500 µm	0	0%	32
Purple Nitrile Glove	n/a	0	0%	4
Pallflex® 40	n/a	144	4%	4
Versapor® R 1200	1.2 µm	178	9%	4
TS6	n/a	569	1%	4
Versapor® 1200	1.2 µm	600	9%	4
				4

n/a – not applicable

A number of the membranes that were tested were impervious to toluene (PTFE, Melinex and nitrile rubber) and many others provided only a limited barrier to the diffusion of toluene. Two membranes were unstable in toluene showing visible damage to the membrane structure (Pelnac and TV2) and four produced an unstable diffusion process, reflected in rapidly varying toluene concentrations in the test cell (Pallflex RO1569J, PO1618, KO1601K and Anodisc).

The variability in the permeation data was similar across most of the membranes that allowed some diffusion through the membrane. The relative standard deviation varied from 1% to 9%

4.3.4 Membrane Selection

From the literature review, it was clear that the dermal permeation rate for neat toluene was somewhere within those figures stated above, i.e. between about 10 and 1,200 $\mu g/cm^2/hr$, with the likely flux being somewhere in the middle of this range, i.e. between about 100 – 200 $\mu g/cm^2/hr$. Comparing these figures with the data from our membrane permeation tests suggests that the Pallflex AO1603 would be most suitable although its permeation rate was considerably higher than we would have really wished. The mean permeation rate of toluene through this was 78,000 $\mu g/cm^2/hr$.

However, the Pallflex AO1603 was also hydrophobic, flexible, robust and contained an EVA binder which was suitable for heat welding materials, such as the backing material. We investigated using multiple layers of the membrane in an attempt to reduce the permeation rate further but it was impracticable to construct a practical sampler in this way. Because of time constraints and the difficulties we had experienced in identifying a membrane that would allow toluene to diffuse slowly through we felt it was necessary to proceed with the sampler design to enable us to further investigate the practicability of the design concept.

The Pallflex AO1603 membrane was therefore selected as the most suitable membrane for the prototype IOM dermal sampler.

4.4 SELECTION OF THE BACKING MATERIAL

A literature review and internet search was carried out to identify suitable backing materials. We had decided the backing material had to be chemically stable, impervious, strong and suitable for sealing to other materials, most importantly the membrane material. We also wished it to be flexible and provide good thermal contact with the skin; allowing simulation of the evaporative effect caused by the warm surface of the skin. Following discussion at the start of the project, it was decided that the most suitable backing material was aluminium foil, which encompassed all of the characteristics required for the sampling device. Aluminium foil is impervious, resistant to organic solvents, flexible, robust and provides good thermal conductivity properties. We were able to source a coated aluminium foil from GTS Flexible Materials, in Wales. They manufacture laminated aluminium foil for a wide range of uses. Their aluminium foil (26 μm thick) was coated with a clear laminate in the laboratory which was sufficient to form a strong thermal weld with the Pallflex AO1603 membrane.

Several sections of the coated aluminium foil were sealed to sections of the membrane using various time settings on the heat sealer until a satisfactory seal was achieved. This was tested by informal tension testing, pulling sections apart to determine the strength of the seal. A suitable midway setting on the heat sealer provided a suitable seal.

Coated aluminium foil from GTS Flexible was selected as the backing for the sampler.

4.5 CONSTRUCTION OF THE SAMPLER

4.5.1 Fabrication of the Sampler

The sampler design was to comprise the membrane sealed to the backing material with the adsorbent sandwiched between. Following an initial evaluation of the prototype sampler design, we judged it was possible for liquid toluene on the membrane surface of sampler to wick directly through to the adsorbent, i.e. without diffusing through an air gap. In order to minimise this possibility we investigated the introduction of some form of spacer between the membrane and the adsorbent. Aluminium mesh was initially investigated, but this was unsuitable because of the possibility for it to tear the membrane and so we investigated the possibility of using an inert plastic mesh. A PTFE mesh, manufactured by the Pall Corporation, was sourced. This was more flexible and easier to cut than aluminium, and did not damage the sampler diffusion membrane. We do not believe this PTFE mesh would have any affect on the uptake of the ACC, for a number of reasons. The PTFE mesh was not fixed to the ACC and size of the spaces in the mesh were large in relation to the overall size of the prototype IOM dermal sampler. The PTFE mesh only acted as a physical spacer between the ACC and membrane, not a physical barrier.

The component parts of the prototype sampler are shown in Figure 5.

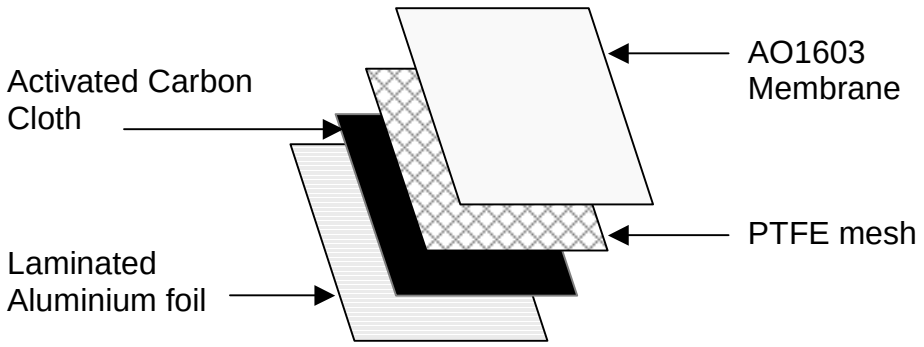


Figure 5 - Schematic of sampler components

The sampler was designed to fit on the back of a hand or wrist, although we believe that there is little constraint on scaling the design up or down in size, e.g. to sample on a finger. For the prototype testing we had arbitrarily selected the wrist as the sampling location. To allow enough space in the sampler for an adequate layer of ACC cloth, the dimensions of the sampler were arbitrarily set at 6 cm by 9 cm. Sections of the membrane and backing material were accurately marked out and cut using a guillotine to give a straight edge. Sections of the ACC and PTFE mesh were also cut using the guillotine, this time to approximately 5cm by 8 cm; these dimensions were smaller to allow space for the thermal weld at all four edges of the sampler. The top surface of the membrane was therefore 54 cm^2, although the actual effective sampling area of the membrane was approximately 34 cm^2.

All edges of the sampler were thermally welded using a commercial heat sealer (Hulme Martin 240V Impulse). The heating element was set to a 4 second cycle and both sections were held together during this process, using normal hand pressure. Each seal formed a flat, secure weld between components. The sampler was constructed in stages. First, a section of the backing foil and the membrane were thermally welded along one long side. A section of PTFE mesh was placed on top of a section of ACC and both were inserted into the unit, so as to be aligned against the welded edge. Every other side was then thermally welded to seal the

sampler. Finished samplers were placed into a desiccator to minimise water adsorption on the ACC.

The prototype IOM dermal sampler is shown in Figure 6.

Figure 6 - Pictures of the prototype, illustrating the diffusive membrane on the front and the laminated foil on the back

4.5.2 Determination of the vapour uptake rate of the sampler

It was important to know how the final version of the sampler would behave in an atmosphere of toluene vapour since it is conceptually similar to conventional diffusive samplers used for evaluating the inhalation exposure of workers. With information about the relative rate of uptake from liquid and vapour it will be possible to identify the relative contribution of both, provided we have an independent assessment of the vapour concentration. This work was also undertaken for ACC since in the laboratory and field trials this type of sampler will be used to provide comparative data.

The vapour uptake rate for the IOM dermal sampler was calculated in relation to 3M 3500 diffusive samplers and pumped charcoal adsorbent tubes. These were placed into a closed chamber which was injected with a known concentration of toluene vapour, which was confirmed from the measurements made with the diffusive and pumped tube samplers. All samples were then desorbed in carbon disulphide and analysed by gas chromatography. The uptake rate was calculated to be 336.5 cc/min or 0.336 l/ min.

4.5.3 Seal Integrity

Satisfactory sampler performance requires the seal between the membrane and backing foil to be leak proof. This was tested using units composed of foil on both sides with an ACC patch inside. Approximately every eighth sampler was manufactured in this way. These foil units were immersed in neat toluene for 1 hour. They were then removed, left in the fume cupboard for a short time to allow surface toluene to evaporate and they were then left in a drying oven overnight. Each unit was then opened, the ACC was removed and then analysed by gas

chromatography to determine the mass of toluene on the ACC (Table 4). The presence of a significant mass of toluene on the ACC was considered to indicate either a perforation in the foil and/or that the thermal weld had been compromised.

The results of these tests are shown in Table 4.

Table 4 – Seal integrity test results

Foil Unit Number	Mass of Toluene (μg)
1	0.3
2	0.4
3	0.3
4	0.7
5	0.7
6	0.2
7	0.3
8	0.3
9	0.4
10	358
11	0.6
12	0.2
13	0.6
14	0.3

The results demonstrate that the seals were generally satisfactory. Most samples indicated negligible masses of toluene, with the exception of sample 10 (358 μg) which appears to be indicative of a small break in the heat seal or a microscopic tear in the foil permitting ingress of toluene. However, this frequency of (7%) and magnitude of leakage was considered acceptable in a prototype device.

5. LABORATORY AND FIELD TRIALS

5.1 INTRODUCTION

Evaluation of the prototype IOM dermal sampler was conducted in two stages. A number of laboratory evaluations were undertaken in order to understand the basic performance of the sampler in a range of controlled exposure situations. These consisted of spray tests, where varying concentrations of toluene were sprayed onto the surface of the prototype IOM dermal samplers, pour tests where varying concentrations of toluene were poured down the surface of the sampler and immersion tests where prototype dermal samplers were fully immersed in varying toluene mixtures. Once these were completed we conducted two short field tests of the sampler: one in a factory making rubber goods and the second in a plant that printed onto metal foil. In each case we have compared the prototype dermal sampler with ACC patches.

5.2 LABORATORY TRIALS METHODS

5.2.1 Spray Tests

Spray tests were carried out by attaching four samplers (two ACC samplers and two prototype IOM dermal samplers) to a vertical cylinder (Figure 7, below) and directing a spray of a liquid mixture containing toluene at 90^{o} to the cylinder. The cylinder was made to slowly rotate so that all four samplers passed in front of the spray gun.

