HSE
Health and Safety Executive

Organic isocyanates in air

Laboratory method with derivatisation in situ either on treated glass fibre filters or in solution using impingers with a treated back-up filter in series, followed by high-performance liquid chromatography analysis

MDHS25/4

Methods for the Determination of Hazardous Substances
Health and Safety Laboratory

Scope

1 The procedure can be used for the determination of time-weighted average concentrations of organic isocyanates in workplace atmospheres. It is suitable for a wide range of organic compounds containing isocyanate functional groups, including isocyanate monomers such as toluene diisocyanate (TDI) (both 2,4-TDI (CAS No. 585-84-9) and 2,6-TDI (CAS No. 91-08-7) isomers), 1,5-diisocyanatonaphthalene (NDI, CAS No. 3173-72-6), 1,6-hexamethylene diisocyanate (HDI, CAS No. 822-06-0) and methylenebis(4-phenylisocyanate) (MDI, CAS No. 101-68-8) and prepolymers derived from diisocyanate monomers.

2 The key derivatising agent 1-(2-methoxyphenyl)piperazine (1,2-MP) used during this analysis is subject to supply restrictions and currently alternative methods of analysis are under investigation to alleviate this issue (see Appendix 1).

Summary

3 A measured volume of air is drawn through a glass impinger containing 1-(2-methoxyphenyl)piperazine (1,2-MP) absorbing solution backed with a filter impregnated with 1,2-MP reagent (isocyanate aerosols) or alternatively a single filter impregnated with the 1,2-MP reagent (isocyanate vapour). The organic isocyanates present in the air will react with the 1,2-MP to form non-volatile urea derivatives.

4 After extraction and concentration, the sample solutions can be analysed by high-performance liquid chromatography (HPLC) with ultraviolet (UV) and electrochemical (EC) detection. Isocyanate-derived peaks can be identified on the basis of the ratio of EC and UV responses; by diode array detection (DAD) spectral library matching and comparison with derivatised bulk formulations (where available).

5 Quantification can be achieved by comparison with the relevant isocyanate monomer standard. Total isocyanate-in-air concentration are then determined from the sum of all the isocyanate-derived peaks.

6 The use of alternative methods not included in the MDHS series is acceptable provided they can demonstrate the accuracy and reliability appropriate to the application.

Recommended sampling

7 Both filters impregnated with derivatising reagent and impingers containing solutions of derivatising reagent have been used to collect mixtures of airborne particles and vapour. However, neither of these systems has been found to be effective alone for all isocyanate environments. Mixtures of airborne particles and/or

vapours (isocyanate aerosols) are not collected satisfactorily on coated filters alone because the isocyanate may react with other compounds, either in the airborne particle or already collected on the filter.

Furthermore, impingers appear unsuitable for sampling the range of isocyanate particle sizes likely to be encountered in the workplace, as particles of less than about 1 µm diameter are inefficiently collected (see further information in appendix 2). Similarly, isocyanate species present in large particles (>10 µm) and collected on reagent coated filters may not be efficiently derivatised. The combination of an impinger with a reagent-coated filter in series will collect both isocyanate aerosols and vapours efficiently[1] and mitigate these issues".

8 When employing fixed point sampling, the samplers should be positioned at approximately head height, away from obstructions, fresh-air inlets or strong winds. The sampling procedures are otherwise the same as for personal sampling.

9 Air monitoring should be representative of the working periods of individuals exposed. General guidance on workplace monitoring is given in the HSE publication *Monitoring strategies for toxic substances* (HSG173).[2]

Filter samples (vapours)

10 Recommended air volume: 20 l to 900 l, collected at 2 $l.min^{-1}$. It is recommended to collect several shorter samples instead of one of full duration if heavily loaded filters are expected. This procedure is recommended for both personal and static sampling.

Impinger with filter in series (aerosols)

11 Recommended flow rate: up to 1 $l.min^{-1}$. Maximum sampled volume 480 l. Minimum recommended sample volume 15 l.

12 For long-term samples, select a sampling period of appropriate duration so that the back-up filter does not become overloaded with particulate matter. For sampling over shorter periods, the flow rate should not exceed 1 $l.min^{-1}$ to minimise evaporation of toluene. It may be necessary to top up the impinger with toluene due to evaporation during sampling. This sampling train is not recommended for personal sampling for reasons outlined in Appendix 2 and an alternative sampler is described.

