



Permeation Tests of Glove and Clothing Materials Against Sensitizing Chemicals Using Diphenylmethane Diisocyanate as an Example

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ABSTRACT

Diphenylmethane diisocyanate (MDI) is a sensitizing chemical that can cause allergic contact dermatitis and asthma. Protective gloves and clothing are necessary to prevent skin exposure. Breakthrough times are used for the selection of chemical protective gloves and clothing. In the EN 374-3:2003 European standard, breakthrough time is defined as the time in which the permeation reaches the rate of $1.0 \mu\text{g min}^{-1} \text{cm}^{-2}$ through the material. Such breakthrough times do not necessarily represent safe limits for sensitizing chemicals. We studied the permeation of 4,4'-MDI through eight glove materials and one clothing material. The test method was derived from the EN 374-3 and ASTM F 739 standards. All measured permeation rates were below $0.1 \mu\text{g min}^{-1} \text{cm}^{-2}$, and thus, the breakthrough times for all the tested materials were over 480 min, when the definitions of EN 374-3 and ASTM F 739 for the breakthrough time were used. Based on the sensitizing capacity of MDI, we concluded that a cumulative permeation of $1.0 \mu\text{g cm}^{-2}$ should be used as the end point of the breakthrough time determination for materials used for protection against direct contact with MDI. Using this criterion for the breakthrough time, seven tested materials were permeated in <480 min (range: 23–406 min). Affordable chemical protective glove materials that had a breakthrough time of over 75 min were natural rubber, thick polyvinylchloride, neoprene-natural rubber, and thin and thick nitrile rubber. We suggest that the current definitions of breakthrough times in the standard requirements for protective materials should be critically evaluated as regards MDI and other sensitizing chemicals, or chemicals highly toxic via the skin.

KEYWORDS: breakthrough time; clothing; dermal exposure; gloves; isocyanates; MDI; permeability; permeation; PPE; sensitizers

INTRODUCTION

Isocyanates are known worldwide as respiratory and skin sensitizers, which cause occupational allergic contact dermatitis and asthma in particular. The most

used isocyanates are diphenylmethane diisocyanate (MDI), toluene diisocyanate (TDI), and hexamethylene diisocyanate (HDI), and their variants and prepolymers. MDI is often used as a mixture of its

monomeric isomers, 2,4' and 4,4'-MDI, and higher molar mass oligomers of MDI. The mixture is called polymeric MDI (PMDI). It is used extensively to produce polyurethane foams, adhesives, and coatings. In construction, PMDI is used in, for example, the thermal insulation of windows, the coating of roofs or floors, and sewer relining. In the boat industry, PMDI is needed in adhesion and flotation applications. Fully cured, finished products are usually regarded as safe. Workers are at risk of sensitization when they handle uncured PMDI during manual mixing of polyurethane components or the application of foams, adhesives, or coatings. The non-occupational, extensive use of MDI polyurethane foam in construction and renovation has raised concerns regarding consumer health (REACH amendment, 2009; EPA, 2011).

Prohibiting skin contact is essential in the prevention of isocyanate-induced allergic contact dermatitis. Skin protection against isocyanates may also play a role in the prevention of asthma (Bello *et al.*, 2007; Redlich, 2010). For successful skin protection, instructions, regulations, and motivation are needed, and efficient, comfortable personal protective equipment (PPE) is essential.

Protection provided by chemical protective gloves or clothing is studied by measuring the permeability of the chemical through the materials, and clothing seams and closures. We were unable to identify any reports of MDI permeation studies with a clear method description. Currently, permeation testing is carried out by commercial, accredited testing laboratories, and in accordance with PPE standards (EN 374-3, 2003; ASTM F 739, 2012). The test results can be found in PPE packaging, and if the chemical list is long, it can be obtained from the retailer or on the Internet. A compendium of all found permeation test data has been published by Forsberg and Mansdorf (2007). According to this, butyl rubber (BR), Viton, Silver Shield/4H, and some of the Dupont's Tychem range clothing are effective protective materials against 4,4'-MDI, as they all have a breakthrough time of over 480 min for 4,4'-MDI. The compendium has no MDI permeation information regarding other materials or PMDI. According to the German database GESTIS, breakthrough times of 4,4'-MDI and PMDI are over 8 h for natural rubber (NR), polychloroprene (CR), BR, and polyvinylchloride (PVC) when the thicknesses of the materials are at least 0.5 mm, for nitrile

rubber (NBR) when the thickness is at least 0.35 mm, and for fluorocarbon rubber when it is 0.4 mm (GESTIS, 2013). According to data published by the American Chemistry Counsel (2013), many materials are suitable for protection against PMDI. However, the effectiveness of NBR material's protection against PMDI and solvent mixtures was much poorer.

