DEVELOPMENT OF A METHOD FOR QUANTIFICATION OF TOLUENE DIISOCYANATE AND METHYLENEDIPHENYL DIISOCYANATE MIGRATION FROM POLYURETHANE FOAM SAMPLE SURFACE TO ARTIFICIAL SWEAT BY HPLC-UV-MS

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Abstract

The US Environmental protection agency (EPA) has published guidance that includes test procedures for evaluating indoor exposure to chemicals from products. One of the test procedures represents the migration test for evaluating potential dermal exposure from home furniture. Such an evaluation involves the chemical measurement of the sweat which is currently unavailable in the literature. The objective of this project was to develop and validate an analytical method for quantification of migration of 4,4'-methylenediphenyl diisocyanate (MDI), 2,6-toluene diisocyanate (2,6-TDI) and 2,4-toluene diisocyanate (2,4-TDI) from a polyurethane (PU) flexible foam to artificial sweat that meets the recommendations of the EPA test protocol. Following the EPA protocol, six synthetic sweat solutions were prepared and used in evaluation of isocyanate recovery performance. The migration tests were conducted using five foam types that were chosen and supplied by PU foam manufacturers to represent the types most commonly found in commercial products, and with formulations anticipated to have the highest potential residual TDI or MDI. Migration tests were conducted using glass fiber filters (GFF) coated with 1-(2-methoxyphenyl)piperazine (1,2-MP) and analyzed using HPLC equipped with a UV detector for quantification and a MS detector to qualify peaks. The detection limits of the method were 0.002µg/mL for 2,6-TDI, 0.011µg/mL for 2,4-TDI, and 0.003µg/mL for MDI. Quantification limits were 0.006µg/mL, 0.037µg/mL, and 0.010µg/mL, respectively. The recovery tests on a Teflon surface for 5 of the 6 EPA-recommended synthetic sweat solutions indicate the recovery percentage was approximately 80% for diisocyanates. Recovery for the sixth sweat solution was low, approximately 30%. TDI and MDI migration was not observed when testing was conducted on foam samples.

Keywords: isocyanate, polyurethane, artificial sweat, migration, 1-(2-methoxyphenyl) piperazine, HPLC-UV.

1. Introduction

Toluene diisocyanate (TDI) and methylenediphenyl diisocyanate (MDI) are organic compounds that have two isocyanate (NCO) groups in their molecules. These two diisocyanates are largely used in polyurethane (PU) production. The polymer is formed by chemical reaction between an isocyanate with two or more NCO groups and a diol or polyol in the presence of a catalyst, a chain extender and other additives [1]. The different nature of isocyanates and polyols used for polymerization create a wide variety of materials, from high performance elastomers to tough thermoplastics and foams that can be used in applications such as construction (for thermal insulation), furniture (bedding, mattresses, chairs, sofas), and automobiles (molded rigid foams), among others. Increasing the temperature during polymerization can cause a reverse reaction that leaves some residual isocyanate attached to the formed product [2]. The concentration of free isocyanate in freshly prepared foam will decrease within a few days after production [1]. The method of quantification of diisocyanate migration studied in this project can confirm or determine at what point the diisocyanates are no longer available to migrate to a sweat solution. Therefore, this can be a useful tool in the estimation of the potential risk for dermal exposure. However, isocyanates analysis has not yet been reported from sweat samples and needs to be addressed.

TDI and MDI are known to cause respiratory tract, eye and skin irritation [3-6]. Over-exposure can lead to sensitization and asthma [7-9]. Possible induction of sensitization to isocyanates due to dermal exposure has been studied in animals [10-12]. It can also cause contact dermatitis on a sensible person [6, 13, 14]. Furthermore, if MDI or TDI are able to migrate, they will eventually hydrolyse to the corresponding MDA or TDA side products [15]. The latter has

been classified category 2B, as a potential cancer suspect agent for human by the *International Agency for research on cancer* [16]. It is also known that the MDA can be absorbed via skin contact [17]. Because of the frequent and prolonged contact with PU foam based furniture's in every day life, it is of the outmost importance to develop an efficient method to determine the migration of potential residual diisocyanates from such foams.

There are exposure limits established by the governmental agencies for these chemicals that are intended for use to determine airborne concentrations [18-20]. Unfortunately, there are no exposure limits for diisocyanates on surfaces or on skin so it is impossible to evaluate the concentrations of these substances being transferred via skin contact and their subsequent health effect.

