Emission of methylene diphenyl diisocyanate and methylene dianiline during use of cure-in-place methylene diphenyl diisocyanate-based consumer products

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Abstract
The aim of this study was to provide realistic isocyanate and amine emission data when using different methylene diphenyl diisocyanate (MDI)-based polyurethane consumer products. Emission testing (air sampling) of diisocyanates and corresponding diamines was performed in a full-scale controlled-environment chamber during different work operations, such as gluing, mixing and foaming. The polyurethane products used were construction glue, one-component foam and two different two-component adhesives used in parquet flooring. Air sampling for isocyanates and amines was performed in the breathing zone of the worker and at different positions inside the controlled-environment chamber while the work operations were performed. Air sampling was also performed after the application, at different positions inside the chamber, to cover the post-curing phase. Low air concentrations (0.1–0.7 μg MDI/m³, 0.03–0.2 μg isocyanate group (NCO)/m³) were found in the breathing zone and close to the work operation for some of the gluing applications. No methylene diphenyl diamine (MDA) concentrations above the limit of quantification were found for any of the applications in the breathing zone air. These results indicated that inhalation exposure to MDA or MDI would be expected to be minimal during application of do-it-yourself consumer products containing MDI.

Keywords
Environmental chamber, exposure assessment, methylene diphenyl diisocyanate, methylene dianiline, do-it-yourself products

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Introduction
Diisocyanates are mainly used to produce polyurethane (PU). PU are valuable polymers that are used in a wide range of applications and can be found in almost every sector of the industry (Baysal & Kasapbasi, 2017). Exposure to isocyanates is widely known as a common cause for developing occupational asthma (Ameille et al., 2003; Lefkowitz et al., 2015). Although cases of diisocyanate work-related asthma have been decreasing globally in recent years (Buyantseva et al., 2011; Paris et al., 2012; Reilly et al., 2020), exposure considerations are still important. Diisocyanates are irritants of the upper airways, skin, and eye, as well as dermal and respiratory sensitizers (European Chemicals Association (ECHA), 2021a). High peak exposures have been implicated in the induction of respiratory sensitization (Plehiers et al., 2020). In the case of the diisocyanate considered in the present work, methylene diphenyl diisocyanate (MDI), the No Observed Adverse Effect Level for histopathological pulmonary effects found in mammalian inhalation toxicology studies was 0.2 mg/m³ (Feron et al., 2001).

Occupational exposure to isocyanates is regulated by authorities at the national level and isocyanates are among the group of compounds having the lowest

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occupational exposure limits (OEL) (ECHA, 2019); a
typical OEL for MDI is 0.05 mg/m³ as an 8h time
weighted average (Deutsche Forschungsgemeinschaft,
2020).

Reaction of isocyanates with water results in the
formation of polymeric ureas, and if the isocyanate
concentration is low enough, can additionally lead to
the formation of low levels of the corresponding di-
amine (methylene diamine (MDA) in the case of
MDI). MDA is classified as a carcinogen presumed to
have carcinogenic potential for humans (IARC, 1986),
to which human exposure should be kept as low as
possible. A typical OEL for MDA is 80 μg MDA/m³
[10 ppb] (United States Department of Labor (2019)).

In addition to industrial and professional applica-
tions, diisocyanates are also used in ‘do-it-yourself’
(DIY) products that are intended for use in the ren-
ovation of homes by both professional and non-
professional users (consumers). For studying emis-
sion of hazardous compounds and evaluating different
exposure scenarios from various consumer products,
controlled-environment chamber studies have been
used (Even et al., 2020; Schaeffer et al., 1996; Vojta
et al., 2017). Emissions of diisocyanates have been
tested in controlled-environment chambers during
curing of different PU adhesives (Wirtz et al., 2003;
Wirtz & Saltzhammer, 2002) and from other PU
products such as various foams, varnishes and sealants
(Kelly et al., 1999). It was observed that during curing,
the isocyanate emission was temperature dependent
and occurred in two phases: surface emission and
internal diffusion. Typically, chamber volumes of less
than 10 L have been used for product testing. Full scale
testing of work operations using DIY consumer products
was evaluated for emission of hazardous compounds
(MEFD, 2018). That study included a one-component
PU sealing foam based on MDI, noting an applicator
breathing zone concentration of 6 μg MDI/m³ (com-
pared to typical occupational exposure limit of 50 μg
MDI/m³ in the EU). The risk assessment indicated a risk
for developing airway and skin allergy when applying
the foam based on the content of MDI in the product, and
the use of protective gloves and respiratory protection
during application was recommended. It was noted as
well that there was no risk in remaining in the room
during curing.