Current standard permeation test methods were developed over 30 years ago (ASTM Standard F 739, 1981; Henry and Schlatter, 1989). The sensitivity of the analytical techniques varied, and thus, breakthrough could not be accurately measured from the first appearance of the chemical on the inside of the protective material. A criterion limit for the detection of the chemicals was needed to normalize the calculation of the breakthrough time (Leinster *et al.*, 1986). Thus, the breakthrough time was defined as the time from the application of the test chemical to the outside of the protective material to the point at which the permeation rate exceeds a specific rate through the material (Leinster *et al.*, 1986; EN 374, 2003; ASTM F 739, 2012; ASTM D 6978, 2013). The specific rate differs according to standards: $0.1 \mu\text{g min}^{-1} \text{cm}^{-2}$ in ASTM F 739 for protective clothing materials, $0.01 \mu\text{g min}^{-1} \text{cm}^{-2}$ in ASTM D 6978 for gloves protecting against cytotoxic drugs, and $1.0 \mu\text{g min}^{-1} \text{cm}^{-2}$ in EN 374-3 for chemical protective gloves. The ASTM F 739 standard also requires the reporting of cumulative permeation ($\mu\text{g cm}^{-2}$), but there is no maximum limit for this. The toxicity of chemicals has not been widely taken into account in the criteria for breakthrough time.

For a sensitizing chemical such as MDI, the question is how much of it is allowed to permeate through the protective material. Dose per unit area ($\mu\text{g cm}^{-2}$) is considered the most important factor in skin sensitization (Upadhye and Maibach, 1992). In patch testing of patients at dermatology clinics, a concentration of ~1% PMDI or 2% 4,4'-MDI in petrolatum, corresponding to $320\text{--}800 \mu\text{g cm}^{-2}$, is considered capable of eliciting contact allergy to MDI without causing sensitization (Frick-Engfeldt *et al.*, 2007). However, in 2012, Hamada *et al.* reported that a 4,4'-MDI concentration of $800 \mu\text{g cm}^{-2}$ caused active sensitization in two volunteers when applied on rather large skin areas of 12.5 and 31 cm². On the basis of the results, it has been recommended in Europe that the patch test concentration should be lowered to 0.5% of 4,4'-MDI in petrolatum. This was reported in the same article by

Hamada *et al.* A larger area of skin exposure results in a higher total dose, which may also play a role in the risk of sensitization (Fischer *et al.*, 2007). Workplace conditions and individual factors such as repeated exposure, skin condition, other skin irritating factors, etc. must also be taken into account when deciding on the acceptable level of exposure. The diameter of the clinical patch test exposure is 8 mm. If not properly protected, the workers may be exposed to many such droplets per day, sometimes on much larger skin areas. The threshold limit value for the allowable amount of MDI inside the protective material should therefore be clearly smaller than the patch test dose per unit area.

The aim of the study was to enhance the means for protecting workers' skin when handling PMDI without solvents. The study is part of a recent research project in which working methods, skin protection, skin contamination, and MDI exposure were studied in construction work and the boat industry in Finland.

This paper describes *in detail* the test method used to determine the permeation of small amounts of 4,4'-MDI through the glove and clothing materials commonly used in Finnish workplaces, using commercial PMDI as the test chemical. Here we report the permeation test results for eight glove materials and one clothing material. For comparison, the breakthrough times were calculated using both permeation rates and cumulative permeation (cumulative permeated mass per area of the protective material). We suggest and use an acceptable cumulative permeation rate through protective materials for evaluation. We then discuss test requirements set by present standards.

