INTERPRETATION

Benchmark Guidance Values(BGVs) are set at a level around the 90th pecentile of available validated data, collected from representative workplaces with good occupational hygiene practices. If a result is greater than a BGV it does not necessarily mean that ill health will occur, but it does mean that exposure is not being adequately controlled. Under these circumstances employers will need to look at current work practices to see how they can be improved to reduce exposure.

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BIOLOGICAL MONITORING METHODS

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HEALTH & SAFETY LABORATORY

Method for Isocyanate Metabolites in Urine

Hazardous Substance:
Hexamethylene diisocyanate
Isophorone diisocyanate
Toluene diisocyanate
MDI

Workplace Exposure Limit = 0.02 µg m^{-3} total NCO

Biological Monitoring Guidance value:
Benchmark = 1 µmol isocyanate-derived diamine/mol creatinine

❑ Sample Collection

When: Collect urine samples at the end of exposure - the urinary half-life is around 2 hours and results reflect exposure over the previous 2 - 4 hours.

How: Collect samples in a polystyrene universal container (30ml) containing 0.5g citric acid and close the container securely to prevent leaks.

❑ Description of Suggested Method

Add internal standards (100 µl of heptane diamine 1µM and ethylenedianiline 5µM) to urine (2 ml). Acidified with concentrated sulphuric acid (200 µl). Cap the tubes and incubate at 100 oC for 90 min. After cooling add sodium hydroxide (2ml, 10M) and diethyl ether (4ml) and mix for 20 min. Centrifuge and remove 3ml of each ether layer to a clean tube and remove the solvent under nitrogen. Derivatise the residue with heptafluorobutyric anhydride (50 µl) in toluene (500 µl) in closed tubes at 55oC for 1h. Cool and remove the derivatising reagent under nitrogen and reconstitute in toluene (100µl). Inject (1µl) splitless (350oC, 30 sec) into a capillary column (30m x 0.3 mm BP5 1µm) at 150 oC increasing at 10 oC/min to 240 oC then 20 oC/min to 300 oC. Detect by mass spectrometry with negative ion chemical ionization (methane) monitoring ions at m/z 488, 449, 462, 495 and 542 from 4 to 10 min and m/z 571 and 585 from 11 to 15 min.

❑ References

Williams NR, Jones K, Cocker J. Occup Environ Med. 1999 Sep;56(9):598-601.

❑ Alternative Method

Marand A, Karlsson D, Dalene M, Skarping G. Analyst. 2004 Jun;129(6):522-8.

❑ Sample Transport to Laboratory

Send samples by first class post (or equivalent) to arrive within 48h of collection. If any delay anticipated, store at -20oC. Packaging must comply with Post Office regulations.

❑ Analytical Evaluation

Precision

- within day <5% RSD at 200 nmol/l
- day to day <12% RSD at 200 nmol/l

Detection limit

-3 x background - 1 nmol/l (approximately 0.1 µmol/mol creatinine)

Limit of Quantitation

- 5 x LoD - 5 nmol/l (approximately 0.5 µmol/mol creatinine)

Calibration range

- typically 50 - 300 nmol/l

Sample Stability

-2 days at ambient, > 3 months at -20 oC

Analytical interferences

-None known

❑ Other Information

Elimination half-time

-The half-life for HDI and TDI is around 2 hours so the previous days exposure will not affect the results. The half-life for MDI is much longer (over 50 hours has been reported for repeated exposures) and so previous days' exposures will influence results.

❑ Confounding Factors

Exposure to free hexamethylene diamine, toluenediamine, isophoronediamine and methylene dianiline will also contribute to their respective urinary diamine levels and may confound assessment of exposure to the isocyanates. A pre-exposure sample for MDI may help in these cases .

Unexposed Levels

< 0.5 µmol /mol creatinine

❑ Quality Assurance

Internal QC - must be established

External QA - German Society of Occupatonal & Environmental Medicine (for MDI only)