The aim of this study was to provide representative
emission data for different applications when using
MDI-based DIY consumer products such as different
kinds of glues and a one-component foam. Concentra-
tion measurements in the work environment
focused on the emission of diisocyanates and di-
amines, and the tests were conducted at high humidity
conditions since these would be expected to promote
any potential amine formation from the isocyanate.

Materials and methods

Chemicals

Dibutyl amine (DBA), acetonitrile, acetic acid, formic
acid, methanol, toluene, 4,4’-methylene dianiline
(MDA) and ethyl chloroformate (ET) were obtained
from Merck (Darmstadt, Germany). Technical grade
MDI (containing 2,4’-MDI and 4,4’-MDI at a ratio of
0.04/1) were obtained from Huntsman (Everberg,
Belgium). Deuterium-labelled DBA [NH(C₄H₉)(C₄D₉)]
and dideuterium-labelled 4,4’-MDA [CD₂(C₆H₄NH₂)₂]
were obtained from Ramidus (Lund, Sweden).

Reference solutions

Solutions of the urea and carbamate ester derivatives
of MDI and MDA, respectively, were prepared and quan-
titatively characterised using LC-Chemiluminescence
detection (CLND) and LC-Mass spectrometry (MS)
according to the method developed, described and
validated by Marand et al. (2004), Karlsson et al. (2002)
and Gylestam et al. (2014) that forms the basis for ISO
17334-1 and 17334-2 (ISO, 2013a, 2013b). This
method uses DBA to derivatize the isocyanates, which
are then measured as the corresponding bis-ureas. The
amines are reacted with ET and are measured as the
 corresponding acetyl derivatives.

The solutions of the urea and carbamate ester deri-
atives of MDI and MDA were diluted in acetonitrile
to appropriate concentrations for the use of calibration
standards and internal standards.

Instrumentation

A triple quadrupole mass spectrometer (MS), Quattro
Micro (Waters, Altrincham, Cheshire, UK) was used
for analysis of air samples. Isocyanate–DBA and
amine-ET derivatives were monitored using positive
electrospray ionization (ES+) and multiple reaction
monitoring (MRM). Quantitative measurements were
made by monitoring the reaction [MH]+→[DBAH]+
for the isocyanate derivatives and [MH]+→[M-46]+
for the diamine derivatives and for the corresponding
deuterium-labelled internal standards ([MH]+→[d9-
DBAH]+ and [d2-MH]+→[d2-M-46]+). For the MS
instrument, the capillary voltage was 3 kV. The temperature of the ion source was 130°C and the desolvation gas temperature was 250°C. The desolvation gas flow was set to 700 L/h. Argon was used as collision gas. Entrance cone voltage and collision energies were optimized individually for the different derivatives. For chromatographic separation of the derivatives, gradient elution was performed, using Shimadzu LC10ADVP micro-LC pumps (Shimadzu Corporation, Kyoto, Japan). The gradient was linear from 40/60/0.05 (v/v/v) acetonitrile/H2O/formic acid to 95/5/0.05 (v/v/v) acetonitrile/H2O/formic acid in 10 min at a flow rate of 0.4 mL/min. Sample injections of 1 μL were made with an LC-Pal autosampler (CTC Analytics AG, Zwingen, Switzerland). The analytical column used was an Ascentis Express 5 cm × 2.2 mm, 2.7 μm C18 (Supelco, Bellefonte, PA, USA). A more detailed description of the instrumental parameters for the analysis of isocyanate–DBA and amine-ET derivatives using LC-MS is available elsewhere (Gylestam et al., 2014; Karlsson et al., 2002; ISO, 2013a, 2013b).

