Electronic Supplementary Information (ESI)

Methods

Chemicals

The MDI (98%); N-methyl-amino-methyl-9 anthracene (MAMA) (98%); dibutylamine; DBA (> 99%); acetone (HPLC grade), and acetic anhydride, AA, (98%) were purchased from Sigma-Aldrich (USA) and were used without further purification. MDI-DBA and the MDI-DBA-d9 standard kits were supplied by Supelco (USA). MAMA-MDI was prepared by Nuchem Therapeutics (Canada). Acetonitrile (ACN), water (H_2O), formic acid (FA) (optima grade), and phosphoric acid (H3PO4) (> 99%) were obtained from Fisher Scientific (Canada). Toluene (> 99%) was purchased from EMD Millipore (USA) and dimethylformamide from the J.T. Baker Company (Fisher Scientific, Canada). The glacial acetic and sulfuric (96%) acids, dimethylformamide, triethylamine (HPLC grade), DMF (HPLC grade), and methanol, MeOH (HPLC grade) were obtained from J.T. Baker (Fisher Scientific, Canada).

Instrumentation

Lab preparation involved the use of an Eberbach shaker (Michigan, USA), a Branson B-52 ultrasonic bath (Danbury, USA), and a Sorvall ST 40R centrifuge (Thermo Scientific, Canada). A Zymark Turbovap LV-ZW700 evaporator was used (Biotage, USA). The two MAMA methods samples were analyzed using an ultra-high-performance liquid chromatographic (UPLC)–photodiode array (PDA) system consisting of an LC1290 from Agilent (USA) with a Zorbax Bonus RP 3.0 X 100 mm 1,8 µm (Agilent, USA). Impinger method samples were analyzed using the same instrumentation with a Zorbax Bonus RP 4.6 X 150 mm, 3.5µm (Agilent, USA).

The software used to operate this system and analyze the data was OpenLab CDS, also from Agilent. Asset samples were analyzed using an ultra-high-performance liquid chromatographic–mass spectrometry (UPLC-MS/MS) system consisting of a Waters Acquity UPLC coupled with a Waters Xevo TQ triple quadrupole MS (USA) equipped with an electrospray source and an autosampler having a partial loop and a needle overfill feature (10 µL). The column was an Acquity UPLC BEH C18, 1.7 µm, 2.1 mm x 100 mm, from Waters (Santry, Ireland). The software used to operate the system and analyze the data was Masslynx, V4.1, from Waters (USA).

Analysis

MDI-MAMA Methods

Calibration standards with MAMA-MDI derivative were prepared in DMF to cover a concentration range of 0.015 to 0.700 µg of MDI per 2 mL. The mobile phase consisted of trimethylamine (TEA) buffer (30 mL TEA + 940 mL H2O, pH 3 with H3PO4) (eluant A) and ACN (eluant B), respectively. Each sample was desorbed in 2 mL of desorption solution (60 mL TEA buffer + 140 mL ACN and 400 mL DMF). The LC method used an isocratic elution program, 25% A and 75% B, at 1 mL/min, 8 µL sample injection and column kept at 30°C. PDA detection was performed at λ = 254 nm. All calibration standards and samples were filtered on 0.22 µm

(polytetrafluoroethylene) prior their transfer in 2 mL vials. Run time for each analysis was 8 minutes.

MAMA (as analyte) method

Calibration standards were prepared by dissolving MAMA in ACN in order to obtain concentrations from 2.5 µg/mL to 20 µg/mL. Samples were extracted in 1 mL of ACN and vortexed for a few seconds. The same LC method than the one for MAMA-MDI was applied with the exception of the injection volume of 4 µL and a run time of 4 minutes. All calibration standards and samples were filtered on 0.22 µm prior their transfer in 2 mL vials.