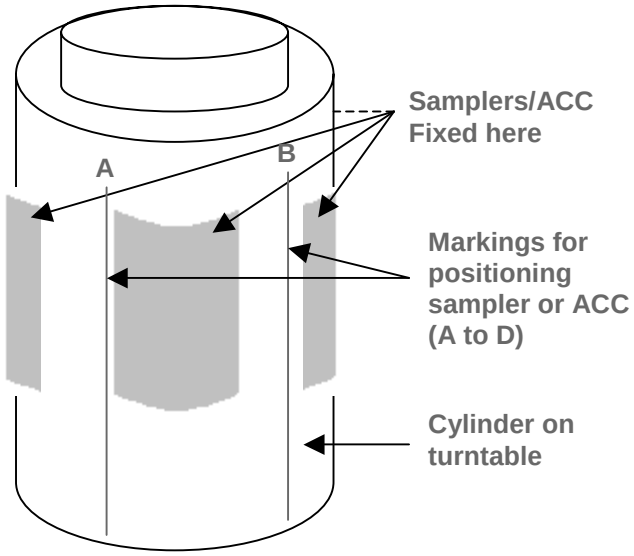


Figure 7 – Schematic diagram of cylinder, illustrating sample positions

ACC samplers and the prototype IOM dermal samplers were exposed to a range of toluene mixtures of differing concentration. Toluene was diluted with ethanol to a predetermined concentration and each solution was sprayed at the ACC samplers or IOM dermal samplers, which were mounted on the rotating cylinder. The experiment took place inside a fume cupboard; the experimental set up is illustrated in Figure 8.

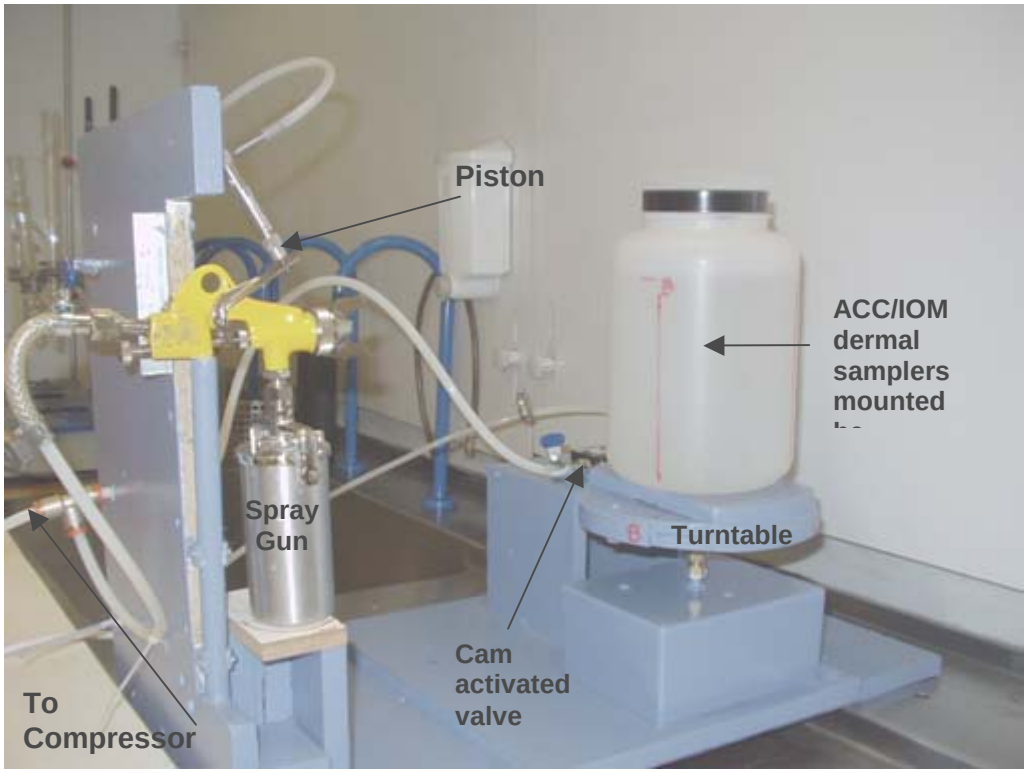


Figure 8 - Spray test experimental setup

Two IOM dermal samplers and two ACC patches were attached at positions marked A to D, marked on the cylinder in both Figure 7 and 8. The sampler type was alternated to minimise the potential for bias in the experiment. The samplers were fixed to the surface of the bottle using double sided sticky tape. The bottle was filled with water to provide ballast as the turntable rotated.

The turntable platform on which the bottle was placed had four sections removed from the wood round its circumference. A cam valve at the side of the turntable platform was activated as the turntable rotated. This valve permitted compressed air to pass through the tubing and activate a piston which was attached to the trigger of the spray gun. The piston depressed the trigger on the spray gun which then sprayed a fine mist of toluene/ethanol solution until the cam valve was closed. In each rotation of the turntable, there were four sprays of the solution over the surface of the samplers.

Initial testing of the experimental setup was carried out by spraying four plain ACC patches with a 25% toluene solution for 10 minutes on each run. There was one blank ACC patch for each of these runs. All were analysed to determine the total mass of toluene present.

Samplers were exposed to toluene at a range of different concentrations, but with the same total mass of toluene being sprayed during the test. Eight IOM dermal samplers were subjected to the spray test at each concentration. These tests were: 100% toluene for 2.5 minutes, a 75% solution for 3.33 minutes, a 50% solution for 5 minutes, 25% for 10 minutes and 5% for 50 minutes. In addition, eight samplers were sprayed with 100% toluene for 10 minutes. For every eight IOM or ACC samplers analysed there was a plain ACC patch as an experimental blank.

5.2.2 Pour Tests

In the pour tests a sampler was fixed onto an angled board using double sided sticky tape. A mixture of toluene and ethanol was then poured over the surface of the sampler for a predetermined period of time. This was achieved with the apparatus shown in Figure 9.

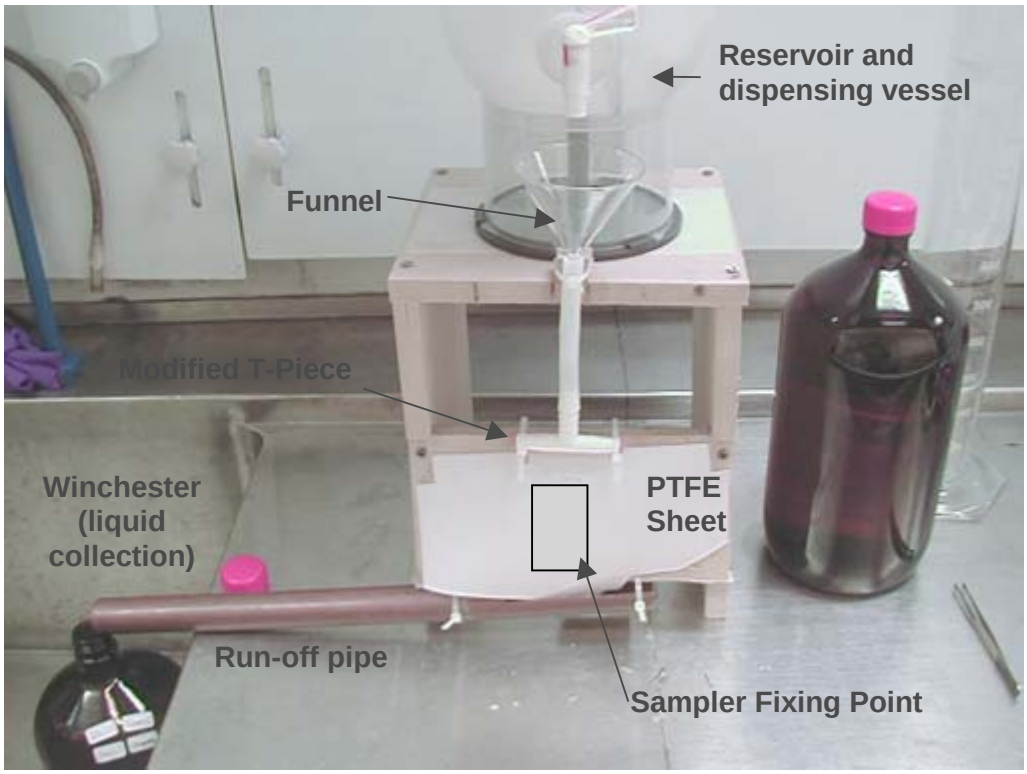


Figure 9 - Pour test experimental setup

A PTFE T-piece, located above the sampler, was connected to a section of PTFE tubing and a funnel. The T-piece has been sealed at both ends and the length of the T-piece has a number of small holes drilled into it. A large bottle with a tap was placed above the funnel and different concentrations of toluene solution were poured into this vessel. As the tap opened, the liquid passed down the funnel and into the T-piece where it escaped via the holes, cascading down the surface of the sampler. Run-off was collected by a piece of copper tubing which drained into a Winchester bottle. The residue was recycled.

In a series of three separate experiments, eight IOM dermal samplers and two ACC samplers were exposed to a 100% toluene for 2.5 minutes, 50% toluene: 50% ethanol solution for five minutes and 25% toluene: 75% ethanol solution for ten minutes. One blank ACC patch was retained from each run and analysed at the same time as the others.

5.2.3 Immersion Tests

IOM prototype diffusive samplers and ACC samplers were immersed in different concentrations of toluene solution for different lengths of time. They were placed into a glass container along with the solution and totally immersed. The container was covered and left in the fume cupboard for the required length of time.

Two IOM diffusive samplers and two ACC samplers were immersed in 100% toluene for 10 seconds, two IOM dermal samplers and two ACC patches were immersed in 25% toluene

solution for 10 seconds and four IOM dermal samplers and two ACC patches were immersed in 100% toluene for one hour.

5.3 RESULTS FROM THE LABORATORY TRIALS

5.3.1 Spray Tests

The results from these and the other tests that were carried out are presented to bring out the important features of the sampler rather than in the order that the tests were carried out. For this reason the number of samples may vary from one experimental condition to another.

Note, the effective area of the prototype IOM dermal sampler was 34 cm^2, while the area of the ACC was 23 cm^2.

Table 5 shows the results from these tests, expressed as mass of toluene per unit area.

Table 5 – Results from laboratory spray tests by test (mass per unit area of sampler)

		Mass per unit area (mg/cm^2)			
Toluene (%)	**Duration of Test (mins)**	**Number of tests**	**IOM dermal sampler (± 1 SD)**	**Number of tests**	**ACC (± 1 SD)**
5	50	4	0.24 (±) 0.02	0	No data
25	10	16	0.28 (±) 0.05	24	2.2 (±) 0.33
50	5	4	0.46 (±) 0.04	8	3.1 (±) 0.24
75	3.33	3	0.51 (±) 0.07	8	1.3 (±) 0.18
100	2.5	7	0.47 (±) 0.14	7	3.9 (±) 0.55

SD – standard deviation

In these tests the average mass of toluene per unit are ranged from 0.24 to 0.51 mg/cm^2 for the prototype IOM dermal sampler and from 1.3 to 3.9 mg/cm^2 for the ACC patches. In general the standard deviation for both types of sampler was about 10% of the mean.