MATERIALS AND METHODS

Glove and clothing samples

The tested materials widely represented different types of materials worn in Finnish workplaces in the handling of PMDI or uncured polyurethane. Twelve workplaces were visited to determine the gloves and clothing used to protect against PMDI and uncured polyurethane.

1. Arm shield, protection against dust, non-woven polypropylene fabric with microporous polyethylene film, L. Brador DC 20
2. PVC gloves (vinyl gloves), disposable examination gloves for healthcare
3. Natural rubber gloves, chemical protection

4. NBR gloves, disposable, chemical protection/healthcare, Worksafe Nimex Premium
5. Winter gloves, Guide 49W, leather gloves with thermoplastic polyurethane insulation and double fleece lining, for protection against mechanical hazards
6. Natural (NR)—neoprene rubber gloves, chemical protection, Bicolour 87–800, Ansell
7. PVC mittens with textile lining, chemical protection, JokaOiler, JokaSafe
8. NBR gloves with textile lining, NitriKnit, chemical protection, North
9. Textile gloves with NBR coating up to the knuckles, KP Grip, for protection against mechanical hazards
10. Leather gloves, for protection against mechanical hazards

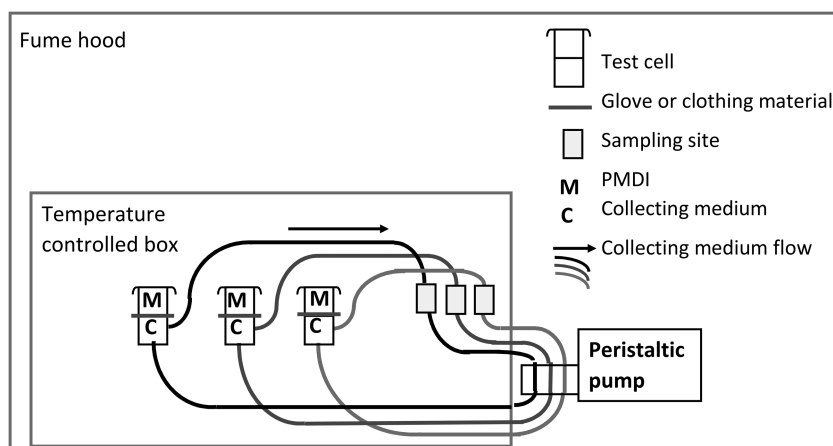
Chemicals

A commercial PMDI from Huntsman (Everberg, Belgium) containing, according to analysis, 9% 2,4'-MDI, 64% 4,4'-MDI, and 7% MDI trimer (4,4') was used as a test chemical. We also used 4,4'-Methylenedianiline (4,4'-MDA) (CAS 101-77-9) from Sigma Aldrich (purity > 97%), acetonitrile (CAS 75-05-8) from Rathburn (HPLC grade > 99.8%), acetic acid (CAS 64-19-7) from Merck (purity > 99.8%), and ammonium acetate (CAS 631-61-8) from Merck (purity > 98%).

Permeation test method

Permeation was tested using test cells in which the glove material separates the test chemical from the collecting medium (Fig. 1). The permeated concentrations ($\mu\text{g ml}^{-1}$) of the test chemical in the collecting medium were measured using the analytical measurement technique described below. The permeation rates, permeated cumulative masses, and the breakthrough times were calculated from these concentrations. Permeation testing was carried out until the permeation rate did not change in the collecting medium chamber or the testing time of 8 h was reached. Triplicate testing of each PMDI/material pair was carried out. The lowest breakthrough time for each triplicate is given as a result.

The glove sample specimens were cut from the palms of the gloves. Thickness and mass per unit area were measured for each sample specimen (Table 1). The thickness was measured in accordance with the



1 Test system.

Table 1. Breakthrough times of 4,4'-MDI through nine different glove materials and one clothing material (No. 1) determined using both permeation rate and cumulative permeation as the end point of the breakthrough time. The shortest of each triplicate breakthrough time is shown; the longest time is given in parenthesis