Impinger method

Calibration standards were prepared by mixing, in glass tubes, MDI solutions of various concentration in toluene with MP in toluene at 0,1 mg/mL. The resulting MDI-MP derivative standard solutions, of concentration range 0.05 µg/mL to 0.96 µg/mL, were obtained by evaporating the toluene followed by a re-dissolution in 1 mL of acetic anhydride 0.5% in ACN. The mobile phase consisted of sodium acetate buffer 0.1% in water at pH 6 (acetic acid) (eluant A) and ACN (eluant B), respectively. The LC method used an isocratic elution program, 38% A and 62% B, at 1 mL/min, 20 µL sample injection and column kept at 30°C. PDA detection was performed at λ = 250 nm. Run time for each analysis was 8 minutes. Filter samples, already immersed in toluene, and impinger samples were quantitatively transferred in glass tubes and the toluene were evaporated. The samples were then dissolved in 1 mL of acetic anhydride 0.5% in ACN. All calibration standards and samples were filtered on 0.22 µm prior their transfer in 2 mL vials.

Asset Method

Asset standards and samples were prepared according to Halpenny et al.(1) The prepared solutions were injected (10 µL) into the UPLC-MS via its autosampler, set at 15°C. The mobile phase was composed of ACN + 0.1% FA (eluant A) and water + 0.1% FA (eluant B). The run started with a gradient of 70% eluant A (0.5 min.), ramped to 90% eluant A (2.5 min.), held at 90% eluant A (2 min.), ramped to 100% eluant A (3 min.), and finally equilibrated at 70% eluant A (2 min.). The flow rate in the column was 0.6 mL/min. and the temperature was maintained at 50°C. The Xevo TQ was used in positive mode with the capillary voltage set at 2 kV and the source temperature at 150°C. The desolvation temperature and flow were 500°C and 1,000 L/h, respectively, while the collision gas flow was set at 0.15 mL/min. The [M+H]+ for MDI-DBA is m/z 509.3 and that of the internal standard, MDI-DBA-d18, is m/z 527.4. The data were acquired in multiple reaction monitoring (MRM) mode (Table S1). Manual adjustments were made on the integrations to ensure that the entire peak was covered before the data were recorded. The results were used to create a regression calibration curve with linear fit.

Table S1. MRM species calculated and measured.

Substances	Calculated [M+H]+	MRM transitions	Cone (V)	Collision energy (eV)
MDI-DBA	509	509.3–130.2	35	20
MDI-DBA-d18	527	451.2–139.1	45	30

Quality Control

For each method, all analytical sequences incorporated quality control samples (QCS). For each sequence, the calibration standards were analyzed, followed by a reagent blank (RB), a QC at a value representing 50% of the dynamic range (QC50%) and then followed by the samples. Every 10 samples, the QC50% was analyzed to verify the calibration of the analytical run. At the end of the sequence, the RB, and QC50% were analyzed again, followed by the calibration standards. Each result was reported considering the fact that the QCS were in the acceptable range, which were ± 20% for the QC50.