**Products tested**

The products tested were chosen as representative applications of those available DIY products in the EU market. The selection was based on a preceding market study performed in relation to the ECHA Community Rolling Action Plan (CoRAP) review for MDI (ECHA, 2021b). One criterion for DIY product selection was that the products should represent the ‘extreme-case’ for exposure. This was determined by selecting representative products with the highest MDI content based on the information available (safety data sheets, information from the producers as well as measurements of the monomeric MDI content presented in Table 1. The method used in making these measurements is described in Supplementary Material 1). Additionally, as a second criterion, the products should also represent a complete range of available application types in the EU’s DIY market, that is, a one-component foam (OCF), a one-component adhesive product, and a two-component adhesive product with a mixing step. Further details on the process used to select the products tested are provided in the Supplementary Material 1. The products tested were all commercially available in different states within the EU in DIY supply stores during the study phase. However, they were obtained by purchasing them directly from the producers. All products were used in accordance with the manufacturer’s instructions.

Specifically, two kinds of two-component parquet glue (Parquet glue I and Parquet glue II; the main difference between those was the proportion of fillers to active ingredient used in the recipe), an OCF and a one-component construction glue were used. All products were tested during application and the two different parquet glues were also tested during mixing of the two components.

**Controlled-environment test chamber**

The controlled-environment chamber used for the emission testing was a full-scale chamber with an inside

| Test | Product (handling operation) | Container sizes | Number of containers used | 4,4’-MDI content in the product (% w/w) | 2,4’-MDI content in the product (% w/w) | Duration of handling operation (min) | Total operation time (min) |
|------|------------------------------|----------------|---------------------------|----------------------------------------|----------------------------------------|------------------------------------|---------------------------|
| 1    | One-component foam (application) | 500 mL | 2 | 8 | 0.1 | 60 | 120 |
| 2    | Construction glue (application) | 750 g | 1 | 16 | 2 | 120 | 120 |
| 3    | Parquet glue I (mixing) | 5.0 kg (A) + 0.7 kg (B) | 3 | 44 | 5 | 30 | 120 |
| 4    | Parquet glue II (mixing) | 5.0 kg (A) + 0.7 kg (B) | 3 | 41 | 5 | 30 | 120 |
| 5    | Parquet glue I (application) | 5.0 kg (A) + 0.7 kg (B) | 1 | 44 | 5 | 120 | 120 |
| 6    | Parquet glue II (application) | 5.0 kg (A) + 0.7 kg (B) | 1 | 41 | 5 | 120 | 120 |

MDI: methylene diphenyl isocyanate.

*The determination of MDI concentration in the products were performed elsewhere prior to this study (see Supplemental Information). No 2,2'-MDI content was reported for any of the products (LOQ = 0.05%).

*bSingle component, or A and B components, as applicable.

Table 1. Summary of the different products used and handling operations undertaken during the air sampling.
volume of 20.25 m³ (depth = 3.0 m, width = 2.8 m and height = 2.4 m). The inner walls, floor, ceiling and ventilation channels were all made of stainless steel. The air exchange rate was set to 10 m³/h. The air humidity was maintained in the range of 70–80% RH with temperatures in the range of 21.1–22.5°C. Due to the system set-up and to enable the low air exchange rate, there was a small variation in air humidity during and within the tests. However, the humidity remained always within the range of 70–80%.

Emission testing

Emission testing (air sampling) was performed during six different work operations using different PU products (Table 1). The different work tasks included 1: application of OCF; 2: Application of construction glue; 3: Mixing of two component parquet glues A; 4: Mixing of two component parquet glues B; 5: Application of parquet glue I and 6: Application of parquet glue II. Each of the six work operations were performed in duplicates (A & B) resulting in a total of 12 emission tests. All work operations were performed according to the manufacturer’s instructions, modelling real life situations.