Figure 10 shows the data from the spray tests carried out with IOM and ACC samplers with pure toluene sprayed over 2.5 minutes, 75% toluene over 3.33 minutes and 50% toluene over 5 minutes and 25% over 10 minutes. Data in Figure 10 is illustrated as a box plot. The box represents the portion of the results that fell between the 25^{th} and 75^{th} percentiles. The indented line in the box represents the median. Marks outside the box are outliers, i.e. extreme values.

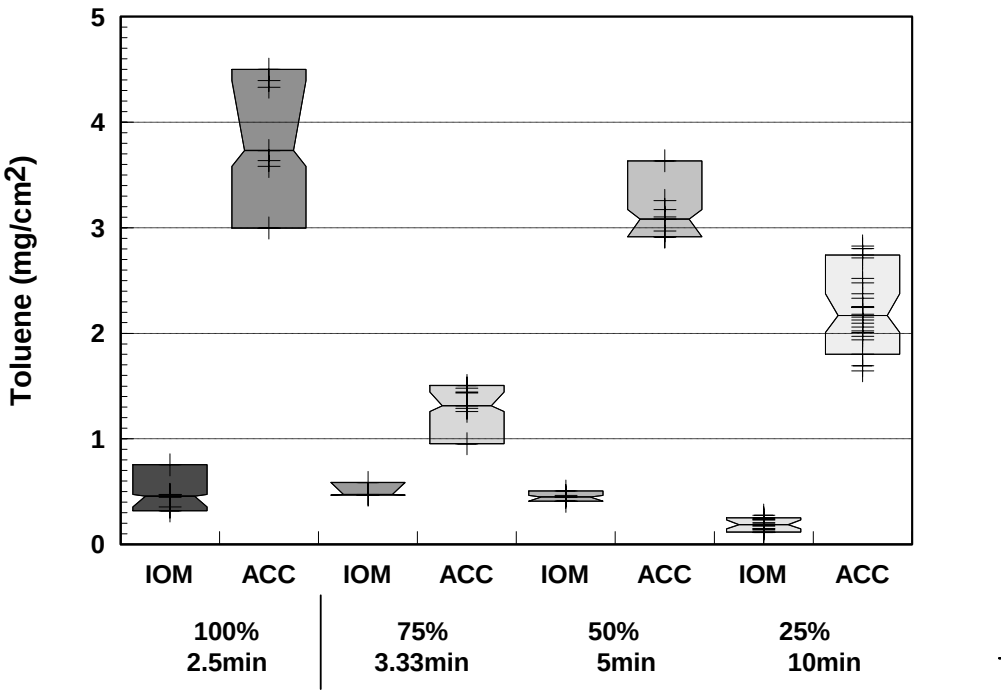


Figure 10 – Results from spray tests, varying concentrations and times (IOM and ACC sampler)

In each case the ACC samplers collected higher levels of toluene per unit area than the prototype IOM dermal samplers under the same conditions. These experiments were intended to provide conditions where the mass of toluene sprayed was identical in each case.

We therefore expected the mass of toluene to be, on average, constant across the range of conditions tested. Firstly, the results for the ACC samplers for the 75% toluene mixtures appear anomalous, being just over twice as high as the corresponding IOM prototype sampler results. These data have been carefully checked and there is no apparent reason for the low masses sampled. In general, the ACC generally collected approximately six times more than the prototype IOM dermal sampler per unit area. More importantly, it appears that the ACC patches are or are very close to saturation point. We believe that the 25% contains less toluene than the 100% solution as a result of saturation of the ACC and the high load of ethanol competing for adsorbent sites on the ACC. This can be seen in both trends; as the ratio of toluene to ethanol decreases so does the total mass of toluene even though it should remain fairly constant.

These results clearly show that the prototype IOM dermal sampler collects much lower quantities of toluene than simple ACC samplers. The diffusion barrier, like the skin gives the opportunity for some of the solvent to evaporate or run off before it is absorbed, while the ACC acts like a "sink" adsorbing most of the solvent that comes into contact with it. The mean mass of toluene on the ACC samplers was 51 mg (or 2.22 mg/cm^2) and on the IOM dermal sampler 6.4 mg (0.19 mg/cm^2).

Figure 11 shows data for the prototype IOM dermal sampler for another series of tests where five different toluene mixtures were sprayed onto the samplers for a fixed period of time (10 minutes). Here it was expected that the mass detected on the sampler would decrease as the toluene concentration (percentage in the mixture) decreased, which is just what was found. For the 100% toluene the average mass collected was approximately 1.39 mg/cm^2. The corresponding figures for the 75%, 50%, 25% and 5% mixtures were 0.81, 0.69, 0.28 and 0.05 mg/cm^2.

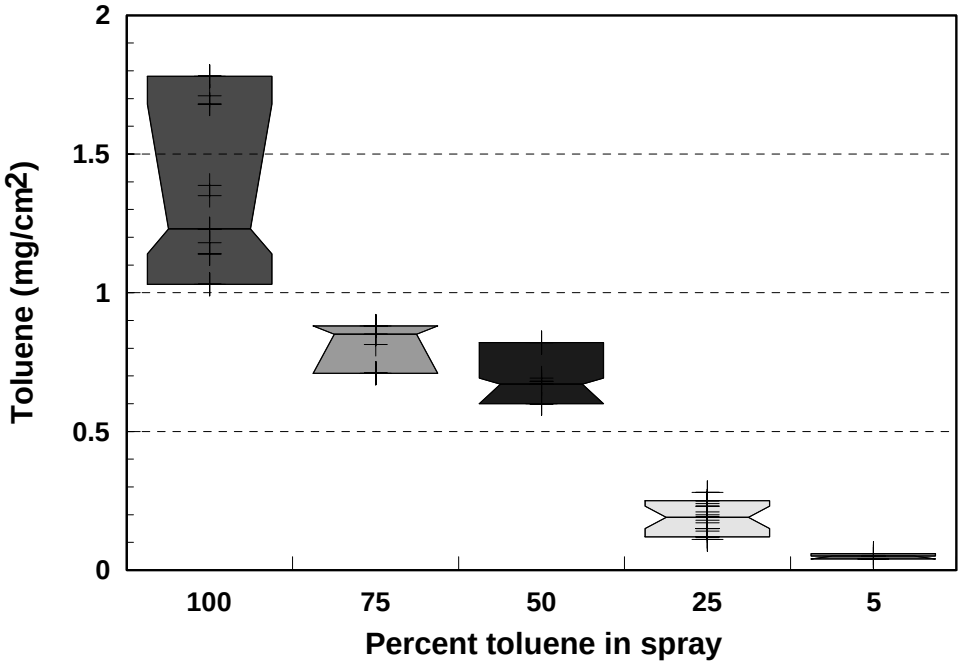


Figure 11 – Results of spray test, varying toluene concentrations over 10 minutes (prototype IOM dermal sampler only)

The data in the previous two figures is shown combined in Figure 12 but in this case expressed as an average uptake rate in mg/cm^2/hour. The average uptake rate for the pure toluene was 6.6 mg/cm^2/hr. This is about ten times lower than we measured during the evaluation of the membrane (Section 4.3) and we believe that this is because the spraying process does not fully or continuously cover the membrane surface with liquid toluene. Observation of the samplers during the testing suggested that the liquid landed on the sampler as fine droplets, which quickly evaporated.

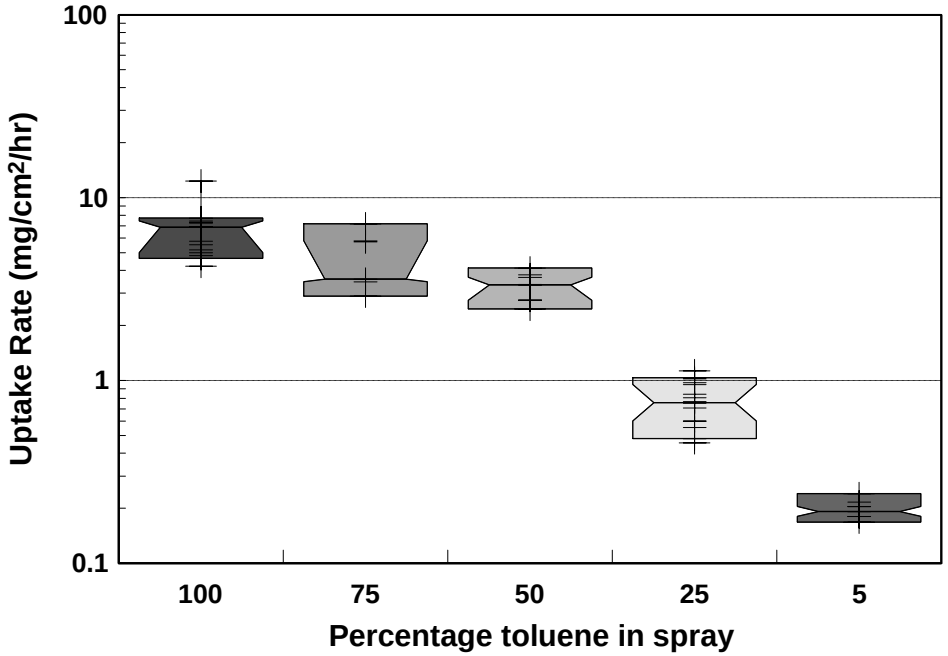


Figure 12 – Average uptake rate for the prototype IOM dermal sampler

The mean uptake rates for the other test mixtures were lower than for the pure toluene. For the 75% mixture the average uptake rate was 4.8 mg/cm^2/hr, for the 50% mixture the figure was 3.2 mg/cm^2/hr, for the 25% mixture it was 0.78 and for the 5% toluene mixture it was 0.19 mg/cm^2/hr. These data have been normalised to the pure toluene uptake rate in Table 6.

Table 6 - Comparison of uptake rates with that of pure toluene

% toluene in the mixture	100%	75%	50%	25%	5%
Average uptake rate normalised to pure toluene	1	0.72	0.49	0.12	0.03

The pattern of these uptake rates was in good agreement with that expected with the exception of the 25% mixture, where the average uptake rate was about half of what was expected.

5.3.2 Pour Test

The results from the pouring tests are summarised in Table 7. These data were for pure toluene and two toluene mixtures (50% and 25%). The duration of the tests were again adjusted so that the same mass of toluene was used in each case. For the ACC samples there are only two measurements contributing to each mixture (these correspond to the top and bottom of the box). In the case of the IOM prototype sampler there are eight measurements for each test condition.