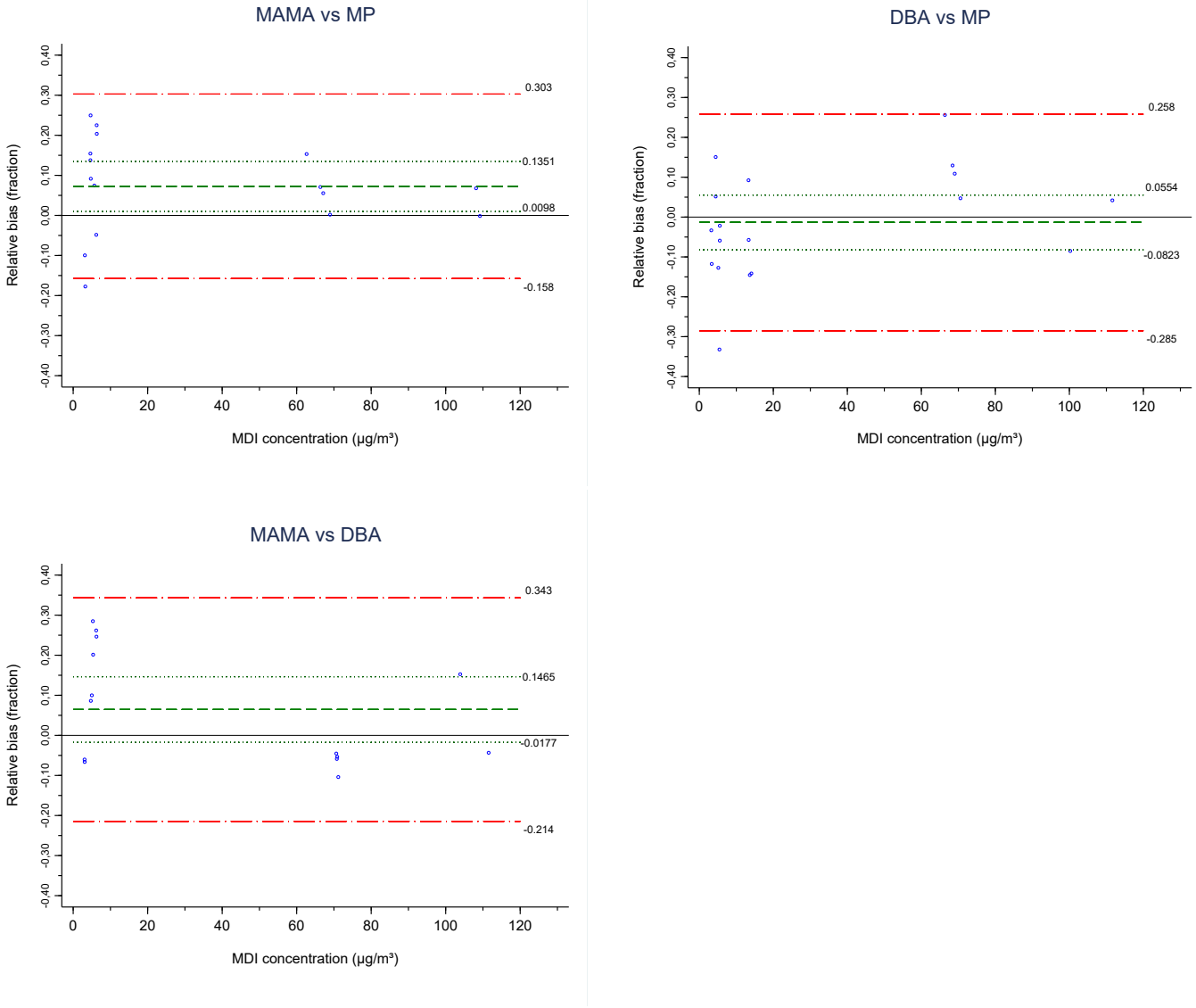

Figure S1. B&A plots of intercomparison of the derivatizing reagents, The relative bias (y axis) consists of the difference between the two paired measurements divided by the mean of these two measurements. The MDI concentration (x axis) consists of the mean of the two paired measurements.