Wood used during the testing was conditioned at 20°C and 70–80% RH for at least 24 h prior start of the testing.

Test 1: One-component foam application. The OCF was applied in a wooden frame with spaces simulating filling of cavities or fixing and insulating door/window frames. The frame consisted of wooden roof batten with an approximate width between the batten of 5 cm (Figure 1). The OCF was repeatedly applied for 15 s, paused for 45 s, then reapplied for 15 s; this cycle was repeated continuously until two OCF cans were emptied. The total application time, with the repeated pausing included, was approximately 1 h (each can could be used approximately 30 min before it was empty). The total operation time was 120 min.

Test 2: Application of construction glue. The glue was applied using a fine-grained spatula to one side of two 50-by-5 cm wood pieces before pressing them together, followed by a 5-min wait time (Figure 2). This was repeated for 120 min.

Test 3: Parquet glue I mixing and test 4: Parquet glue II mixing. The mixing of the two-component parquet glues was performed by opening the containers and loading the 0.7 kg isocyanate component into the 5 kg container containing the polyol component (an operation that took 5 min), followed by 10 min of mixing (Figure 3). After the mixing, the lid was placed on the container and a 15-min waiting time elapsed. The procedure was then repeated for a new set of two-component containers. A total of three sets of two-component containers were mixed for each test. Between the second and last mixing, the container was closed but after the last mixing procedure, the lid was...
not placed on the container and a 45-min waiting time elapsed to simulate material in container that is not fully cured yet would be present in the vicinity of the product user. This resulted in a total mixing time of 30 min and a total sampling time of 120 min.

Tests 5 and 6: Parquet glue I and II applications. The mixing of the parquet glue for these tests was performed outside the controlled-environment chamber to avoid contamination. The freshly mixed glue was applied in accordance with the manufacturer’s instructions. The glue was applied on three wood panels at a time (Figure 4), resulting in a total application surface of 0.43 m² (1.6 m × 0.27 m). Five minutes after completion of the first glue application, three new wood panels were placed on top of the glue surface and a new glue application was performed on the second set of wood panels. The procedure was then repeated for a total operation time of 120 min.

Air sampling

For diisocyanate monitoring, samples were collected using a solvent-free sampler (ASSET™ EZ4-NCO Dry Sampler, Supelco, Bellefonte, PA, US) at a flow rate of approximately 0.2 L/min. For amine monitoring, samples were collected using impinger flasks containing 10 mL 0.01 M DBA in toluene and a glass fibre filter in series at a flow rate of approximately 1 L/min. For the 12 tests conducted (i.e. Tests 1–6, A–B each), duplicate samples were collected both in the breathing zone of the worker as well as at stationary locations in the working area for 120 min. One set of duplicate stationary samples were collected close to the work operation and another set 2 m away from the work operation (Figure 5). The samplers used for collecting air samples of the breathing zone were attached to the workers clothing and positioned in such a way that representative sampling of the breathing zone was enabled. The samplers close to the work operation and in the worker’s breathing zone can be seen in Figures 1–3.

This sampling plan resulted in six ASSET samplers for diisocyanate monitoring and six impinger-filter samples for diamine monitoring during the work operation for each of the 12 tests. In addition, immediately after the end of each work operation, new duplicate stationary sampling was performed (close to the work operation and 2 m away from the work operation) for an additional 120 min to assess the post-application curing phase. This resulted in an additional four ASSET samplers for diisocyanate monitoring and four impinger-filter samples for diamine monitoring and was done for all the emission tests except mixing of parquet glue (Test 3 and Test 4).

To ensure that there was no contamination inside the controlled-environment chamber, prior to the start of each test two ASSET samplers and two impinger samplers were collected for 120 min inside the chamber (these were all found negative).