Table 7 – Results from pour test, varying concentrations and times

		Mass per unit area (mg/cm^2)			
Toluene (%)	**Duration of Test (mins)**	**Number of tests**	**IOM dermal sampler (± 1SD)**	**Number of tests**	**ACC (± 1SD)**
25	10	8	2.2 (±) 0.34	2	3.1 (±) 0.48
50	5	8	2.9 (±) 0.16	2	4.7 (±) 0.49
100	2.5	8	3.0 (±) 0.44	2	5.5 (±) 0.43

Here the toluene mass per unit area ranged from 2.2 to 3.0 mg/cm^2 for the prototype IOM dermal sampler and from 3.1 to 5.5 mg/cm^2 for the ACC patches.

The difference between the two types of sampler was smaller than was observed with the spraying tests. Here we have some doubts about the reliability of the data for the pure toluene since we believe that the charcoal in the ACC and possibly the IOM dermal samplers are almost certainly saturated. Nevertheless, the general patterns are similar to those we have seen earlier; the IOM dermal sampler produces lower sampled masses and as the duration of the tests increased and the concentrations decreased, so too did the sampled mass of toluene, again possibly as a result of the increased ethanol load.

5.3.3 Immersion Test

Table 8 shows the results from the immersion tests: in each case there were two of each type of sampler tested. Here there were two very short term tests lasting 0.17 minutes (10 seconds) and a one hour immersion test in pure toluene. In the latter test we assume that both samplers were saturated.

Table 8 – Results from immersion tests

		Mass per unit area (mg/cm^2)			
Toluene (%)	**Duration of Test (mins)**	**Number of tests**	**IOM dermal sampler (± 1SD)**	**Number of tests**	**ACC (± 1SD)**
25	0.17 (10sec)	2	0.53 (±) 0.03	2	3.8 (±) 0.19
100	0.17 (10sec)	2	1.8 (±) 0.49	2	4.6 (±) 0.80
100	60	4	3.1 (±) 0.27	2	5.4 (±) 0.28

As before there are differences between the IOM and ACC samplers, with the IOM dermal sampler lower than the ACC samplers, and the lower concentration toluene mixtures producing lower mass uptake for both types of sampler when compared to pure toluene. Both the IOM dermal sampler and ACC are clearly saturated after immersion in the 100% toluene solution for 60 minutes and it appears that even a 10 second immersion in pure toluene may be close to saturation point.

5.3.4 Summary data

We have summarised the data presented in the preceding sections as estimated uptake rates (mg/cm^2/hour) in Figure 13. Each series of three box plots represents the data from spraying, pouring and immersion, respectively. The first block of results are for pure toluene, and then for 50% and 25% mixtures. Note the 60 minute immersion test has been excluded and there are no immersion measurements for the middle toluene mixture.

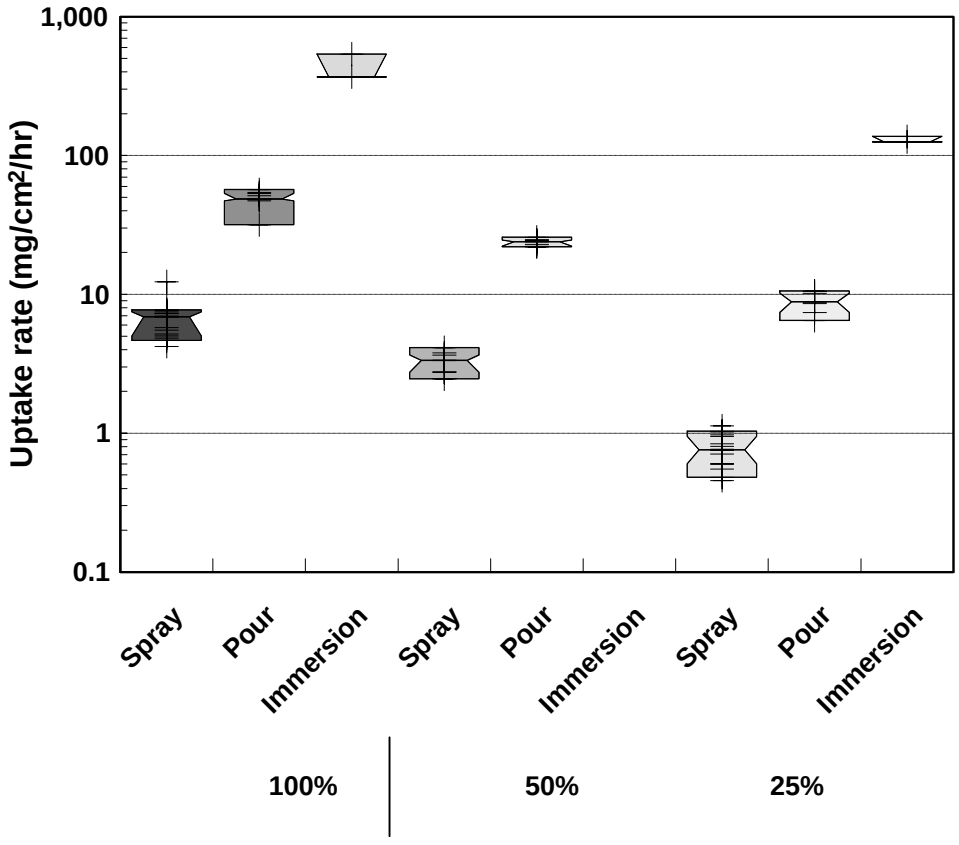


Figure 13 – Estimated uptake rates for the spray, pour and immersion tests

The mean uptake rates for pouring were 48, 24 and 8.9 mg/cm^2/hour, for the 100%, 50% and 25% toluene mixtures respectively. For the immersion tests they were 450 and 130 mg/cm^2/hour for the 100% and 25% toluene mixtures.

We have used the information from the tests with the prototype IOM dermal sampler to estimate the average concentration over the surface of the sampler during the test. Here we have assumed that there was steady state diffusion through the sampler membrane throughout each test and that the permeation rate for the membrane that we measured in the development work was applicable. Therefore the concentration on the sampler (C_{sk}) is given by:

$$C_{sk} = \frac{M_{IOM}}{k_{IOM}.A_{IOM}.t}$$

where M_{IOM} is the mass of toluene detected on the charcoal (mg),
k_{IOM} is the permeation rate (mg/cm^2/hr),
A_{IOM} is the sampling area of the prototype IOM dermal sampler (cm^2) and
t the sampling duration (hr).

C_{sk} is a dimensionless concentration, i.e. the ratio of mass of toluene to the mass of the mixture.

These data have then been compared with the toluene concentration in the bulk liquid in Figure 14.

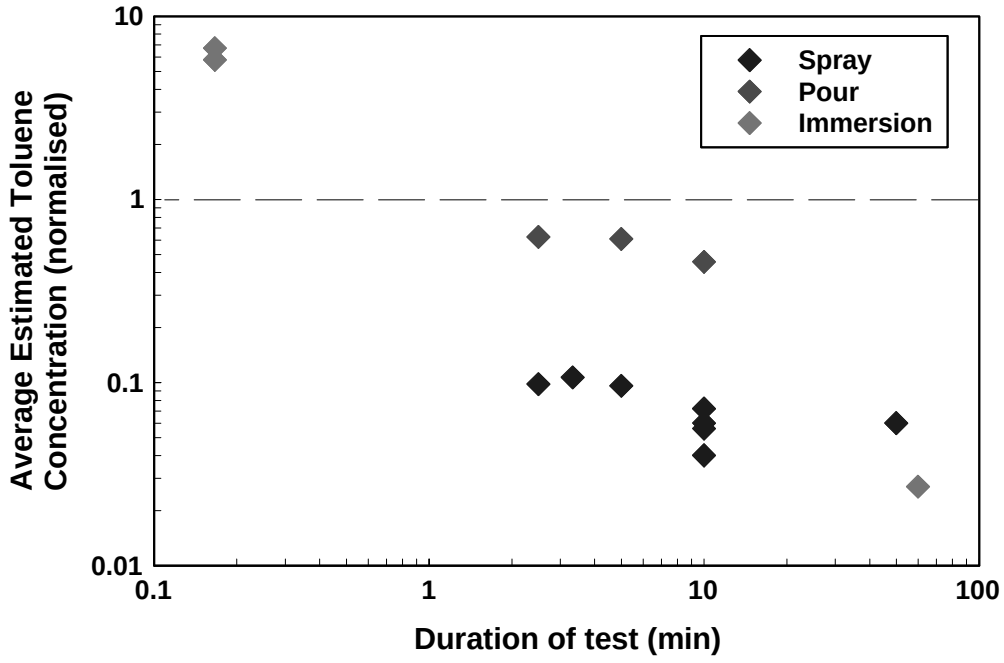


Figure 14 – Average estimated toluene concentration

The differences between test conditions are clearly apparent. We have already indicated that we believe the spray test did not uniformly or continuously cover the sampler membrane. Clearly the pouring test provides a greater coverage of the sampler surface with the test liquid. Here the ratio of the measured concentration to the toluene concentration in the bulk liquid is

closer to expected, although still somewhat lower (on average about one third of the bulk toluene concentration). On the short duration immersion tests the estimated toluene concentration was much higher than expected from the bulk liquid concentration and for the long-term sample it was much lower. In the latter case the adsorbent was clearly saturated and this is the explanation for this anomalous result. In the short duration samples we believe that it was unlikely that the actual duration of the test would properly reflect the time that toluene was permeating through the membrane, because after removal from the liquid there would still be some toluene in the membrane that would continue to diffuse towards the adsorbent. However, this would also occur with dermal exposure on the skin, suggesting that short-term exposure may lead to relatively more uptake than longer term exposure.

At the end of the laboratory tests of the prototype dermal sampler we concluded that:

- there was considerably less toluene present on the prototype IOM dermal sampler than on the ACC patches;
- the ACC was saturated in most cases;
- results from the IOM dermal sampler were reproducible;
- changing conditions give sensible, but certainly not prefect results and,
- with further development, we would consider this a great step forward for measuring dermal exposure to volatile substances.

It should be remembered that the purpose of the project was to develop a sampling device and method that could be used to measure the concentration of toluene on the skin. As a consequence the development of testing methods was necessarily short to enable preliminary experiments to be completed and ideas to be developed, the results reflect this.

5.4 FIELD TRIALS METHODS

Two sites were chosen for limited field trials; both were based in Lothian and were identified through IOM's industrial contacts. These sites are identified as Company A and Company B in this report. Both sites use significant volumes of toluene in quite different processes.

5.4.1 Company A - Rubber goods manufacturing

Company A manufacture a range of specialist printing blankets and rubber coated fabrics, including specialist blankets for use in the security printing industry. They are a small to medium sized enterprise, based in Edinburgh. The process comprised mixing of supplied rubber compound with toluene, spreading of this mixture onto cloth and then curing to form the final product.