Prerequisites

13 Users of this method will need to be familiar with the content of PD ISO/TR 17737,[3] BS ISO 16702,[4] and MDHS14.[5]

Safety

14 Users of this method should be familiar with standard laboratory practice and carry out a suitable risk assessment. It is the user's responsibility to establish appropriate health and safety practices and to ensure compliance with regulatory requirements.

Sampling equipment

15 Filter holders: An IOM sampler fitted with a stainless-steel cassette, for collection of vapour phase isocyanates, and a 25 mm Swinnex filter holder, for use in series with the impinger for aerosol sampling, have been found suitable for supporting 1,2-MP impregnated filters. Samplers should be pre-cleaned and operated according to the manufacturer's instructions.

16 Glass-fibre filters (for impregnation with 1,2-MP reagent): Binder-free filters with capture efficiency of not less than 95%, eg Whatman GF/A, 25 mm have been found suitable for use with both the IOM and Swinnex holders.

17 Spill-proof midget impinger: The two parts should be matched so that the distance between the inlet tube and the receiver bottom is 1–2 mm. Clean in laboratory detergent solution, rinse thoroughly with distilled water and dry or alternatively use a laboratory washing machine.

18 Personal sampling pumps that meet the requirements of BS EN ISO 13137.[6]

19 A portable flow meter calibrated against a primary standard, with a measurement uncertainty typically less than ±2%.

20 Flexible plastic tubing of a suitable diameter for making a leak-proof connection from the sampling train to the pump; belts and harnesses to facilitate attachment of sampling apparatus to sample subjects; flat-tipped tweezers for handling filters; sample vials with PTFE lined caps for filter and impinger solutions and a container to transport them from site to the analytical laboratory.

Laboratory reagents and equipment

Reagents

21 During the analysis, use only reagents of recognised analytical grade.

22 1-(2-Methoxyphenyl)piperazine) (1,2-MP, >98% by mass).

23 Toluene: Dried over anhydrous calcium chloride or magnesium sulphate for preparation of impregnated filters or monomer standards (this step may be omitted for preparation of absorbing solution).

24 Acetonitrile: HPLC grade.

25 Hexane: HPLC grade.

26 Dichloromethane: HPLC grade"

27 Water: HPLC grade.

28 Anhydrous sodium acetate.

29 Acetic anhydride.

1,2-MP impregnated filters

30 Prepare the 1,2-MP impregnated filters as follows: Accurately weigh out approximately 0.25 g of 1,2-MP and transfer to a 25 ml volumetric flask. Make up to the mark with anhydrous toluene and shake to mix (solution A). In an area free from dust and isocyanates, using flat-tipped tweezers, place a number of 25 mm glass-fibre filters on a clean glass plate so that no filters touch. Add 200 µl of solution A onto the surface of each filter, ensuring that the reagent soaks the whole filter. Allow the filters to dry in air for several hours and transfer to a screw-cap amber bottle. Store in a dark cupboard or refrigerator for up to 6 months.

Impinger absorbing solution (50 µg.ml^{-1})

31 Accurately weigh approximately 50 mg of 1,2-MP and transfer to a dry 100 ml volumetric flask. Dissolve and make up to volume with dry toluene. Dilute 10 ml to 100 ml with dry toluene in a second volumetric flask to give the 260 µM absorbing solution. Prepare fresh solution weekly.

Monomer derivatives

32 Add 0.1 g of the appropriate isocyanate (~1 mmol for the common diisocyanates such as HDI, TDI and MDI) to 0.6 g (~3 mmol) of 1,2-MP dissolved in dry toluene (10 ml) and leave to stand for 1 h. A white crystalline urea will precipitate. Collect the precipitate on a filter paper (eg Whatman No 1) and wash several times with dry toluene to remove excess reagent. Re-crystallise the urea from toluene, by warming to about 60 °C and slowly adding methanol to dissolve the urea. Allow to cool then filter the resulting crystals, washing with cold, dry toluene. Dry the solid in air. The urea derivatives of the mono and most of the diisocyanates are only slightly soluble in toluene but readily soluble in methanol or acetonitrile.