During all the sampling with the impinger-filter samplers, the reagent solution (0.01 M DBA in toluene)
was refilled at regular intervals in the impinger bottle to ensure a sufficient volume of reagent in the sampler.

**Work-up and analysis**

After sampling of diisocyanates using the ASSET samplers, the isocyanate-DBA derivatives were extracted from the filters. Deuterium-labelled isocyanate-DBA derivative (used as internal standard) was added to the extraction solutions. Isocyanate groups were derivatised by DBA immediately upon being captured by the sampler during sampling. The amine groups were derivatised in subsequent two-phase derivatisation procedure with ET to form carbamate esters. The excess reagent and solvent were evaporated, and the samples were re-dissolved in acetonitrile. The samples were analysed using reversed-phase liquid chromatography (LC) and electrospray (ESP) mass spectrometric (MS) detection, monitoring positive ions. Calibration was performed in the range of 0.008–0.56 μg for MDA. Quantification was made by MRM. The LOQ was 0.01 μg for 4,4'-MDA. Sampling at 1000 mL/min for 120 min resulted in a LOQ of 0.09 μg/m³ (The MDA isomers were quantified as a sum and reported as 4,4'-MDA).

A more detailed description of the work-up and analysis procedures for the ASSET sampler and impinger-filter sampler is available elsewhere (Gylestam et al., 2014; Karlsson et al., 2002; ISO, 2013a, 2013b).

**Results**

The complete results of the emission sampling are shown in Table 2. No MDA concentrations above the LOQ were found in any of the samples collected. No diisocyanate concentrations above the LOQ were found in the stationary samples that were collected 2 m from the source during application, nor in any stationary samples during the post-application/curing phase. For the glue mixing and OCF application, no MDI concentrations above the LOQ were found in any of the samples collected. For all gluing applications (1-component glue and 2-component glue after mixing), MDI concentrations in the range of 0.1–0.7 μg/m³ (0.03–0.2 μg NCO/m³) were measured in some of the samples collected in the breathing zone of the operator and in the stationary (area) samples that were collected close to the source. If greater than the LOQ, mainly 4,4'-MDI was detected in the vapour phase and to some extent also the 2,4'-MDI isomer (See Table 2).

**Discussion**

It is important to obtain information regarding the risk of exposure from hazardous compounds during applications that involve the use of consumer products in
Table 2. Methylene diphenyl isocyanate (MDI) concentration in the collected samples from the different emission tests. Test 1: Application of one-component foam; Test 2: Application of construction glue; Test 3: Mixing of two-component parquet glue I; Test 4: Mixing of two-component parquet glue II; Test 5: Application of parquet glue I and test 6: Application of parquet glue II. The concentrations are given in μg/m³. Values that were less than the limit of quantification of 0.03 for MDI and 0.09 for methylene diphenyl diamine (120 min of sampling at 200 mL/min) are marked with ‘-’. ‘A’ and ‘B’ in the test numbers refer to duplicate experiments. The 120–240 min sampling was not performed for Tests 3 and 4; therefore, these are marked as N/A (not applicable) in the table.

| Sampling position | Test 1A | Test 1B | Test 2A | Test 2B | Test 3A | Test 3B | Test 4A | Test 4B | Test 5A | Test 5B | Test 6A | Test 6B |
|-------------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| Breathing zone of the worker, 0–120 min | 2,4'-MDI | 4,4'-MDI | 2,4'-MDI | 4,4'-MDI | 2,4'-MDI | 4,4'-MDI | 2,4'-MDI | 4,4'-MDI | 2,4'-MDI | 4,4'-MDI | 2,4'-MDI | 4,4'-MDI |
| Close to work operation, 0–120 min | — | — | — | 0.1 | 0.7 | — | — | — | — | — | — | — |
| 2 m from work operation, 0–120 min | — | — | — | — | — | — | — | — | — | — | — | — |
| Close to work operation, 120–240 min | — | — | — | — | — | — | — | N/A | N/A | N/A | N/A | N/A |
| 2 m from work operation, 120–240 min | — | — | — | — | — | — | — | N/A | N/A | N/A | N/A | N/A |