The mixing room was located at the back of the factory, by the stores. The mixing machine was located adjacent to the warehouse door which remained open all day, providing general ventilation to the area. The mixing machine had one section of local exhaust ventilation which was located at the top of the mixing bucket, a curved face covering approximately one third of the circumference of the mixing drum. This was attached to a specific centrifugal fan which exhausted to the outside of the factory at roof height. This system was not part of a larger LEV system and was self contained, for use with the mixer. The employee wore jogging trousers and a T-shirt while working. There were no overalls, gloves or respirators used at any time during the shift. In the spreading hall there was a range of LEV extraction points on each spreading machine, each connected to a larger LEV system. Employees involved in spreading tasks wore overalls but did not wear any protective gloves.

Rubber compounds are purchased form a variety of manufacturers depending on specific production requirements. They are delivered in drums and these are emptied by hand into a large mixing drum (Figure 15) by the 'mixing' employee. The mixer is started and the worker

gradually adds neat toluene from a jug into the mixer (see Figure 16). Toluene is poured into the drum until the correct consistency of the mixture is obtained. Once the mixing process is complete, the compound is again removed by hand, from the mixing container back into a drum for the next stage of the process.

Figure 15 - Mixing Drum

Figure 16 - Adding neat toluene to mix

While the mixer was operating there were visible signs of toluene splashing out of the container in all directions. The quantity emitted was largely dependant on the speed of the mixing head. During sampling there were a number of splashes of rubber observed on the operator's arms and even one on the surface of the prototype IOM dermal sampler.

The mixed rubber compound is passed onto the production line. This is where the product backing, such as cotton cloth is fed into the spreading machine from a large roll. Employees lift large handfuls of the rubber compound and place it onto a roller at the start of the spreading line. They then spread the rubber along the length of the roller, again by hand. As the machine feeds the material through the rubber is pressed onto the cloth by a series of rollers, set to the desired thickness required for the finished product. The sheet then passes through a series of drying ovens to cure the rubber onto the material and the cloth is then rolled at the end of the production line, ready for use.

Figure 17 - Start of spreading line

Figure 18 - Spreader line rollers

Employees wore overalls but did not wear gloves. They regularly wash their hands in a bucket of soapy water.

Four employees were selected for sampling, the mixing employee and three 'spreaders'. They were each sampled for two hours in the morning and then this was repeated again in the afternoon with the same employees. Each employee wore a prototype IOM dermal sampler and an ACC sampler, side-by-side on both the forearm and the chest. Prototype samplers were attached to the forearm, using a Velcro strap and the chest using a safety pin. ACC patches were attached to the forearm using double sided adhesive tape and the chest using a safety pin, see Figure 19. The figure illustrates the positioning of the relative samplers on the

operator. Please note, the prototype IOM dermal sampler on the chest is partially obscuring the ACC patch sampler due to the position of the T-shirt and safety pin. The IOM dermal sampler was not fixed in position over the ACC sampler and moved as the operator and his clothing moved. It is unlikely that this partial obscuring prevented air movement over the ACC patch.

Figure 19 - Employee wearing sampling equipment (Mixer)

In addition to the dermal samplers each worker also wore a 3M diffusive vapour sampling badge to determine the airborne concentration of toluene. These samples were also worn on the chest within the breathing zone of the operator throughout the period of sampling. A number of fixed location vapour measurements were also taken at various points throughout the factory, also using 3M diffusive vapour badges.

5.4.2 Company B - Printing onto Metal Foils

Company B manufacture stamping foils for a wide range of uses. They produce coloured foils for use as security foils, security holograms, foil stamped packaging and many other applications. This large factory site in Lothian is part of a global organisation. Photographs were not permitted due to commercial sensitivity.

Toluene is used in both the pigment mixing process and in the coating process. In the pigment mixing process toluene is a constituent of the pigment. It is normally piped directly into mixing vats from a large bulk storage tank in the factory yard. However, it is often necessary for the employees to transfer small volumes of toluene up the mixing vats in small jugs and add them during the pigment production process. The main exposure of the mixing operator occurs during the dispensing of the final pigment into drums located below the mixing vat. These pigments are used to produce a wide range of coloured foils. There was also possible significant exposure from smaller mixing machines which were not fully enclosed, from jugging of neat toluene to the mixing vat or from dispensing of waste pigment into storage drums.

A large local exhaust ventilation system was installed in the mixing hall. This was connected directly to all mixing machines. As stated above, toluene is piped directly from bulk storage

into the mixing vats, eliminating a potentially large source of exposure, except where open jugs are required for topping up in the vats. Employees in this area wore disposable overalls (Tyvek) and nitrile gloves during their shift.

In the high speed gravure coating process, rolls of metal foil are fed into the machine and pass through a series of rollers. Toluene and pigment are fed into the machine at one end and the roll is coated. The foil passes through a series of drying ovens on top of the machine to evaporate the solvent and then into additional rollers at the opposite end of the gravure printing machine, where a backing material was applied. A small amount of exposure to toluene can be attributed to fugitive toluene emission on this line, but the main source of exposure occurs during the cleaning of rollers with solvent rags and the changing of drums of solvent used in the process. Apart from these tasks, employees spend the remainder of their time monitoring the machine, loading or unloading rolls of foil and product, and completing paperwork.

The gravure printing machine has a number of LEV extraction points connected directly to it to extract solvent vapour as it was generated. The employees on this line wore overalls during their shift. When they required to wash down the rollers or move solvent drums they wore nitrile gloves.

Four employees were selected for sampling in the morning shift and two in the afternoon. There were only two workers selected in the afternoon because less people were employed on these processes during the afternoon. During the morning shift, two pigment mixing staff and two coating line staff were selected. During the afternoon, one mixer and one coater were selected. Unlike Factory A, there were six individuals sampled. Each employee was sampled for two hours during each shift. They wore a prototype IOM dermal sampler and ACC sampler side-by-side on their forearm and chest. IOM dermal samplers were attached to the forearm using a Velcro strap and onto the chest using a safety pin. ACC samplers were attached to the forearm using double sided adhesive tape and on the chest using a safety pin.

In addition, they also wore a 3M diffusive vapour sampling badge to assess the airborne concentration of toluene. A number of fixed location measurements were taken at various points throughout the factory, also using 3M badges.

5.5 RESULTS FROM THE FIELD TRIALS

5.5.1 Company A - Rubber goods manufacturing

Three spreaders and one mixer were sampled at company A.

The results from the inhalation exposure measurements are shown in Table 9. Note these measurements were made over time periods relevant to the dermal exposure measurements and so do not represent 8-hour time-weighted average exposures.

Table 9 - Toluene inhalation exposure levels from factory A

Spreading employees were exposed to toluene by handling freshly mixed rubber compound. As they did not wear gloves their dermal exposure was likely to be very high, coupled with their inhalation exposure as toluene vapour was released from the compound during handling. Once the compound was spread on the machine, exposure was greatly reduced as the extraction on the machine removed most vapour. The odour of toluene was present throughout the spreading hall and this is reflected by the ambient air concentration measured on the spreading employees and the static points. The situation in the mixing hall was very different; there was an exceptionally strong odour of toluene in the area and splashes of toluene liquid could clearly be seen spraying out of the mixing drum into the surrounding area and onto the mixing employee. In addition, once a batch of rubber was finished, this was removed to another drum. To do this, the mixer removed the mixed rubber compound by hand and when nearing the bottom of the drum he would lean his whole upper torso right into the drum to scrape the bottom and sides. Clearly there will be significant dermal exposure as the product was moved by hand (without gloves). Additionally, toluene vapour released from the compound and residual vapour in the drum may have contributed to the high inhalation dose reported in Table 9.

The personal toluene exposure measurements from the operators ranged from 78 to 230 mg/m^3, or 21 to 60 ppm. The highest two measurements were obtained from Worker 1 and the lowest two measurements form Worker 2. The exposure of the mixer was much greater than the spreader operators, with both measurements around 4400 mg/m^3 (1200 ppm). It is likely that the 3M badges were saturated with a combination of high vapour concentrations and as a result of toluene splashing onto the surface of the badge from the mixing drum adding to the overall exposure. The static samples varied from 52 to 205 mg/m^3, or 14 to 54 ppm.

By using data obtained from section 4.5.2 (Determination of vapour uptake by the prototype IOM dermal sampler) and data from the personal inhalation exposure measurement, we estimated the mass of toluene that would have been sampled by both the prototype IOM dermal and ACC samplers. These ranged from 0.3 to 17 mg of toluene for the IOM dermal sampler and from 3.1 to 180 mg for the ACC samplers. In both cases the highest figures were for the mixer. These data suggest that for the mixer operator the ACC cloth, and possibly the prototype IOM dermal sampler, would be saturated by vapour uptake alone and we have therefore not included data for this worker in the subsequent data presentations. On average vapour contributed 9.6% of the toluene mass on the IOM dermal sampler and 23% of the mass on the ACC samplers.

Table 10 shows the results from the dermal samplers adjusted for uptake from toluene vapour in the air. All employees were spreading operators.

Table 10 - Dermal exposure measurements for toluene in Factory A, adjusted for vapour uptake

			Toluene (mg/cm^2)			
Worker	**Task**	**Shift**	**IOM dermal sampler Forearm**	**ACC Forearm**	**IOM dermal sampler Chest**	**ACC Chest**
1	Spreader	AM	0.65	2.1	0.30	1.2
		PM	0.32	1.2	0.13	0.79
2	Spreader	AM	0.91	1.8	0.11	0.61
		PM	0.58	1.1	0.11	0.66
3	Spreader	AM	0.35	1.1	0.21	1.6
		PM	0.67	0.79	0.14	0.94

The measurements for the samplers on the workers' chest were generally lower than corresponding data from the forearm. The maximum mass density on the IOM prototype dermal sampler in the forearm was 0.91 mg/cm^2 and the highest from the chest sample location was 0.30 mg/cm^2. The average mass for the chest was 0.17 mg/cm^2 and the corresponding figure for the forearm was 0.58 mg/cm^2. The measurements made with the ACC were higher than the corresponding IOM prototype dermal sampler data. The average mass of toluene per unit area collected in the chest was 1.3 mg/cm^2 and on the chest 0.97 mg/cm^2.

5.5.2 Company B - Printing onto Metal Foils

The results from the inhalation exposure measurements are shown in Table 11.

The engineering controls for tasks in Company B were very good; this is reflected by the results in Table 10. The mixer, as expected, had the highest exposure as this job involved more direct exposure to toluene in pigment mixes. Employees on the coating line were only directly exposed during cleaning of the rollers and this was infrequent. LEV on the coating machine removed nearly all toluene vapour during the production process.