To be able to analyze diisocyanates it is necessary to stabilize the NCO groups by a derivatization reaction. Secondary amines used in this reaction can include 1-(9-anthracenylmethyl)piperazine (MAP), N-(4-nitrobenzyl)-N-propylamine (OSHA method 18), 1-(2-Pyridyl)piperazine (1,2-PP) (OSHA 42 and 47 methods), 1-(2-methoxyphenyl)piperazine (1,2-MP) and are routinely used for derivatization of isocyanates. These stable derivatives can be further analyzed in laboratory using reversed phase chromatography with UV, diode-array or Mass Spectrometry (MS) detection [21, 22].

It's been demonstrated in some studies that residual TDI can be extracted from foam using organic solvents, treated with a derivatizing agent and then analyzed [23-25]. The concentrations of TDI extracted from foam are very low and usually decrease with foam aging. It was also reported that the concentration of TDI found depends on the solvent used for extraction [24].

Assuming that solvent extraction may lead to detection of unreacted TDI, those concentrations should not be considered 'free TDI' which is available for migration to surface of the foam, leading to skin contact from articles made with PU foams. For this reason, another approach was needed for evaluation of diisocyanate that may migrate from polyurethane products and potentially result in dermal exposure.

US EPA's Office of Pollution Prevention and Toxics (OPPT) has published ten testing protocols providing general information and descriptions of sampling and analytical procedures used to evaluate indoor exposure to chemicals in consumer products and articles [26]. The latter include building materials used in the indoor environment. One of the testing procedures described in the protocol is for migration to simulated sweat to determine the quantity of a chemical accumulated on skin surface from direct contact with an object. Five simulated sweat solutions containing typical components of sweat (i.e., water, lactate, urea, sodium, potassium, calcium, magnesium cations) at different pH (5.4; 4.5; 2.8) were proposed by EPA (Table 1).

A sixth artificial sweat solution (Table 2) was added to the protocol later, and is more likely to represent the composition of a biological fluid [27-30]. All six simulated sweat solutions were used in this study to evaluate TDI and MDI migration from a polyurethane flexible foam sample. Even if these sweat mixtures are available from EPA, there is no example reported on how the samples should be prepared for analytical measurements. The development of an efficient method is therefore needed to extract isocyanates from the sweat.

The objective of this study was to develop and validate a method for the quantification of diisocyanate from synthetic sweat samples according to the EPA published protocol described

above in order to assess the migration potential from foam furniture. Glass fiber (GF) filters coated with 1,2-MP were used to collect isocyanates, simultaneously transforming them into stable derivatives that were analyzed by HPLC coupled with both UV-and mass detectors. Five polyurethane foam samples, representing the types most commonly found in commercial products and with formulations anticipated to have the highest potential residual TDI or MDI were supplied by manufacturers and were analyzed using the developed method. Synthetic sweat solutions (6 proposed by EPA) were used to evaluate each of the five foams for determining optimum recovery results. The use of a mass detector allowed simultaneous confirmation of the identity of the peaks detected by UV.

2. Methods

2.1. Chemicals

All chemicals were used without any further purification. 2,4-TDI (96% purity), 2,6-TDI (97% purity), 4,4'-MDI (98% purity), 1-(2-Methoxyphenyl)piperazine (1,2-MP; 98% purity), Acetic anhydride (AcA; 98% purity), Amino acid mix, Squalene, Glyceryl trioleate, Cetylpalmitate, N-Butyric acid were obtained from Sigma-Aldrich (Milwaukee, USA). Sodium sulfate (99% purity), Lead reference 1000 ppm, Manganese-reference 1000 ppm, Nickel-reference 1000 ppm, Zinc-reference 1000 ppm, Calcium chloride, Copper chloride, Ammonium hydroxide (trace metal grade), Creatinine were obtained from Fisher Scientific (Markham, ON, Canada). Cholesteryl oleate, Sulfur (99%) and Lactic acid were obtained from Alfa Aesar (Tewksbury, MA, USA). Ammonium chloride, Sodium chloride and Iron sulfate (>99% purity) were obtained from VWR (Ville Mont-Royal, QC, Canada). Sodium phosphate and Sodium bicarbonate were obtained from Bioshop (Burlington, ON, Canada). Urea was obtained from Bio

Basic (Markham, ON, Canada). Acetonitrile (ACN) and water (H_2O), both HPLC grade were obtained from Fisher Scientific (Canada). Glacial acetic acid was obtained from J.T. Baker. Potassium chloride (99 % purity) and D-Glucose were obtained from EMD Millipore Corp. (Billerica, MA, USA). Ammonium acetate (99% purity) was obtained from Fluka Chemical Corp. (Ronkonkoma, NY).