33 MDI and HDI have low solubility in toluene and therefore the following procedure will be more suitable for these compounds: Slowly add a solution of the appropriate isocyanate (0.25 g, ~2 mmol NCO for MDI and HDI) in dichloromethane (25 ml) to a solution of 1,2-MP (1 g,~5 mmol) in dichloromethane (50 ml). A white suspension will form. Pipette this drop-wise to a beaker of hexane (500 ml) while stirring. Filter the resultant precipitate and dissolve in a minimum volume of dichloromethane. Add hexane to re-precipitate the solid, filter and wash with hexane. Dry the urea derivative in air. This procedure may also be used for isocyanate oligomers, polymers and prepolymers.

HPLC mobile phase

34 The preferred composition of the mobile phase depends on the isocyanate formulation of interest. The greater the proportion of acetonitrile in the mobile phase, the faster the peaks will elute. A ‘slow’ mobile phase is recommended for monomeric diisocyanates and monoisocyanate 1,2-MP derivatives. For polymeric isocyanate 1,2-MP derivatives, a ‘fast’ mobile phase is more suitable. Gradient elution with an appropriate mobile phase concentration can also be adopted to optimise elution times. Care must be taken to elute all the polymeric 1,2-MP derivatives and not to co-elute any monomeric species with the acetylated 1,2-MP reagent peak at the start of the chromatogram.

35 ‘Slow’ mobile phase: Dissolve 5 g of anhydrous sodium acetate in 1 l water. Adjust the pH of this solution to 6.0 by drop-wise addition of glacial acetic acid. Add 550 ml of this solution to acetonitrile (450 ml) to give a volume mixture of 45% acetonitrile and 55% sodium acetate buffer.

36 'Fast' mobile phase: Dissolve 5 g of anhydrous sodium acetate in 1 l water. Adjust the pH of this solution to 6.0 with glacial acetic acid. Add 400 ml of this solution to acetonitrile (600 ml) to give a volume mixture of 60% acetonitrile and 40% sodium acetate buffer.

Equipment

37 A balance, calibrated against a primary standard, for the preparation of the internal standard solution and calibration standards. The balance should be capable of weighing to ±0.1 mg over the range 0 to 100 mg.

38 A selection of laboratory glassware, including pipettes, beakers, measuring cylinders and volumetric flasks, Class A, complying with the requirements of BS EN ISO 1042:2000.[7]

39 Piston-operated micropipettes complying with the requirements of BS EN 8655-6:2002.[8]

HPLC system

40 An HPLC system with ultraviolet (UV) and electrochemical (EC) detectors in series. The EC detector should be used in the oxidation mode. A diode array detector (DAD) is also recommended for confirmation of identity. Temperature fluctuations must be avoided in order to obtain the required analytical sensitivity. This can be achieved by fitting the HPLC column and EC detector with a thermostat. EC performance can be improved by recirculating the mobile phase in a closed loop and by use of a guard cell (set to ~50 mV above analytical cell potential) before the injector. A pulse dampener will also decrease the LC system noise (pulse ripple) and so increase signal to noise ratio.

41 Typical instrumental conditions are given in Table 1. Conditions will depend on the presence of interfering compounds and the type of isocyanate formulation.

Column dimensions	Length, 100 mm; internal diameter, 4.6 mm	
Column packing	Octadecylsilane (C18), 5 µm or similar	
Column temperature	20 °C	
Flow rate	1 ml.min^{-1}	
UV detector	242 nm and/or DAD	
EC detector	Porous graphite electrode, operating potential of + 0.8 V	
Typical isocyanate retention times (min)	'Slow' conditions	'Fast' conditions
HDI	6	3
MDI	11.5	4.5
2,6-TDI	5	-
2,4-TDI	6.7	-
HDI (polymers)	-	6 to 45
MDI (polymers)	-	6 to 45

Table 1 Typical HPLC conditions and retention times for some common isocyanate monomers and polymers

42 The analytical conditions should be optimised for the isocyanates or formulation being investigated. The excess 1,2-MP reagent peak may mask the isocyanate monomer peak. To improve the separation, decrease the acetonitrile concentration of the mobile phase and acetylate the sample. For a more rapid analysis of MDI, modify the mobile phase by increasing acetonitrile concentration, eg with the above system 56% acetonitrile gave an MDI retention time of 7 minutes. Where high concentrations are found, dilute the sample solutions with acetonitrile to bring the concentration back within the calibration range.