Six personal exposure measurements were made, three on mixing operators and three on coating operators. The measured toluene levels for mixers ranged from 27 to 140 mg/m^3, (7.2 to 37 ppm). The corresponding range for the coating operators was lower, i.e. from 2.6 to 32 mg/m^3, (0.7 to 8.4 ppm). The static concentrations in the work area were comparable to those measured on the coating workers (6.8 to 33 mg/m^3), although these were measured over a longer period.

Table 11 - Toluene Inhalation Exposure Measurements in Factory B

Sample Description	AM or PM	Sampling Time (mins)	Toluene Inhalation Exposure Level	
			mg/m^3	ppm
Worker 1 - Mixing	AM	120	140	37
Worker 2 - Mixing	AM	120	59	16
Worker 3 - Coating	AM	120	32	8.4
Worker 4 - Coating	AM	120	14	3.6
Worker 5 - Mixing	AM	120	27	7.2
Worker 6 - Coating	AM/PM	208	2.6	0.7
Static - at entrance to mixing room	AM/PM	300	15	3.9
Static - by pigment mix tanks	AM/PM	300	32	8.4
Static - Coaing line, at coating end	AM/PM	295	33	8.6
Static - Coating line by operator workstation	AM/PM	295	6.8	1.8

The dermal exposure measurement data from Factory B are shown in Table 12, again adjusted for vapour uptake.

Table 12 - Dermal toluene exposure measurements for Factory B, adjusted for vapour uptake

			Toluene (mg/cm^2)			
Worker	Task	Shift	IOM dermal sampler Forearm	ACC Forearm	IOM dermal sampler Chest	ACC Chest
1	Mixing	AM	0.24	0.63	0.06	0.02
2	Mixing	AM	0.09	0.42	0.05	0.20
3	Coating	AM	0.04	0.22	0.04	0.18
4	Coating	AM	0.03	0.10	0.01	0.07
5	Mixing	PM	0.05	0.35	0.04	0.17
6	Coating	PM	0.005	0.03	0	0

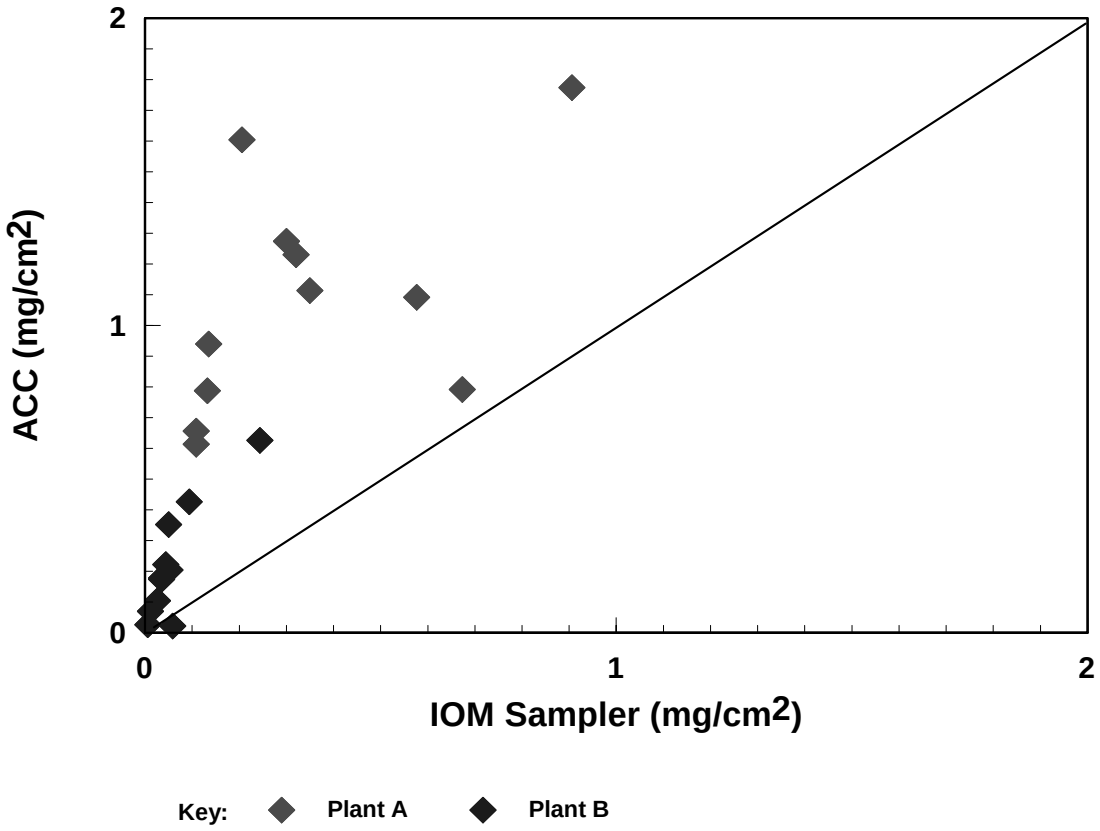
The dermal toluene exposures measured with the prototype IOM dermal sampler were lower than seen in Factory A, which reflects the much lower level of contact with toluene containing mixtures. For the mixer operators the IOM dermal sampler measurements from the chest ranged from 0.04 to 0.06 mg/cm^2, with an average 0.05 mg/cm^2. The corresponding values for the forearm were 0.05 to 0.24 mg/cm^2, average 0.13 mg/cm^2. For coating operators the chest samples ranged from zero to 0.04 mg/cm^2, average 0.02 mg/cm^2; and for the forearm from 0.005 to 0.04 mg/cm^2, average 0.03 mg/cm^2. These lower exposures for coating operators are explicable by the lower level of contact with toluene for these workers compared with mixing operators.

As before the data from the ACC samplers were higher, although there were still differences between the chest and forearm. The chest the ACC measurements ranged from zero to 0.20 mg/cm^2, average 0.10 mg/cm^2. On the forearm the results ranged from 0.03 to 0.63 mg/cm^2, average 0.29 mg/cm^2.

5.5.3 Comparison of the data from both surveys

Figure 20 shows the toluene dermal exposure measurements form both factories, with the diagonal showing the line of equality. The red points are from Factory A and the blue from Factory B. As we saw earlier the measurements at the second plant were generally lower than the data from the first factory.

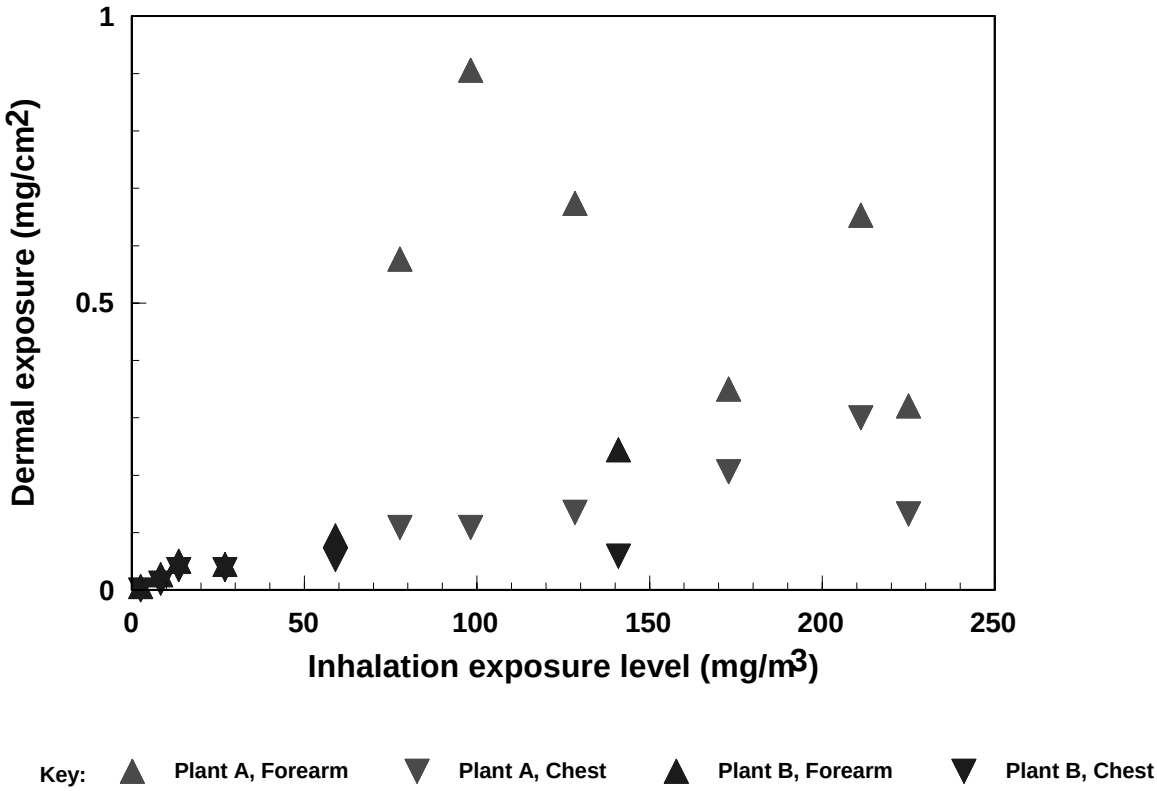
Figure 20 - Comparison of measurements from the prototype IOM dermal sampler with the ACC samplers



This scatter plot confirms that the ACC measurements were generally higher than the corresponding IOM dermal sampler. There is also a reasonable correlation between the two types of measurement (correlation coefficient = 0.8), suggesting that both samplers are responding to the contact the operators made with toluene.

Figure 21 shows a scatter plot of the inhalation exposure levels and dermal exposures measured using the prototype IOM dermal sampler. For each inhalation exposure measurement there are two dermal data points, one for the chest and a second for the forearm. The key for the symbols used in the figure is shown below the plot.

Figure 21 - Scatter plot of inhalation and dermal exposure measurements



NOTE – the symbols which appear to be stars are triangles representing Plant B Forearm and Chest, which are positioned on top of one another.

From the graph there appears to be little indication of any association between these two sets of data. However, the correlation coefficient between the inhalation exposure level and the IOM chest samples was 0.83 and for the forearm samples it was 0.56. The main reason for the lower correlation coefficient for the forearm samples was the negative correlation between the forearm measurements and inhalation exposure level for Plant A (r = -0.5).

6. DISCUSSION

6.1 DEVELOPMENT OF THE PROTOTYPE SAMPLER

The main purpose of the project was to provide a practical demonstration of the previously developed design concept for a dermal sampler for volatile substances (Cherrie and Robertson, 1995). The original concept was to measure concentration of volatile materials on the skin, by developing a simple diffusion sampler incorporating an adsorbent and diffusion membrane. Having chosen to use toluene as the volatile substance for this work the selection of adsorbent and backing material was relatively straightforward. Our main difficulty has been sourcing a suitable diffusion membrane for the sampler.