Materials	Thickness, mm	Mass per unit area, g m ⁻²	Breakthrough time, min		
			Calculated using permeation rate, 0.01 µg min ⁻¹ cm ⁻²	Calculated using cumulative permeation, 0.25 µg cm ⁻²	Calculated using cumulative permeation, 1.0 µg cm ⁻²
1 Arm shield	0.22	58	4.2 ^a (4.5 ^a)	10 ^a (12 ^a)	24 (30)
2 PVC (vinyl)	0.07	93	5.4 ^a (5.9 ^a)	12 ^a (14 ^a)	23 (29)
3 Natural rubber, NR	0.53	430	30 ^a (36)	43 ^a (52)	78 (102)
4 Nitrile rubber	0.10	100	29 ^a (35 ^a)	42 ^a (52)	90 (130)
5 Winter gloves	1.9	540	9 ^a (71 ^a)	23 (88)	65 (>330)
6 NR—neoprene rubber	0.78	750	231 (>275)	132 (154)	224 (255)
7 PVC mittens	1.7	1400	>480	256 (335)	406 (>480)
8 Nitrile rubber with textile lining	0.96	510	>480	>480	>480
9 Textile with nitrile coating	0.80	580	>480	>480	>480
10 Leather	1.0	520	—	—	—

—, Permeation could not be measured. Material permeated collecting medium.

^aBreakthrough time calculated from two consecutive collecting medium samples, from first of which MDA could not be detected.

ISO 4648 standard (1991). The fleece lining inside the winter gloves siphoned the collecting medium out of the test cell and was thus removed from the samples before the permeation tests.

Test cells in accordance with the superseded version of the EN ISO 6529 standard (2001) were selected for the study. The PMDI test chemical is difficult to wash off the test chamber. Thus, a test cell with a simple

chamber structure for the test chemical was needed. The permeation cell was divided into an upper chamber, into which the test chemical was applied at the beginning of the test, and a collection medium chamber. The upper chamber was a glass cone (diameter: 2.5 cm) with a ground joint at one end. A glove or clothing sample specimen separated the two chambers of the permeation cell, with the outer surface of the material on the test chemical side of the permeation cell.

We used a closed loop test system (Fig. 1) in which the collecting medium was circulated with a peristaltic pump between the test cell and the point at which samples were taken from the collecting medium flow of each test cell for the analysis. Three separate tubing loops were used, each with a pump head, test cell, and sampling site. The sample size was 1.0 ml, and after each discrete sampling, the collecting medium was replenished by 1.0 ml of fresh collecting medium solution. The sampling times were 0, 5, 15, 30, 45, 60, 75, 105, 135, 165, 210, 270, 330, 390, 450, 475, and 485 min. The collecting medium was 1.0% acetic acid, in which the 4,4'-MDI rapidly reacted to form 4,4'-MDA, because of acidic hydrolysis, which is a reaction of isocyanates (Morrison and Boyd, 1975) and used in the well-known Marcali (1957) method for determination of aromatic diisocyanates in the atmosphere.

The volume of the collecting medium in the test cell and the test loop was 33 ml, and the volume of the test chemical PMDI was 5 ml. The flow rate of the collecting medium, 32 ml min⁻¹, was checked at the beginning of each test. The collecting medium and the test chemical were tempered to test temperature (23.0 ± 1.0°C) prior to the tests. The test system was built into a plastic box, which had thermostatically controlled heating with forced convection. The temperature inside the box was adjusted to 23.0 ± 1.0°C and monitored by a calibrated temperature data logger. The pump was set as close as possible, outside of the box.

The average permeation rate $\bar{P}_i$ over a period from t_{i-1} to t_i was calculated as (ASTM F 739, 2012):

$$\bar{P}_i = \frac{\left[c_i - c_{i-1} \left(\frac{V_t - V_s}{V_t} \right) \right] V_t}{(t_i - t_{i-1}) A}$$

The cumulative permeation of the test chemical inside the protective material was calculated as:

$$K_i = \frac{c_i V_t}{A} + \sum_{s=1}^{i-1} \frac{c_{si} V_s}{A}$$

The symbols are as follows: P is the permeation rate, in $\mu\text{g min}^{-1} \text{cm}^{-2}$; K is the cumulative permeation (cumulative permeated mass per area of the test specimen); A is the area of the material specimen in contact with the test chemical; i is an indexing number assigned to each discrete sample taken from the collecting medium, starting from $i = 0$ at the beginning of the test; t is time, starting from the application of the test chemical to the test cell; c is the concentration of the test chemical in the collecting medium; c_s is the concentration of the test chemical in the discrete sample removed from the collecting medium; V_t is the total volume of the collecting medium; and V_s is the volume of the discrete sample removed from the collecting medium.