Preparation and sampling

Preparation of filter samplers (isocyanate vapour)

43 In an area free from isocyanates, load the 1,2-MP impregnated filters into clean, dry IOM samplers using clean flat-tipped tweezers.

44 Connect each loaded sampler to a sampling pump using plastic tubing ensuring that no leaks can occur.

45 Switch on the pump, allow to stabilise and attach the calibrated flow meter to the sampler so that it measures the flow through the sampler inlet orifice. Set the flow rate to 2 $l.min^{-1}$. Switch off the pump and seal the sampler with its protective cover to prevent contamination during transport to the sampling position.

Preparation of impinger and filter in series samplers (isocyanate aerosols)

46 In an area free from isocyanates, load the 1,2-MP impregnated filters into clean, dry Swinnex samplers using clean flat-tipped tweezers and cap.

47 Immediately before sampling, transfer 10 ml of the absorbing solution into the impinger.

48 Attach the inlet of Swinnex filter holder containing the 1,2-MP impregnated filter to the outlet of the impinger using a short length of tubing.

49 Connect the sampling train via the outlet of the filter holder to the sampling pump using plastic tubing ensuring that no leaks can occur.

50 Switch on the pump, allow to stabilise and attach the calibrated flow meter to the inlet of the impinger and set the flow rate to 1 $l.min^{-1}$. Switch off the pump and cap the inlet to the impinger.

Collection of filter samples (vapour phase samples)

51 In an area free from isocyanates, attach the sampler in the worker's breathing zone within 300 mm of the nose and mouth.

52 When ready to begin sampling, remove the protective cover and switch on the pump and adjust the flow rate if necessary using the calibrated flow meter.

53 Record the time at the start of the sampling period, and if the pump is equipped with an elapsed time indicator, ensure that this is set to zero. The recommended air volume is within the range 20 l to 900 l at 2 $l.min^{-1}$.

54 Monitor the performance of the sampler periodically, a minimum of every 2 hours (or more frequently if heavy filter loadings are suspected). It is preferable to

take several short-term samples instead of one long period sample if a heavy loading is expected.

55 Terminate sampling and check the flow rate with the calibrated flow meter and consider the sample to be invalid if the flow rate was not maintained to within ±5% of the nominal value throughout the sampling period.

56 In a clean environment, remove the filter from the sampler and place in a glass vial, with PTFE-lined cap, containing 1,2-MP absorbing solution (2 ml). If deposition of aerosol on the sampler walls is suspected, rinse with a little dilute 1,2-MP solution and add the washings to the vial.

Collection of impinger backed by filter samples

57 When ready to begin sampling, remove the protective cap to the impinger and switch on the pump.

58 Record the time at the start of the sampling period, and if the pump is equipped with an elapsed time indicator, ensure that this is set to zero.

59 Draw a measured volume of air through the sampler at a flow rate of no more than 1 $l.min^{-1}$.

60 Monitor the performance of the sampler periodically, and top up the impinger with toluene if significant evaporation has occurred.

61 Terminate sampling and check the flow rate with the calibrated flow meter and consider the sample to be invalid if the flow rate was not maintained to within ±5% of the nominal value throughout the sampling period.

62 In a clean environment, remove the filter from the sampler and place in a glass vial containing 1,2-MP absorbing solution (2 ml).

63 Transfer the contents of the impinger to a glass vial with PTFE-lined cap. Rinse the impinger and inlet tube with a little toluene and add the washings to the vial and cap.

Blanks

64 Field blanks should be prepared by using samplers identical to those used for sampling and subjecting them to the same handling procedure as the samples except for the actual period of sampling.

Calibration

65 Weigh out a known mass of the urea derivative, place in a 100 ml volumetric flask and make up to the mark with acetonitrile or methanol.

66 Take aliquots of this solution and dilute volumetrically in acetonitrile or HPLC mobile phase to generate a series of standard solutions over the NCO concentration range 0.01 $\mu g.ml^{-1}$ to 1.0 $\mu g.ml^{-1}$. Prepare at least six calibration standards to overlap the analytical range.