2.2. Instruments and analytical conditions

The HPLC-UV-QDa system was an Acquity Arc from Waters (Beverly, Massachusetts, USA). The analyses were carried out using a Kinetex core shell C_{18} column of 2.6 µm (2.1 mm × 100 mm) from Phenomenex. A SecurityGuard™ Ultra Cartridge System (C18 4.6mm) was also used to protect the analytical column from an accumulation of any possible precipitants.

The elution was effectuated using an isocratic method with 50% of aqueous phase (2 mM ammonium acetate buffer at pH 6 adjusted using acetic acid) and 50% of organic phase (acetonitrile) for 4 minutes. The column temperature was maintained at 35 °C and a constant eluent flow rate of 0.5 mL/min was used. The injection volume was 10 µL and the sample temperature was maintained at 18 °C. The UV spectrum was obtained using a photodiode array detector operating between 200 and 400 nm. The quantification was done at 242 nm for 2,6-TDI, 2,4-TDI and 250 nm for MDI. Areas for TDI and MDI quantification were determined using the automatic integration feature and manual adjustments were done only where auto-integrations did not cover the entire peak. The calibration curve regression equation was determined using least-squares linear regression fitted of the peak area versus concentration data, with a concentration weighting factor of 1/x.

The QDa was operated in positive mode. Cone voltage was adjusted to 15 V, capillary voltage was set at 0.8 kV and the probe temperature was set at 600^{o}C. The detector was scanning the ion masses between 100-700 Da. The peaks of TDI-1,2-MP were confirmed by the ion mass 559Da and the peak of MDI-1,2-MP had the ion mass 635Da.

2.3. Synthetic sweat solutions

Artificial sweat solutions were prepared for use as sample collection solvents in migration tests with foam samples and on a Teflon surface for transfer efficiency.

Five sweat solutions were prepared in water using sodium, potassium, calcium, magnesium, lactate and urea in different concentrations as shown in Table 1. The sixth sweat solution was prepared partially in water and partially in a mixture of organic solvents (3 parts chloroform and 1 part methanol). These two parts were mixed together in a 1:1 proportion and mixed on a Vortex mixer prior to the experiment (Table 2).

2.4. Standard curve preparation

The stock solution of isocyanates mixture (200 µg/mL of MDI and 124.4 µg/mL for the 2,6-TDI, 2,4-TDI isomers) used to make the calibration standards was prepared in ACN. For the stock solution, about 20 mg of MDI was weighted accurately on a microbalance and dissolved in 80 mL of ACN; 10 µL of each isomer of TDI were added to the volumetric flask and was placed in a sonicating bath for 1 minute; then ACN was added to a flask up to 100 mL. Several dilutions of the stock solution used for the calibration curve were also done in ACN. The preparation of the calibration curve samples was as follows: known aliquots from diluted stock solutions were spiked into 0.1 mg/mL 1,2-MP/ACN followed by addition of 0.5% AcA. One blank and 5 calibration solutions containing TDI-1,2-MP derivatives of concentrations ranging from 0.025

µg/mL to 0.490 µg/mL (0 µg/mL, 0.025 µg/mL, 0.050 µg/mL, 0.125 µg/mL, 0.250 µg/mL, 0.490 µg/mL); and from 0.04 µg/mL to 0.8 µg/mL (0 µg/mL, 0.040 µg/mL, 0.080 µg/mL, 0.200 µg/mL, 0.400 µg/mL, 0.800 µg/mL) for MDI-1,2-MP derivative were made. The blank values were always used according to an analytical protocol to check if there was a blank value to be considered for any kind of contamination. In the current work, no blank subtraction was mandatory due to unexpected contamination. The blank value was not included in the calibration curve. All the calibration samples were filtered on a syringe cartridge containing a 0.22 µm pore size filter. Final sample concentration solutions were obtained by adding 500 µL of the above solutions and 500 µL of water as mobile phase solvents.