MDI: methylene diphenyl isocyanate.
general; this is even more important with DIY consumer products that involve reactive components (i.e. those that ‘cure’). Safety precautions such as ventilation, work routines and personal respiratory protection cannot be guaranteed in the same way for DIY applications as for handling of diisocyanate products in industrial or professional settings. Under the experimental conditions in this study, which were considered to be representative of typical DIY consumer use of these products, no MDA emission was measured above the LOQ, MDI was only measured above the LOQ in a few of the collected samples during the different tests performed and no MDI or MDA emissions were measured during the post-application/curing phase. The LOQ of 0.09 μg/m$^3$ for MDA is three orders of magnitude below the existing occupational exposure limits (OELs) (typical occupational exposure limit of 80 μg MDA/m$^3$ [10 ppb] (United States Department of Labor (2019)). In addition, a theoretical estimation based on the maximum level of MDA found in the curing products (Supplementary Material 2) indicates that the maximum possible MDA air concentration during curing of the products tested would be 0.002 μg/m$^3$ (2 ng/m$^3$).

The air concentrations of MDI that were greater than the LOQ were found in the breathing zone samples or the stationary samples close to the emission source. The levels found were almost two orders of magnitude below existing OELs (typical occupational exposure limit of 50 μg MDI/m$^3$ in the EU) and the no observable effect level (NOEL) in animal tests was 0.2 mg/m$^2$ for MDI (Feron et al. (2001). The DIY consumer products tested were selected as having the highest MDI concentration among products on the market in their category. The results of this study demonstrated that airborne exposure to MDI and MDA during preparation, application and post-application curing of MDI-based DIY consumer products is minimal. It is important to emphasize that, when handling DIY consumer products, instructions for safe handling of the products must be followed and adequate protective gloves and clothing should be used to minimize the risk of dermal exposure.

The diisocyanate and diamine emission found from the different work operations studied are most likely to occur as a vapour. Impinger-filter sampling can be used for simultaneous selective sampling of isocyanates and amines (ISO, 2013a, 2013b). However, there is a risk of underestimating MDI vapour concentrations using impinger flasks due to potential condensation of MDI in the impinger inlet glass tubing. To avoid this, ASSET samplers were used for isocyanate monitoring and impinger-filter samplers for selective amine monitoring after DBA derivatisation of any isocyanate groups captured during sampling. Sampling of isocyanates using ASSET samplers and the determination of their DBA derivatives using LC-MS/MS provides a convenient sampling approach with low detection limits. The LOQs presented in this study for diisocyanate monomers can be lowered even further by increasing the enrichment and optimisation of the MS data acquisition. This would be beneficial if there was a need to compare sampling results to a lower exposure limit or guideline.

### Summary and conclusions

The air emission potential of the DIY consumer products studied was determined under extreme application conditions of high humidity (70–80% RH) in a specialized controlled-environment chamber. No concentrations of airborne MDA were found greater than the LOQ in any of the samples collected during the extreme-case conditions (i.e. high humidity) for any of the applications studied. In addition, airborne MDI concentrations from DIY consumer products were less than the LOQ for the mixing and foaming applications; airborne MDI concentrations were found to be just above the LOQ, in the range of 0.1–0.7 μg/m$^3$ (0.03–0.2 μg NCO/m$^3$), in the breathing zone and close to the work operation for the different gluing operations.

Since the MDI results were almost two orders of magnitude less than the relevant OEL of 50 μg MDI/m$^3$, these results indicated that only incidental exposure to MDI at insignificant levels would be expected from application of MDI-based DIY consumer products. For MDA, the results indicated that no inhalation exposure at any significant levels would be expected during applications of such DIY consumer products. These results provide user exposure estimates under realistic exposure scenarios which could be used in risk assessment/characterisation.

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Supplemental material

Supplemental material for this article is available online.

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