67 The concentration of isocyanate groups in the standard is given by:

$$NCO\ \mu g.ml^{-1} = (W \times M_n \times N)/M_u$$

Where:

W = the concentration ($\mu g.ml^{-1}$) of the urea derivative in the standard

M_n = the relative molecular mass of NCO

N = the number of isocyanate groups per molecule

M_u = is the relative molecular mass of the urea derivative

68 Inject a known fixed volume (10 µl to 20 µl) of each standard solution into the HPLC and measure the UV response of the target compound at 242 nm (as a peak height or area). Plot the UV response against the corresponding analyte concentration of the standard, in $\mu g.ml^{-1}$, and construct the line of best fit. The slope of this line is the detector response factor (R_F) for the target compound.

Sample analysis

Pre-reaction of sample and blank impinger samples before HPLC analysis

69 Allow at least 24 hours to elapse from the time of sampling to ensure complete conversion of any isocyanate pre-polymers to 1,2-MP derivatives.

70 Acetylation of unreacted 1,2-MP reagent improves the chromatographic separation of isocyanate derivatives. After sampling, transfer the contents of the impinger to a screw-cap vial; add 100 µl acetic anhydride and mix.

71 Evaporate to dryness, and then dissolve the residue in acetonitrile (2 ml) or mobile phase and transfer to a glass HPLC sample vial.

Pre-reaction of sample and blank filter samples before HPLC analysis

72 Add 100 µl acetic anhydride into each glass vial containing the 1,2-MP desorbing solution and filter paper and mix.

73 Evaporate to dryness and dissolve the residue in 2 ml acetonitrile or mobile phase.

74 Filter this solution into an HPLC sample vial, using a 0.5 µm syringe filter.

Determination of airborne isocyanate for monomeric isocyanates (UV detection)

75 Inject the same fixed volume of the sample and blank solutions as used for the calibration standards. Measure the UV response at 242 nm (or other appropriate wavelength) of the target compound(s) and convert this value to an analyte concentration, in µg.ml-1, by dividing by the RF value obtained from the calibration standards. Analyse any samples used to determine sampling efficiency (see Appendix 4) in the same way.

Identification of polymeric isocyanates: EC/UV ratio approach

76 Analytical standards of the polymeric isocyanate 1,2-MP derivatives are not readily available. If the presence of isocyanate oligomers, polymers or prepolymers is suspected, these peaks must be positively identified as isocyanate derivatives before quantitation.

77 Examine all peaks in the HPLC trace and calculate the ratio of the EC to UV response (at a given wavelength) for each peak. Also analyse the corresponding isocyanate monomer derivative standard under the same operating conditions. Usually, the monomer is present in the prepolymer chromatogram, but this may be at very low levels compared to the polymer peaks, eg typically <1% monomeric HDI in poly-HDI-based paints used in the motor vehicle repair industry.

78 The ratio of the peak responses from the two detectors can be calculated as follows:

The polymer peak response ratio, y, is given by Equation 1:

$y = E_{poly}/U_{poly}$ (Equation 1)

Where:

E_{poly} = the polymer peak response of the EC detector

U_{poly} = the polymer peak response of the UV detector

The monomer peak response ratio, x, is given by Equation 2:

$X = E_{mono}/U_{mono}$ (Equation 2)

Where:

E_{mono} = the monomer peak response of the EC detector

U_{mono} = the monomer peak response of the UV detector

79 Peaks which have a detector response ratio, y/x, of 0.6 to 1.7 are assigned as being derived from isocyanates. To calculate the total isocyanate concentration in the sample solution, measure the EC response of these peaks relative to the monomer derivative calibration graph, and sum these values.

80 With some prepolymer preparations, it can take over 40 minutes to elute all the components. In such cases, it is advisable to modify the mobile phase or apply gradient elution after the initial run. Increasing the acetonitrile content will reduce elution times and improve peak shapes in the latter portion of the chromatogram, allowing accurate integrals to be calculated.

81 Ideally the ratio of y/x would be 1, ie polymeric and monomeric isocyanates would have the same EC to UV response ratio. In practice, the UV responses for monomers and polymers are different. It has been found empirically that isocyanates give y/x values between 0.6 and 1.7.[9]

82 The detector response ratio varies with isocyanate type and EC detector conditions. It is also dependent on the wavelength of the UV detector and the potential at which the EC detector is set. However, in a series of analyses performed on the same day, this ratio should remain relatively constant for a given isocyanate monomer and its derived prepolymers.