In the calculation of the breakthrough times, it was assumed that the permeation between two sampling points was linear. It was also taken into account that when plotting average permeation rates as a function of time, the time co-ordinate is the midpoint of the interval over which the average was obtained. In calculations and in figures, we used 0 $\mu\text{g cm}^{-2}$ or 0 $\mu\text{g min}^{-1} \text{cm}^{-2}$ as the cumulative permeation or permeation rate when the permeation did not reach the determination limit of the analytical method.

The breakthrough times were determined (i) as the time when permeation rates exceeded 0.01, 0.1, and 1.0 $\mu\text{g min}^{-1} \text{cm}^{-2}$ and (ii) as the time where the cumulative permeation of the test chemical exceeded 0.25 and 1.0 $\mu\text{g cm}^{-2}$. The expanded uncertainty for the permeation rate was estimated as 21% at a confidence level of 95%. It was calculated for one of the triplicate tests of NR-neoprene gloves, when the permeation rate rose from 0.0087 to 0.011 $\mu\text{g min}^{-1} \text{cm}^{-2}$ in the testing time period from 240 to 300 min. For the cumulative permeation, the expanded uncertainty with the same sample specimen was estimated to be 18% at a confidence level of 95%. The cumulative permeation rose from 0.61 to 1.1 $\mu\text{g cm}^{-2}$ in the testing time period of 105–135 min.

Chemical analysis

4,4'-MDI was determined as 4,4'-MDA in acidic conditions using liquid chromatography with UV detection (LC-UV) (Waters 2690 Alliance Separation

Module/996 Photodiode Array Detector, Milford, MA 01757) at 244 nm. The LC column was Hypersil 5005 (25 cm $\times$ 4.6 mm), and the column temperature was 30°C. The mobile phase (flow 1 ml min⁻¹) consisted of 60% acetonitrile and 40% water with 10 mM ammonium acetate. The injection volume of the sample was 50 μ l. The quantitation limit for 4,4'-MDA was 0.01 μ g ml⁻¹.

Standard solutions of 4,4'-MDA were prepared by dissolving accurately weighed amounts in acetonitrile. The solutions were further diluted in 1% acetic acid in water to the appropriate concentrations. The linear range of standard concentrations used was 0.01–5.0 μ g ml⁻¹.

The stability of 4,4'-MDA in the collecting medium was determined by mixing a solution of 2 μ g ml⁻¹ of the PMDI test chemical in 1.0% acetic acid and measuring the MDA concentration immediately after mixing, then again after 20 h. The changes in concentration were not significant. All collecting medium samples were analyzed within 20 h from sampling. The recovery of the 4,4'-MDI was 68% in 1.0% acetic acid solution when determined as 4,4'-MDA in a concentration of 0.05 μ g ml⁻¹. The recovery was taken into account in the calculation of the permeation rates and cumulative masses. The expanded uncertainty of the analytical test method for MDA was estimated to be 11% at a confidence level of 95% and 19% for 4,4'-MDI.

