

Biological Monitoring Guidance Values

Guidance sheet for:

Isocyanates

Monitored by analysis of isocyanate metabolites in urine

BMGV: $1\mu\text{mol}$ isocyanate-derived diamine/mol creatinine

Hazardous Substances

Hexamethylene diisocyanate (HDI)

CAS number: 822-06-0

Methylene diphenyl diisocyanate (MDI)

CAS number: 101-68-8

Toluene diisocyanate (TDI)

CAS number: 584-84-9

Isophorone diisocyanate (IPDI)

CAS number: 4098-71-9

Workplace Exposure Limits:

8-hour TWA: $0.02\text{mg}/\text{m}^3$ total -NCO

15-minute STEL: $0.07\text{mg}/\text{m}^3$ total -NCO



Biological Monitoring Guidance Values

Isocyanates in urine

Biological Monitoring Guidance Value (BMGV)

Guidance value: 1µmol isocyanate-derived diamine/mol creatinine

Other Guidance Values

The ACGIH BEI for TDI is 5µg/g (approx. 5µmol/mol creatinine) and for HDI is 15µg/g (approx. 15µmol/mol creatinine). The DFG BAT for HDI is 15µg/g (approx. 15µmol/mol creatinine) and for MDI is 10µg/g (approx. 4µmol/mol creatinine)..

Sample Collection

Urine samples should be collected at the end of shift into polystyrene universal containers (30mL) each containing 0.5g citric acid.

Sample Transport to Laboratory

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

Description of Suggested Method

Internal standard solution (100µL, contains 1,6 hexamethylene-¹³C₂-diamine, d8-4,4-methylene dianiline and 1,7 heptane diamine) is added to each urine sample (2mL). The samples are then acidified with concentrated sulphuric acid (200µL), the tubes capped and then incubated

added and the samples mixed for 20 minutes. They are then centrifuged, and 3mL of the ether layer is removed to a clean tube and the solvent evaporated under nitrogen. The residue is derivatised with heptafluorobutyric anhydride (20µL) in toluene (200µL) in closed tubes at 60°C for 1h. Samples are cooled; the derivatising agent is removed under nitrogen and the residue reconstituted in toluene (100µL). This is then injected (2µL, splitless, 350°C) into a capillary column (30m x 0.3mm, ZB-5 1µm) at 150°C, increasing at 5°C/min to 200°C, then 25°C/min to 300°C. Detection is by mass spectrometry with negative ion chemical ionisation (methane), monitoring ions at m/z 462, 488 (448/449), 490, 495, 542, 571 and 574.

Analytical Evaluation

Detection limit:

1nmol/L (3 x background, approx. 0.1µmol/mol creatinine)

Limit of Quantitation:

5nmol/L (5 x detection limit, approx. 0.5 230mol/mol creatinine)

Calibration range:

Typically 0-160 nmol/L

Precision:

- within day <5% RSD at 200nmol/L

- day to day <12% RSD at 200nmol/L

Sample stability:

2 days at ambient temperature, >3 months at 20°C

Analytical Interferences: None known



Biological Monitoring Guidance Values

Isocyanates in urine

Other Information

Elimination half-time:

For HDI and TDI in urine, approximately 2 hours, so exposure from previous day(s) will not affect the results.

For MDI in urine, the half-life 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, toluene diamine, isophorone diamine and methylene dianiline will also contribute to their respective urinary diamine levels and may confound assessment of exposure to the isocyanates.

Unexposed level:

<0.5µmol/mol creatinine

Creatinine correction is advised

Alternative Methods

Marand, Å., Karlsson, D., Dalene, M. and Skarping, G., 2004. Extractable organic compounds in polyurethane foam with special reference to aromatic amines and derivatives thereof. *Analytica chimica acta*, 510(1), pp.109-119.

Quality Assurance

Internal QC:

Must be established

External QA:

G-EQUAS (www.g-equas.de).

Email: G-EQUAS@ipasum.med.uni-erlangen.de.

Telephone: +49-9131-8522312.

Interpretation

Urinary isocyanate metabolite results reflect systematic exposure to isocyanates that may have entered the body by inhalation or through the skin. If biological monitoring results are greater than the guidance value, 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.



Biological Monitoring Guidance Values

Isocyanates in urine

Links

EH40 List of Approved Workplace Exposure Limits

<http://www.hse.gov.uk/pubns/books/eh40.htm>

Biological Monitoring at HSL

<http://www.hsl.gov.uk/online-ordering/analytical-services-and-assays/biological-monitoring>

References

Williams, N.R., Jones, K. and Cocker, J., 1999. Biological monitoring to assess exposure from use of isocyanates in motor vehicle repair. Occupational and environmental medicine, 56(9), pp.598-601.

For further advice, please contact us:

Sample Registration, Health and Safety
Laboratory, Harpur Hill, Buxton. SK17 9JN.

registration.sample@hsl.gsi.gov.uk

01298 218099