The calibration concentration range of the method is equivalent to 0.009 µg/cm^2 to 0.178 µg/cm^2 of TDI at the filter surface and 0.015 µg/cm^2 to 0.291 µg/cm^2 of MDI at the filter surface. To convert units from µg / mL to µg / cm^2, the concentrations were multiplied by 4/11. Given that each 37 mm filter (11cm^2 in surface) was desorbed in 2 mL of desorption solution and then diluted 1:2 and analyzed, 4 mL of sample represents the amount removed from 11 cm^2 of the surface.

2.5. GF/1,2-MP coated filters preparation

The 1,2-MP solution for the coating was prepared by dissolving approximately 750 mg of 1,2-MP in 100 mL of acetonitrile. GF filters were placed in a beaker and soaked with the coating solution for ~ 30 minutes. The filters were removed from the solution, placed on a clean aluminum foil surface and into a drying box; they were allowed to dry under nitrogen atmosphere overnight. Dried filters were transferred to a clean closed container and stored in a dark refrigerated (2-8^{o}C or cooler) place for no longer than 3 months.

2.6. Desorption efficiency tests

Teflon squares used for the tests were cut from a sheet, wiped with methanol and kept in a sealed plastic bag.

Three procedures were attempted to evaluate the desorption efficiency of the spiked isocyanates from the Teflon filter as well as the possibility of hydrolysis to occur:

Procedure 1 Wiping of the Teflon surface with a 37mm GF/1,2-MP impregnated filter:

The desorption efficiency was determined by spiking 40µL of acetonitrile solution containing 19.36µg/mL of each isomer of TDI and 37.77µg/mL of MDI on Teflon and immediately wiping with a 37mm GF/1,2-MP filter. The filter was transferred to a glass jar containing 2 mL of desorption solution (0.5% of acetic anhydride in acetonitrile). The solution in the jar was placed on a shaker for thirty minutes to facilitate desorption and then filtered using a filter syringe with a 0.22µm pore size. 500µL of filtered solution was combined with 500µL of water, mixed on a Vortex mixer, and analyzed.

Procedure 2 and 3 Wiping of the Teflon surface with a sweat solution moistened 37mm GF/1,2-MP impregnated filter VS a sweat solution moistened 37mm filter containing no derivatizing agent*:*

A similar procedure using a GF/1,2-MP filter wetted with 0.5 mL of a synthetic sweat solution (one out of six) and a GF non-impregnated filter wetted with a synthetic sweat solution (one out of five) was used to evaluate the desorption efficiency. Sweat 6 was not evaluated with non-impregnated filters due to low recovery performance with impregnated filters. In this case the filters with diisocyanate migrated were placed in a jar containing 1,2-MP solution (0.1

mg/mL) in acetonitrile for derivatization. In both cases, each filter was transferred to a separate jar after 5 min and 60 min to evaluate possible hydrolysis.

2.7. Analytical performance evaluation

The analytical performance evaluation was completed in accordance with DR-12-VMC method validation [30]. The limit of detection (LOD) and limit of quantification (LOQ) were measured with ten sample replicates (0.025 µg/mL of TDI isomers; 0.040µg/mL of MDI). The concentrations of replicates were distributed over the calibration range. The standard deviation of the sample peak areas was determined. The LOD and LOQ were calculated as three and ten times the standard deviation, respectively.

The influence of the "matrix effect" of the media solution (GF/1,2-MP filter wetted with 0.5 mL of a synthetic sweat solution) was investigated for each isocyanate (2,6-TDI, 2,4-TDI and MDI). This was done by comparing measured concentrations of isocyanates-1,2-MP derivatives, obtained from five replicate samples where a mixture of the three isocyanates was spiked (at five different concentrations) to the media solution, and was compared to those obtained by spiking the same isocyanates mixture to 1,2-MP solution without any GF/1,2-MP filter and synthetic sweat solution.

Intra-day precision was assessed from six replicates of four different concentrations injected the same day. Inter-day precision was also determined using four concentrations and repeated on six different days using the same instrument and analyst. The accuracy of the method was calculated against a different TDI and MDI stock solution that was carried through the entire extraction procedure and injected during each day of the validation period. The concentration of the solutions that were used for the accuracy was 0.250 µg/mL for TDI isomers and 0.400 µg/mL

for MDI. The analytical uncertainty (u) was obtained according to the formula of method DR-12-VMC and incorporated a bias and overall precision. This formula uses the total relative standard deviation (TRSD). The extended uncertainty (U) is also calculated by applying a coverage factor k = 1.96 to u [31].