RESULTS

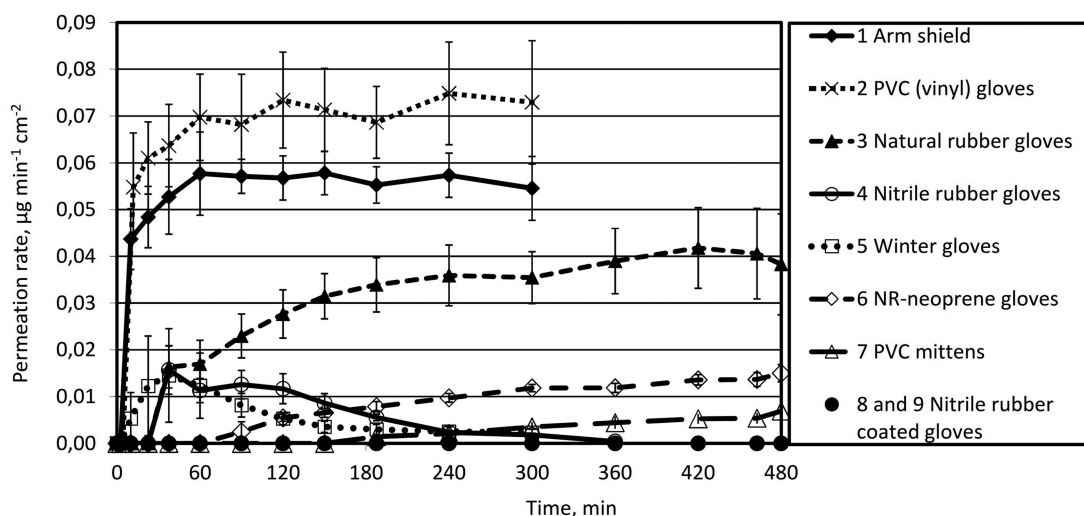
The breakthrough times defined as a permeation rate exceeding 0.01 μ g min⁻¹ cm⁻², 0.25 μ g cm⁻², and 1.0 μ g

cm⁻² are reported in Table 1. The shortest of each triplicate breakthrough time is given as the result as in the EN 374-3 standard (2003). Average permeation rates and average cumulative permeation and the standard deviations of three triplicate samples are shown in Figs 2 and 3.

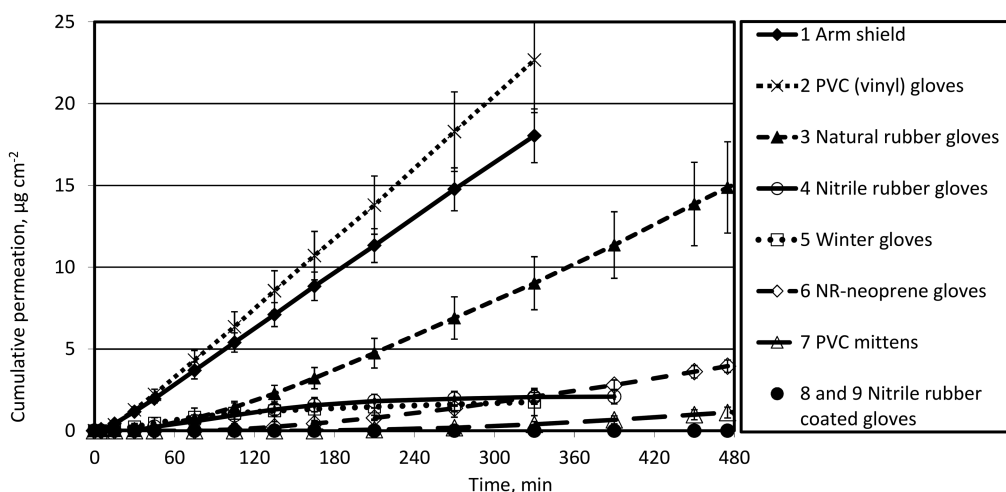
All the permeation rates measured in this study were below 0.1 μ g min⁻¹ cm⁻², and thus, all the breakthrough times were over 480 min when calculated as the normalized breakthrough times in the EN 374-3 and ASTM F 739 standards. For six of the test materials, the breakthrough time could be determined using the normalized permeation limit of 0.01 μ g min⁻¹ cm⁻² (Table 1), which is used in the ASTM D 6978 standard for permeation by chemotherapy drugs. When a cumulative permeation of 0.25 or 1.0 μ g cm⁻² was used as the end point, 480 min was exceeded by only two materials; breakthrough times could be calculated for seven out of nine materials (Table 1).

The permeation rate of disposable PVC gloves and arm shields steadied between 0.06 and 0.07 μ g min⁻¹ cm⁻² after ~60 min (Fig. 2). On the cumulative permeation curve (Fig. 3), steady permeation can be seen as an almost straight line. The disposable PVC gloves and arm shields did not change appearance during testing.