During the development phase we tested 29 different membranes to evaluate their suitability. Their performance fell into three broad categories; either the membrane was impermeable, was highly permeable or was apparently not chemically stable when exposed to toluene. We had already decided that the most appropriate selection criterion for the diffusion membrane was that it should have permeability to toluene that was similar to human skin. This presented us with some difficulty since the available *in vitro* and *in vivo* research literature provides a mixed picture of the rate of uptake of toluene through skin depending on exactly how the investigations were carried out. Some studies were carried out *in vitro* with excised human skin while others were carried out *in vivo* on human subjects. There are substantial differences between the results reported both between methods and within either group of methods. We have assumed that the latter experiments provide a more reliable indicator of uptake through the skin and we believe that the target uptake rate for the sampler should be approximately 1,200 $\mu g/cm^2$/hr. However, none of the candidate membranes had such a low permeation rate; the closest was about 65 times greater than this value. For the practical purposes of the study, it was necessary to use this membrane to test the principle of the sampler, both in the laboratory and in a limited field trial. However, it would be desirable to use a less permeable membrane in further developments of this dermal sampling method. We believe this is technically possible through discussion with the manufacturers of these membranes.

6.2 OVERVIEW OF PERFORMANCE

We have shown that it is possible to produce a practical sampler with a simple construction. We have demonstrated that the sealing is sufficient to exclude leakage into the sampler that might contaminate the adsorbent. In addition, the construction is sufficiently robust to be used in the field without any difficulty. The results obtained with the IOM dermal sampler were reproducible in laboratory trials and followed logical patterns.

Throughout the tests on the prototype dermal sampler we have used activated charcoal cloth (ACC) samplers for comparison, similar to those proposed by Cohen and Popendorf (1989). However it proved difficult to compare results systematically with ACC dermal patch samplers as these became very rapidly saturated. However, where comparisons were possible i.e. when the ACC was not saturated, the IOM dermal sampler collected much less toluene and there was broad correlation between the masses collected by the two techniques ($r=0.8$). Our experience with saturation of the ACC samplers suggested that the ACC patch sampler was not a practicable solution for measuring dermal exposure to volatile organic compounds in an industrial setting.

The compromise we had to make with the membrane selection meant that saturation of the adsorbent also occasionally occurred with the prototype IOM dermal sampler, albeit to a much lesser extent. Saturation limited the range of tests that we were able to successfully undertake. The need to match the properties of the membrane with those of skin is particularly

important. All reported techniques for measuring dermal exposure to volatile chemicals will also act as diffusive samplers for vapours. The ratio of vapour uptake to liquid uptake should be the same for samplers and skin. We do not know whether this is the case for the sampler tested. We therefore simultaneously measured toluene vapour concentration using a conventional vapour diffusion sampler during the field trials so that we could correct the dermal measurements for vapour uptake by the dermal samplers. In the field trials the vapour component was typically about 10 to 20% of the total mass of toluene sampled. We believe that if we were able to identify a more suitable membrane for the sampler, i.e. with uptake properties for vapour and liquid similar to those of skin, it would not be necessary to correct for vapour uptake since the sampler would take up toluene vapour similarly to skin.

In the laboratory spray tests we saw that the relative uptake rate for mixtures of toluene compared with pure toluene was similar to that expected, i.e. reducing the concentration of toluene in the mixture resulted in corresponding decreases in uptake rate. These data suggest that the sampler is responding to the concentration rather than the mass of toluene, as expected. This is supported from the data where we sprayed decreasing concentrations of toluene for longer times and obtained broadly comparable masses of toluene sampled. There is a suggestion of lower total uptake for the longest lowest concentration tests, which may be due to the limited capacity of the charcoal adsorbent. However, overall we believe that the sampler responds as expected.

When we used the spray test measurements to estimate the concentration of the mixture we obtained values much lower than expected (between about 0.05 and 0.1 times the toluene concentration in the bulk liquid). We believe that this was because the whole surface of the sampler was not continually covered with liquid toluene, which was supported by the observations made during the tests. This led us to devise the pouring tests where we were confident that a much greater part of the sampler surface would be covered by toluene. This proved to be the case and we obtained estimates of the concentration of the mixture used in the tests that were much closer to those used (0.5 to 0.6 of the bulk liquid). It is possible that the test conditions still did not result in the whole of the sampler being covered or, more likely, this very harsh test saturated or came close to saturating the absorbent in the IOM dermal sampler.

The data from the short duration immersion tests were also intended to explore the issue of surface coverage but these were also complicated by saturation of both the ACC sampler and the IOM dermal sampler. The relatively permeable membrane meant that we had to use a very short duration test and even then we are uncertain whether the results are free from any bias because of the adsorbent becoming saturated. In addition, the transient effects of such a short test, i.e. the likely continued sampling after the sampler was removed from the liquid because of reservoir effects and some residual liquid on the surface of the sampler, make these data even more difficult to interpret reliably. Note that the ACC sampler was undoubtedly saturated after only a few seconds immersion and that it, and similar surrogate skin techniques, are unsuitable for measuring dermal exposure to liquids where immersion is likely.

In the field study we found that there was an association between the inhalation exposure level and dermal exposure to toluene measured with the IOM prototype sampler. This in part reflected the considerable difference between the two plants studied, with plant A having much poorer control measures than plant B. The correlation was greater for the chest samples than for the forearm samples, which probably reflects the relative contributions of direct contact with contaminated materials to these two sampling locations. In some ways these results are encouraging since it may reflect a general linkage between inhalation and dermal exposures. Schneider *et al* (1999) proposed a conceptual model of dermal exposure that highlights the possible routes of dermal exposure, e.g. source to surfaces to skin, source to air to skin etc. This model clearly shows the interconnected nature of exposure with the air

compartment of the model being somewhat central to many of the routes of exposure. For example, liquids that splash out of sources may land on surrounding surfaces or the skin of the worker, in both cases possibly contributing to dermal exposure. If these liquids are volatile then the splash will evaporate and so add to the concentration in the air compartment. Vermeulen *et al* (2000) looked at this interconnection for rubber fume and showed that there is often moderate correlation between inhalation exposure and dermal exposure.

There has been very little research into the relative sampling efficiency of the skin and of surrogate skin samplers, whether patches or whole body samplers. Many different materials have been used in surrogate skin samplers. Soutar *et al* (2000) listed cotton, cotton polyester, gauze, polyurethane foam, filter paper and charcoal cloth. There are very broad ranges of properties in each of these categories of material. The selection criteria for collection materials have, in the past, been based almost solely on analytical requirements (sample recovery, sample stability and sample blanks being the most important). The only requirement for sampling has been to ensure that the sampler is absorbent. For example, OECD (1997) in their standard method state that the absorbent for dermal sampling of liquids should be "…absorbent enough to retain all liquid residues…". The conceptual model of dermal exposure (Schneider *et al*, 1999) makes it clear that there are complex paths of deposition and transfer of chemicals both to and from the skin. Patch samplers have, up to now, only taken account of deposition and transfer to the skin. Absorbent materials have been selected not to mimic transfer from the skin.

The other major problem in terms of sampling is that there are no criteria for defining the efficiency of the transfer on to the skin. All the materials mentioned above will collect different amounts from, for example, splashing, immersion or contact with contaminated surfaces. Dislodgeable residue is a well-established concept in relation to surface contamination. However, it is likely that the sorts of materials used in patch samplers, glove samplers and whole body samplers will be more efficient collectors than skin. What is not dislodgeable from skin contact, therefore, may or may not be dislodgeable from contact with a cotton patch sampler or a ACC patch sampler.

The sampling concept we have used and demonstrated in this study offers a real opportunity of developing a dermal exposure sampler that will mimic the sampling and transfer properties of the skin in relation to volatile organic compounds. Further development of the concept would therefore provide an excellent opportunity to place dermal exposure sampling on a firmer scientific footing. It will enable the sampling to reflect the properties of skin and it will measure the appropriate metric to assess health risks from either uptake or local effects on the skin.

6.3 THE FUTURE OF THE PROTOTYPE IOM DERMAL SAMPLER

The IOM dermal sampler is the first practical dermal exposure sampler to allow both deposition and transfer to and from its surface. The sampler gives sensible, reproducible results in the laboratory and field trials. These results indicate that the principle does work, further development will improve on this and there is also evidence to prove the concentration effects on adsorption.

The combination of the membrane and activated charcoal cloth meant that the sampler was too permeable, coupled with a low capacity. This resulted in the adsorbent becoming easily saturated during testing.

Any future research will require further development of the membrane material to ensure that it is much less permeable than the current material and closer in collection characteristics to skin. Alternatively, a thicker membrane could be used. Possible routes forward include

development of a membrane with collection efficiencies for a range of materials closer those of skin or even developing a custom-built biological membrane.

In addition, a higher capacity activated carbon cloth may be required. A number of varying density cloths are available in a range of forms, these can be investigated.

7. ACKNOWLEDGEMENTS

We are grateful to help and advice we have received from many different organisations. In particular we would like to thank:

Roy Picken from GTS Flexible Materials, UK.
Dr. Joseph Adiletta from Pall flex/Pall Corporation, USA.
Dr. Alun Fowler, formerly with Pall Corporation, USA.
Manfred Vogel from Pall Corporation, Germany.
Gary Lynch from Maceplast.
Tsugoyoshi Taira from Gunz Medical Materials Centre, Kyoto, Japan.
Karl Moss from Thermo Onix, UK.
Gery Allan at Company B, UK.
Douglas Main at Company A, UK.
Chemviron Carbon, UK.

We would also like to acknowledge the work of our colleagues at the Institute of Occupational Medicine who helped with advice or who commented on the report. Mike Beveridge from IOM helped construct the test rig and Craig Lewis, Carolyn McGonagle and Andrina Cunningham undertook the chemical analysis.

We are grateful to Laura Gordon for devising a way to secure the sampler to forearm with the foil in contact with skin.

Finally, we are very grateful to the Health and Safety Executive for funding this research project.