2.8. Polyurethane foam samples migration tests

The foam used for these experiments was received from the Polyurethane Foam Association (PFA). The Polyurethane Foam Association represents manufacturers and suppliers to the flexible polyurethane foam industry, providing support and education on industry topics, and guidance to members on regulatory compliance. All samples were prepared and packaged for shipping according to the procedures outlined in the CertiPUR program [32] and analyzed in the range of 7-23 days post-production.

The foam samples received were cut in cylinders of 37 mm in diameter (Ø) and 6 cm in height one day before the test, and were kept in a sealed plastic bag. The experimental cell was assembled and a 0.25 mm thick Teflon square, large enough to cover the metal plate at the bottom, was utilized. Two GF/1,2-MP filters wetted with 0.5 mL of synthetic sweat solution (each) were placed on the Teflon square. The sample was then placed on these two filters with two more GF/1,2-MP sweat-wetted filters then placed on top of the sample and covered with another Teflon square. The top metal part of the cell was then installed and the foam was compressed by 25% (1.5 cm) of its height using wing nuts (Fig. 1). The cell was then left overnight at ambient laboratory conditions. The cell was disassembled and each single filter was transferred to a separate glass jar containing 2 mL of desorption solution (0.5% of acetic anhydride in acetonitrile). The solution in the jar was placed on a mechanical shaker for thirty

minutes to facilitate desorption. Lastly, the solution was filtered through a pore size 0.22 µm filter syringe with 500 µL of the filtered solution added to 500 µL of water, mixed by Vortex and analyzed.

3. Results and discussion

3.1. Method strategy

The analysis of isocyanates chemical from sweat samples is novel and it is of high importance in the current scheme where dermal exposure must be evaluated. A typical sweat is a matrix containing several components such as salts, electrolytes and inorganic constituents. It is therefore important to ensure that these constituents won't interfere with the derivatization needed with diisocyanates analysis.

Even though it has been demonstrated that residual TDI and MDI can be extracted from foam samples using organic solvents [23-25], the test procedures outlined in the EPA protocol and used in this study represent a more realistic evaluation of the potential for skin contact. For the derivatization of the isocyanates, 1,2-MP-impregnated glass fiber filters were used due to their efficiency in stabilizing the isocyanate group through formation of a stable derivative [21, 23] that can be easily analyzed using UV detector [22].

The synthetic sweat solutions were used to moisten the surface of the filter to facilitate the migration of the chemicals from the surface in a fashion that is representative of the skin surface environment. The desorption solution was prepared in acetonitrile instead of commonly used toluene [23] or methanol [21], to allow injection directly into the column, avoiding a long evaporation step in the sample work up procedure.

The use of a Waters Acquity Arc with diode-array and QDa detectors with subsequent UV spectrum allowed quantification without the use of an internal standard, which can add some complication due to the matrix effect. Figure 2 (a) shows the UV chromatogram of the 2,6-TDI-1,2-MP, 2,4-TDI-1,2-MP and 4,4'-MDI-1, 2-MP.

The QDa detector allows for validation of peak identities using ion masses, and also allows for the identification of any possible interference in cases where peaks are coeluting or overlapping as shown in Figure 2 (b). Using the Extract Ion Chromatograms (XIC) for the peaks of interest, two peaks with different masses coeluting together can be seen at the place of 2,4-TDI derivative (at 1.5 min Fig. 2 (b)). The peak of unknown interference has a mass of 425Da.

3.2 Dynamic range, detection limits, precision and accuracy

For method validation, analytical performances were determined and are summarized in Table 4. The dynamic ranges were established to cover from 0.025 µg/mL to 0.490 µg/mL for TDI-1,2MP isomers (0.009-0.178µg/cm^2 of foam surface) and from 0.040 µg/mL to 0.800 µg/mL for MDI-1,2-MP (0.015-0.291µg/cm^2 of foam surface) with $R^2 \geq 0.990$. The lowest reported value was chosen as the concentration of the standard with minimal concentration. The detection limits of the method, that correspond to the analytical performance of the instrument, were 0.002µg/mL for 2,6-TDI, 0.011µg/mL for 2,4-TDI, and 0.003µg/mL for MDI. Quantification limits were 0.006µg/mL, 0.037µg/mL, and 0.010µg/mL, respectively. The average intra-day precision is less than 4% for all of the diisocyanates derivatives and average inter-day precision is less than 10% as shown in Table 4. This indicates that the method is robust and can produce quantitative data. The accuracy is > 81% at a target level around 0.250 µg/mL

(for TDI isomers) and 0.400 µg/mL (for MDI). Validated parameters assured that the method can be used for real sample quantification.