The permeation rate through NR and NR-neoprene gloves stopped rising after 3 h. The maximum average permeation rates were 0.04 and 0.015 μ g min⁻¹ cm⁻². The first observed breakthrough for NR gloves was in the 45-min sample and for NR-neoprene gloves in the



2 Average 4,4'-MDI permeation rate and standard deviation of three samples versus time in nine materials.



3 Average 4,4'-MDI cumulative permeation and its standard deviation of three samples versus time in nine materials. Data points are calculated from same data as in Fig. 2.

105-min sample. The materials swelled slightly during testing.

Disposable NBR gloves and the leather of the winter gloves became rigid in contact with PMDI. The NBR samples also changed appearance by swelling. The change of the material state can be seen in Figs 2 and 3. The permeation rates increased at first but after 6 h of testing, the permeation rate for the winter gloves was $0.003 \mu\text{g min}^{-1} \text{cm}^{-2}$, and that of the NBR gloves could no longer be observed. Permeation was first detected at 30 min in the NBR gloves and at 15 min in the winter gloves. The cumulative permeation steadied to a level of $\sim 2 \mu\text{g cm}^{-2}$.

The thick PVC mittens hardened in 8-h testing. Permeation was first observed in the 210-min sample. A cumulative permeation of $1.0 \mu\text{g cm}^{-2}$ was reached in 406 and 450 min in two of the sample specimens and was not exceeded in the 480-min testing of one of the samples.

The NBR gloves with textile lining and the textile gloves with NBR coating (items 8 and 9) were the only gloves through which permeation was not observed in testing. Nevertheless, these materials also swelled and hardened in 480-min contact with the PMDI. The leather gloves were immediately penetrated by the collecting medium and, therefore, could not be tested.

DISCUSSION

In the present study, we showed that the breakthrough time of 4,4'-MDI through various protective clothing

is dependent on the defined endpoint of the breakthrough time: when using the EN 374-1 or ASTM F 739 definition, i.e. the permeation rate (1.0 or $0.1 \mu\text{g min}^{-1} \text{cm}^{-2}$), 4,4'-MDI from the PMDI did not permeate any of the materials, whereas when using cumulative permeation ($0.25 \mu\text{g cm}^{-2}$ or $1.0 \mu\text{g cm}^{-2}$), most of the materials were shown to be permeated by 4,4'-MDI originating from the PMDI. The protection efficacy of the tested materials varied greatly.

Dose per unit area ($\mu\text{g cm}^{-2}$) is considered the most important factor in skin sensitization (Upadhye and Maibach, 1992). Thus, cumulative permeation is useful for chemical safety assessment when the right kind of protection is selected in different kinds of exposure scenarios (ECHA, 2012). Only rough estimates for acceptable skin exposure to a sensitizing substance can be made, but these can be used to assess the limits for the breakthrough time of chemical protective gloves and clothing. Breakthrough times are only meant for comparison of protective materials (Leinster *et al.*, 1986), but the information has to be valid as regards the safe levels of exposure. Based on the present findings, cumulative permeation of MDI, which may be capable of sensitizing the skin, can occur through protective materials before the EN 374-3:2003 permeation rate of $1.0 \mu\text{g min}^{-1} \text{cm}^{-2}$ is reached. It is also likely that the ASTM F 739 standard's limit of $0.1 \mu\text{g min}^{-1} \text{cm}^{-2}$ is not safe. Therefore, the EN 374-3 and ASTM F 739 standards do not produce information that would allow safe comparison of protective materials.

Here, we set the threshold limit value for the cumulative permeation of 4,4'-MDI for protective gloves in close contact with the skin at $1.0 \mu\text{g cm}^{-2}$, which is 800 times less than the amount known to have sensitized patch-tested volunteers (Hamada *et al.*, 2012). With this limit value, we obtained breakthrough times that could be used to compare the protection efficacy of various materials. For clothing we suggest that the endpoint of the breakthrough time be 1.0 or $10 \mu\text{g cm}^{-2}$, depending on how closely in contact the skin is, and also on the likelihood of PMDI touching the clothing surface. We also suggest that commercial PMDI mixtures with high 4,4'-MDI content should be used as test chemical in MDI permeation tests because the higher molar mass oligomers of MDI are not likely to permeate glove or clothing materials. Because we were mainly interested in low levels of MDI permeation, we measured only the dominating monomer 4,4'-MDI as 4,4'-MDA. However, measuring both monomers is an option.