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APPENDIX 1: Membrane materials selected for testing

Manufacturer	Material	Pore Size (µm) and Form	Basic Composition
Amari	PTFE	500 µm Sheet	Polytetrafluoroethylene
DuPont	Tefzel 1000LZ	250 µm Film	Polytetrafluoroethylene
DuPont	Tefzel 500LZ	125 µm Film	Polytetrafluoroethylene
DuPont	Teflon FEP 500A	125 µm Film	Polytetrafluoroethylene
DuPont	Teflon FEP 50A	12.5 µm Film	Polytetrafluoroethylene
Fluorocarbon Company	PFTE	100 µm Film	Polytetrafluoroethylene
Fluorocarbon Company	PTFE	500 µm Sheet	Polytetrafluoroethylene
Gunz	Pelnac	Bilayer	Collagen sponge base, silicon top layer
ICI	Melinex 505	125 µm Film	Polyethylene terephthalate
ICI	Melinex ST505 100um	125 µm Film	Polyethylene terephthalate
Maceplast	PTFE	125 µm Sheet	Polytetrafluoroethylene
Pall	Biodyne®	0.45	Nylon 6,6
Pall	Biodyne®	5.0	Nylon 6,6
Pall	Emflon®	0.02	ePTFE supported with non-woven polyester
Pall	Emflon®	0.2	ePTFE supported with non-woven polyester
Pall	Emflon®	0.45	ePTFE supported with non-woven polyester
Pall	Pallflex® 40	-	Hemp fibre base with glass fibre matrix, EVA binder & hydrophobic/olephobic fluoropolymer formulation
Pall	Pallflex® 8E	-	Manila cellulose paper with glass fibre matrix, VA latex binder & Fluorochemical oil
Pall	TS6	-	Randomly distributed glass microfibres reinforced with woven glass fabric. Saturated with PTFE and silicon formulation.
Pall	TV2	-	Randomly distributed glass microfibres reinforced with woven glass fabric. Saturated with PTFE and silicon formulation.
Pall	TX4	-	PTFE, glass microfibre & fine glass cloth
Pall	Versapor® 1200	1.2	Modified acrylic copolymer cast on non-woven nylon support.
Pall	Versapor® R 1200	1.2	Modified acrylic copolymer cast on non-woven nylon support. Treated with FluoRepel for hydrophobic/Olephobic surface properties
Pall	Pallflex® AO1603	Submicron (<0.1µ)	Unique composition of solvent compatible aramid fibres with EVCL-PVA thermoplastic proprietary binder. Organophobic, flexible membrane with good vapour transmission property
Pall	Pallflex® RO1569J	-	Development Material – not specified
Pall	Pallflex® PO1618	-	Development Material – not specified
Pall	Pallflex® KO1601K	-	Development Material – not specified
Safeskin	Purple Nitrile Glove	-	Purple Nitrile
Whatman	Anodisc	0.02	Aluminium Oxide

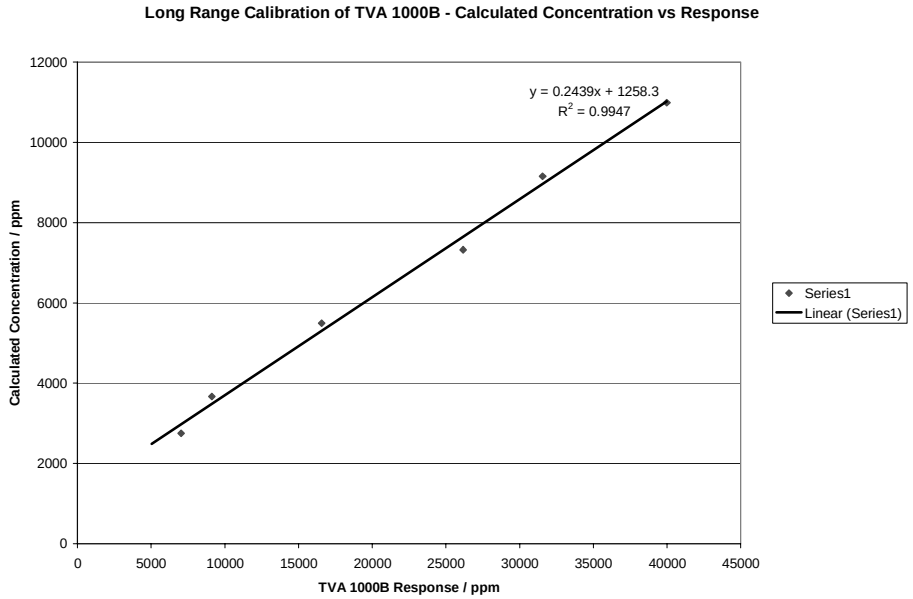
Biodyne, Emflon, Pallflex, and Versapor are trademarks of Pall Corporation. ® indicates a trademark registered in the USA.

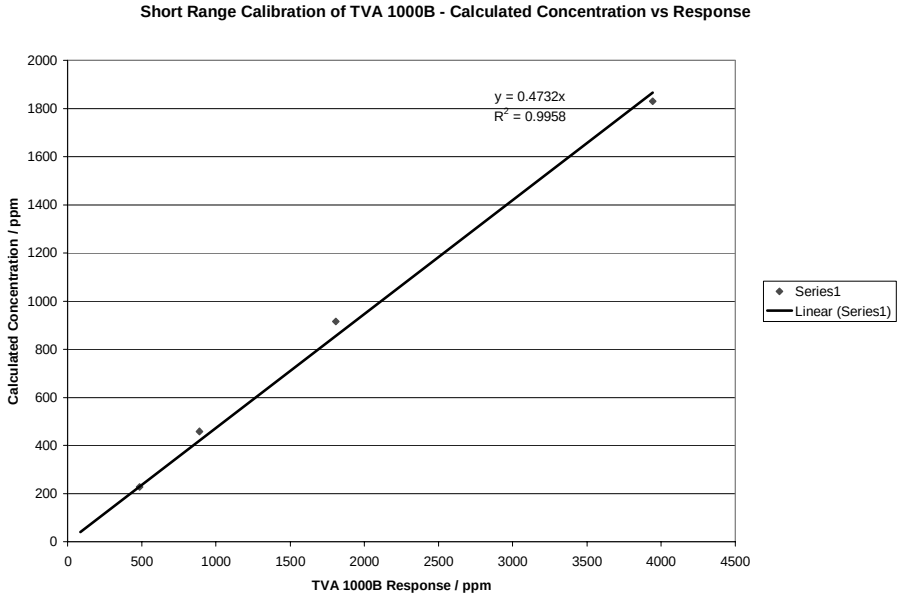
N.B – Those materials marked as ‘film’ were very thin, less than 500µm. Those marked “sheet” were generally greater than 500µm.

APPENDIX 2: CALIBRATION DATA

TVA 1000B Calibration Data

Tedlar Bag Number		**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Volume of Toluene Added (ul)		5	10	20	40	60	80	120	160	200	240
Calculated Concentration		228	458	920	1830	2750	3670	5490	7320	9150	11000
Response (Max value)	*Run 1*	502	877	1830	4200	6900	9960	17500	28700	33500	41100
	Run 2	448	840	1680	3690	7520	8400	16600	27300	29600	39000
	Run 3	504	944	1910	3940	6700	8980	15700	22500	31500	39700
	Mean	**485**	**887**	**1808**	**3943**	**7040**	**9110**	**16571**	**26200**	**31500**	**40000**
	St Devn	**32.00**	**53.1**	**116.0**	**252.0**	**429.0**	**787.0**	**903.0**	**3270.0**	**1950.0**	**1020.0**





APPENDIX 3 - Results of Permeation Tests

		Mean Toluene Conc. At Steady State				Permeation Rate ($mg.cm^{-2}.hr^{-1}$)				
MATERIAL/MEMBRANE	**Pore Size (µm)**	**1st Run**	**2nd Run**	**3rd Run**	**4th Run**	**1st Run**	**2nd Run**	**3rd Run**	**4th Run**	**Mean**
Amari - 0.5mm PTFE	n/a	NO PERMEATION DETECTABLE				0	0	0	0	0
DuPont - Tefzel 1000LZ	n/a	NO PERMEATION DETECTABLE				0	0	0	0	0
DuPont - Tefzel 500LZ	n/a	NO PERMEATION DETECTABLE				0	0	0	0	0
Fluorocarbon Company - 0.1mm PTFE	n/a	NO PERMEATION DETECTABLE				0	0	0	0	0
Fluorocarbon Company - 0.5mm PTFE	n/a	NO PERMEATION DETECTABLE				0	0	0	0	0
Maceplast - PTFE film	n/a	NO PERMEATION DETECTABLE				0	0	0	0	0
ICI - Melinex 505	n/a	NO PERMEATION DETECTABLE				0	0	0	0	0
ICI - Melinex ST505 100um	n/a	NO PERMEATION DETECTABLE				0	0	0	0	0
Safeskin - Purple Nitrile Glove	n/a	NO PERMEATION DETECTABLE				0	0	0	0	0
DuPont - Teflon FEP 500A	n/a	NO PERMEATION DETECTABLE				0	0	0	0	0
DuPont Teflon FEP A 50 Guage (12.5um)	n/a	NO PERMEATION DETECTABLE				0	0	0	0	0
Whatman - Anodisc	0.02	NO STEADY STATE				0	0	0	0	0
Pall - Biodyne	0.45	38.0	34.7	35.9	37.1	604	551	570	590	579
Pall - Biodyne	5.00	31.4	33.4	31.3	31.1	499	530	497	494	505
Pall - Emflon	0.02	39.1	39.5	37.3	35.3	621	628	592	561	601
Pall - Emflon	0.20	40.1	34.0	34.3	34.5	636	541	544	548	567
Pall - Emflon	0.45	38.0	37.0	37.7	37.0	604	587	599	588	595
Pall - Pallflex 40	n/a	9.4	9.0	8.7	9.0	151	143	137	143	144
Pall - Pallflex 8E	n/a	11.5	10.4	10.6	10.6	182	166	168	168	171
Gunz - Pelnac	n/a	UNSTABLE, DEGRADES				0	0	0	0	0
Pall - TS6	n/a	36.3	35.8	35.5	35.8	576	568	565	568	569
Pall - TV2	n/a	UNSTABLE, NO STEADY STATE				0	0	0	0	0
Pall - TX4	n/a	42.2	37.0	36.9	35.6	670	587	586	566	602
Pall - Versapor 1200	1.20	34.0	36.5	38.3	42.2	540	581	609	671	600
Pall - Versapor R 1200	1.20	10.6	12.7	10.4	11.0	169	201	166	175	178
Pall - Pallflex AO1603	n/a	5.0	4.3	5.1	5.3	79	68	81	85	78
Pall - Pallflex RO1569J (both sides)	n/a	NO STEADY STATE				0	0	0	0	0
Pall - Pallflex PO1618 (both sides)	n/a	NO STEADY STATE				0	0	0	0	0
Pall - Pallflex KO1601K (both sides)	n/a	NO STEADY STATE				0	0	0	0	0

n/a – Not Applicable

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C1.25 06/03

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ISBN 0-7176-2223-1