3.3 Recovery and matrix effect

The recovery and the matrix effect were investigated by comparing the derivatives concentrations (obtained by spiking the isocyanate standards into the 1,2-MP solution) without any filter and sweat solution to the one spiked on the GF/1,2-MP wet filter. The results are summarized in Table 4. The low recovery performance is possibly due to insufficient desorption or incomplete derivatization on the filter surface, or the spiking technique.

3.4 Desorption efficiency tests results

To evaluate the recovery percentage of TDI and MDI in all assays, spiking the Teflon surface with a standard solution containing TDI and MDI was performed. Stabilization of the spiked diisocyanates was done both using GF/1,2-MP without any synthetic sweat solution and using all six sweat solutions. In the case of GF filters not coated with 1,2-MP and moisturized with sweat solution, the stabilization with 1,2-MP was done subsequently. According to the results summarized in Table 3, the derivatizing agent needs to be applied directly on the filter surface for good recovery of isocyanates derivatives (entry 2-6). The data (entry 7 -10) also indicate that four of the six synthetic sweat solutions used for these tests give an acceptable recovery (> 80% for TDI isomers and >70% for MDI) and any one of them can be used for the validation of the method and for migration test of real samples. The fifth synthetic sweat solution gives a recovery that is slightly lower (entry 11) than the other four (entry 7-10), probably due to its low pH. The sixth synthetic sweat solution did not provide a good recovery (entry 12). Although the formulation used in the sixth synthetic sweat solution best mimics biological fluid, the

chloroform used as a solvent to solubilize the sebum ingredients cause interferences in the chromatogram when applied to the filter. In addition, it doesn't give a homogeneous solution when mixed with water and it dries very quickly. The recovery percentages were very similar for the filters transferred after 5 or 60 minutes to the desorption solution, thus confirming that there is no interference of isocyanate-1,2-MP derivatization by the five other synthetic sweat solutions.

3.5 Analytical performance

The samples used for evaluating analytical performance were prepared by spiking the isocyanate standards diluted in acetonitrile on the 1,2-MP-coated GF filter wetted with the synthetic sweat solution No. 3 followed by the desorption solution.

3.6 Specificity and selectivity

The chromatographic retention time and the precise wavelength (242 nm for TDI isomers and 250 nm for MDI) were used for the method specificity and selectivity. A possible interference was investigated by comparing the chromatograms of derivatives obtained by spiking the standards in 1,2-MP solution or on a coated filter wetted with the No. 3 sweat solution. One peak of interference was observed while stabilizing the isocyanates with GF/1,2-MP filter. An unknown substance was coeluting with the peak of 2,4-TDI-1,2-MP (Figure 2(b)). The QDa data allows for easily distinguishing between the peaks of interference due to different ion mass. This peak is also observed in the chromatogram of the media blank of GF/1,2-MP filter wetted with the sweat solution. The average concentration of three media blank filters was subtracted from the concentration of the standards during the method validation tests.

3.7. Polyurethane foam samples migration tests results

The validated analytical method was used to evaluate the migration of isocyanates from the surface of the flexible PU foam supplied by the PFA. All the foam samples were analyzed within 7 to 23 days post-production. Results obtained are summarized in Table 5. As can be seen in these assays, none of the analytes (2,4- and 2,6-TDI and MDI) were detected in the migration samples. The results of this study suggest that unreacted diisocyanates (MDI, TDI) would not be expected to be present on the surface of, or migrate to skin in contact with, consumer foam products such as those tested here.

4. Conclusion

A method to quantify diisocyanates from sweat samples according to an EPA protocol was developed and validated in order to establish the potential of migration from foam materials. The method was shown to be robust, reliable and accurate. It is therefore possible to analyze diisocyanates such as TDI and MDI from sweat samples. Among six synthetic sweat solutions proposed by EPA, five resulted in good recovery and can be used as a co-solvent during migration tests. This method can be used to quantify any of the three diisocyanates commonly used in flexible PU production. Testing of five “worst-case” foam samples provided by foam manufacturers showed that free diisocyanates were not detected.

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