The limit of $1.0 \mu\text{g cm}^{-2}$ resulted in breakthrough times from 78 to over 480 min for chemical protective gloves (Table 1). Gloves for different applications, also for direct PMDI contact, could be found even with this rather strict limit. However, in heavy exposure, the gloves have to be discarded after 15 min of use because the polyurethane hardens. Thus, chemical protective gloves of natural rubber and thin NBR, for instance, can be safely used in many applications of short duration.

Glove No. 9 in which the nitrile coating reached only the knuckles on the back of the hand was of an excellent protective material. It was affordable and comfortable to wear. These should be accepted as chemical protective gloves when the back of the hands are not exposed. The standards should take into account glove types that could provide more user comfort than the current requirements. Material from glove No. 10 was penetrated by the collecting medium containing mainly water before the permeation test began. Thus, plain leather gloves should not be used as protection against hazardous chemicals at workplaces.

By using a cumulative permeation of $1.0 \mu\text{g cm}^{-2}$ as the endpoint of breakthrough time, we were able to demonstrate that the breakthrough times (over 480 min) reported by GESTIS (2013) may lead to the unsafe use of NR gloves because we found a

breakthrough time of only 78 min (Table 1) for an NR glove material of the same thickness. We also found that more materials that protect against 4,4'-MDI exist than reported by Forsberg and Mansdorf (2007).

Setting values lower than $1.0 \mu\text{g cm}^{-2}$ as breakthrough time endpoints could cause difficulties owing to limitations in analytical sensitivity. In Table 1, one type of measurement difficulty is marked by an asterisk. In five tests, the 4,4'-MDA concentration did not reach the determination limit of the analytical method in the first of the two consecutive samples from which the breakthrough time was determined, when using $0.25 \mu\text{g cm}^{-2}$ as the endpoint. The breakthrough time measurement was inaccurate, as the exact location of the first point in the cumulative permeation axis (Fig. 3) was unknown.

In closed loop test methods for permeation (Fig. 1), the permeation rates (equation 1) are calculated from the current sample concentration (c_t) by subtracting the previous sample concentration (c_{t-1}) after correcting its concentration loss caused by the sampling with the factor $[(V_t - V_s)/V_t]$. If the permeation rate approaches or steadies onto some level (the c_{t-1} is near the c_t), method uncertainty can cause high irregularity in the permeation rate curve. If the correction factor approaches 1, the permeation rate can occasionally be negative. If the permeation rate steadies to a level near that at which the breakthrough time is determined, the method uncertainty can be hours. Cumulative permeation produces more easily interpreted permeation curves than permeation rates (Figs 2 and 3). The closed loop method is needed for measuring permeation in low concentrations because in the loop, the test chemical concentrates into the collecting medium. It also allows the safe collection of the resulting chemical waste.

We chose to use 1.0% acetic acid as the collecting medium because of the rapid reaction of the MDI to MDA, which was stable in the acidic water solution. Another reason for our choice was that we believe that the collecting medium should resemble the conditions inside the glove as much as possible. Instead of sweat and air, purified water and nitrogen are generally used in permeation studies. We did not consider using strong solvents for the collection of MDI because of their well-known ability to permeate glove materials (Mickelsen *et al.*, 1986): they would have interfered with the tests. Nevertheless, better recovery of the

MDI monomers in the collecting medium is a challenge for future studies.

CONCLUSIONS AND RECOMMENDATIONS

Skin exposure is in general assessed on the basis of dose/unit area. The permeability of chemical protective materials should be estimated using the same definition. The current permeation test standards do not comply with this principle, and the current limit for breakthrough time is too high for sensitizing substances and chemicals very toxic via the skin. Therefore, new standards should be developed. A cumulative permeation of $1.0 \mu\text{g cm}^{-2}$ of 4,4'-MDI should be used as a safety limit for gloves and other clothing in direct contact with PMDI, and $10 \mu\text{g cm}^{-2}$ should be used for clothing meant for protection against light exposure.

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