**Isocyanates**

***Who is this guidance for?***

This guidance is primarily aimed at employers or individuals with delegated responsibility for managing workplace exposure to substances. Whilst it is not exhaustive, the information presented is intended to demonstrate how biomonitoring can help with this duty. Some simple advice is presented to help non-specialist users to get the most out of biomonitoring covering (1) when to take a sample to ensure reliable and comparable results over time; (2) putting the result into context with respect to background (environmental) levels or what can reasonably be achieved with good exposure control; and (3) some basic technical data that can help to evaluate an analytical service provider. For further information you should consult your chosen analytical service provider who should be happy to discuss your specific requirements and find solutions.

**Isocyanates**

Monitored by analysis of isocyanate metabolites in urine

**BMGV**: 1µmol 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: 0.02mg/m3 total -NCO

15-minute STEL: 0.07mg/m3 total -NCO

***Biological Monitoring Guidance Value (BMGV)***

1µmol isocyanate-derived diamine/mol creatinine.

Based on 90th percentile of data from exposed workers judged by expert occupational hygienist to be used good exposure control practices.

***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/L (approx. 4µmol/mol creatinine).

Guidance values set by different organisations will vary, based on factors including available data and scientific knowledge at the time and interpretation of the toxicology data.

***Sample Collection***

Urine samples should be collected at the end of shift into polystyrene universal containers (30mL) 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 samples chilled – ideally frozen if suitable facilities are available. Packaging must comply with relevant postal regulations for biological samples (UN3373).

***Description of Suggested Method***

Urine samples (2ml) are acid-hydrolysed to release free di-amine metabolites. Isotope-labelled analytes are added as internal standard. Following liquid-liquid extraction into diethyl ether, samples are derivatised prior to analysis by gas chromatography with mass spectrometry detection, using negative chemical ionisation (methane). Multiple similar methods have been reported by different laboratories and they can be found in the published scientific literature.

**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 µmol/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

Quality assurance: GEQAS (www.g-equas.de).

***When to take a sample?***

Elimination half-life is a measure of the rate of removal of a substance that has been taken into the body. It helps to identify when it is best to take a sample following potential exposure and indicates the potential ‘exposure window’ that will be reflected by a result.

For HDI, IPDI and TDI, the elimination of their corresponding diamine metabolites into urine has an approximate half-life of between 2 and 3 hours. These are fairly short half-lives, so urine samples should be collected at end of the shift (or even shortly after the end of a task if exposure is anticipated to only occur early in a shift). Results will predominantly reflect that day’s exposure (previous 10 – 15 hours).

For MDI in urine, the half-life is much longer (over 50 hours has been reported for repeated exposures (Dalene et al, 1997) and so previous days’ exposures will influence results. Post-shift urine sampling is still recommended, however, if individuals are potentially exposed over consecutive days, taking a sample towards the end of the working week can be considered. MDI exposure commonly includes a significant component of dermal absorption (via skin exposure) and this is reflected by a longer elimination half-life. Consequently, where dermal exposure is significant, higher urine MDA levels are often observed pre-shift the following day. Determining the optimal time to take samples for biomonitoring MDI exposure therefore requires consideration of when and how product is being used and likely routes of exposure.

**Other Information**

***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. Amines are themselves widely used industrial chemicals and they present their own potential hazards to health that should be properly controlled.

**Unexposed level**

Below the quantitation limit.

There is potential for very low-level exposure to isocyanates from a variety of consumer products, but these are unlikely to be detected in urine samples. Exposure to some DIY products, including foams and adhesives, or application of isocyanate-containing spray paints outside of work could give rise to more elevated levels.

**Creatinine correction is advised**

***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. An elevated result should be re-tested as soon as possible to help establish whether it represents ongoing workplace exposure or a ‘one-off’ event. If necessary, employers will need to look at current work practices to see how they can be improved to reduce exposure.

***Further information***

EH40 List of Approved Workplace Exposure Limits <http://www.hse.gov.uk/pubns/books/eh40.htm>

Further information on undertaking urine sampling for isocyanate exposure measurement is available in HSE’s COSHH essentials general guidance leaflet, G408. <https://www.hse.gov.uk/pubns/guidance/g408.pdf>

Biological Monitoring: A tool for helping to assess workplace exposure (August 2021). Published by British Occupational Hygiene Society (www.bohs.org). [BOHS-Biological-Monitoring-A-tool-for-helping-to-assess-workplace-exposure-rebranded.pdf](https://www.bohs.org/app/uploads/2021/08/BOHS-Biological-Monitoring-A-tool-for-helping-to-assess-workplace-exposure-rebranded.pdf)

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:

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**Biological Monitoring at HSE**

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