MDI 23 µg/m³ MDI 230 µg/m³

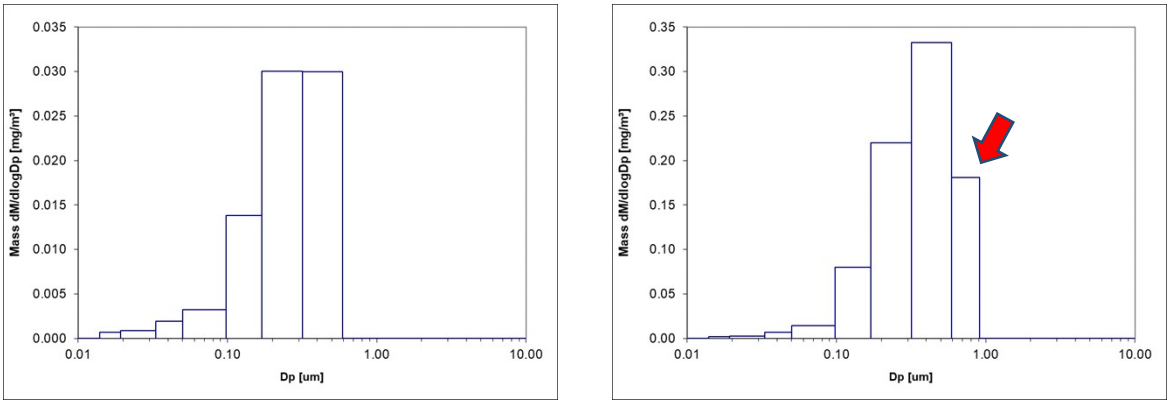

Figure S2. Change in particle-size distribution (mass) measured by ELPI in function of the airborne MDI concentration (2)

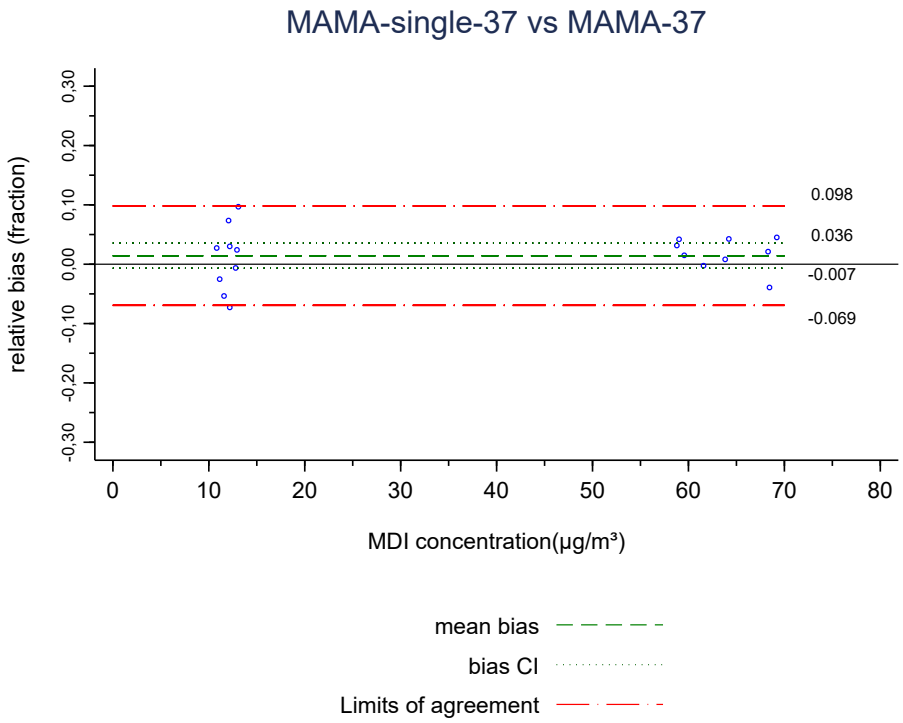

Figure S3. B&A plot of the comparison MAMA-37 vs MAMA-37-single. The relative bias (y axis) consists of the difference between the two paired measurements divided by the mean of these two measurements. The MDI concentration (x axis) consists of the mean of the two paired measurements.

References

1. Halpenny M, Brown J. ASSET™ EZ4-NCO Dry Sampler Extraction Procedure: Sigma-Aldrich; 2013 [Available from: https://www.sigmaaldrich.com/content/dam/sigma-aldrich/docs/Supelco/Instructions/1/ASSET_EZ4-NCO_Extraction.pdf.
2. Aubin S, Wingert L, Gagné S, Breau L, Lesage J. Development and characterization of an adaptable aerosolized methylene diphenyl diisocyanate generation system. Environmental Science: Processes & Impacts. 2021;23(10):1500-8.