83 The EC/UV ratio is a guide to identification only. It is the responsibility of the analyst to correctly identify the major peaks in a chromatogram.

Confirmation of identification for polymeric isocyanates (prepolymers)

Analysis of a bulk sample

84 In addition to the ratio method described above, it may be possible to confirm the presence of polymeric isocyanates (prepolymers) if a bulk sample of the process polymer is available. This can be achieved by comparing retention times in the bulk and sample chromatograms for the 1,2-MP-derivatised material. This approach will not be successful for end-capped, or stoved, isocyanates.

85 It is possible that some peaks in the sample chromatogram may not correspond to those in that of the bulk, as some modification of the prepolymer can take place in the atmosphere, eg by partial reaction with atmospheric polyol compounds. In practice, additional peaks have not been found in the samples routinely analysed.[9,10,11] If partially reacted species exist, the EC response of the prepolymer 1,2-MP derivative should still be proportional to the number of free isocyanate groups remaining, since this is primarily a function of the attached methoxyphenyl groups, not of the isocyanate matrix.

Confirmation of identity using a diode array detector

86 The use of a diode array detector (DAD) can also be of use for confirmation that a peak is derived from an isocyanate[9] and allows retention time matching of the samples to be carried out against monomer and bulk derivative standards. Peak purity routines can be run to detect co-eluting compounds. Library matching of spectra can also be carried out to aid identification as it has been found that isocyanate prepolymers give DAD spectra that closely match that of the parent monomer.[9,11]

87 The DAD also allows the use of gradient elution to decrease run times and improve peak shapes for any later eluting peaks. Running a gradient up to 100% acetonitrile should remove any highly polymerised isocyanates if these compounds are thought to be present. Gradient elution is not suitable for EC detection, as the response factors of the EC are dependent on mobile phase composition.

Confirmation of identity using other techniques

88 HPLC with mass spectroscopic detection has also been used to confirm peak identity.[10,12,13] The use of HPLC with mass selective detection is described further in Appendix 3. Titration or Fourier transform infrared (FT-IR) spectrometry can be used to determine isocyanate content if a non-derivatised bulk sample is available.[10,11,14] Safety data sheets and manufacturer's information are other useful sources of information for underivatised bulks.

Quantification of airborne isocyanate for polymeric isocyanates (EC detection)

89 For routine analysis of monomers, as described above, only UV detection need be used as standards for these compounds are readily available or can be easily synthesised. However, for the majority of industrially used polymeric isocyanates no standards exist. This method quantifies these compounds using the EC detector, which operates by oxidation of the methoxy-group on the isocyanate derivative. As this group is common to all 1,2-MP derivatives, the polymeric species may be calibrated using the corresponding isocyanate monomer.[15]

90 After identification of the isocyanate-derived peaks, as described by the procedures above, the peaks of interest can be quantified using the EC response factor for the relevant isocyanate monomer 1,2-MP derivative, in a similar manner

to that described for UV detection of monomeric isocyanates. The EC detector, used to quantify polymeric isocyanates, is less stable and linear than the UV detector used to quantify the monomeric compounds. The use of an internal standard has been found to dramatically improve the linearity and variability of the EC detector.[15]

Sampling efficiency

91 Sampling efficiency (SE), may be less 100% due to incomplete reaction of the isocyanate with the 1,2-MP reagent on the filter or in the impinger solution, eg if a large air volume is taken or the sampling rate is too high. Low SE can also occur on the filter if the local concentration of 1,2-MP reagent is depleted, eg because of large droplets with a high isocyanate content.

92 Appendix 4 describes a procedure for the determination of SE when using impingers. Usually, sampling efficiencies fall between 95 and 105%. Correction should be made for incomplete absorption if SE falls below 95% under the sampling conditions used. Alternatively, it may be feasible to use two impingers in series and sum the results.

Calculation of results

Volume of air sample

93 Calculate the sampled air volume, V_S, in litres, of each air sample by multiplying the mean volumetric flow rate in litres per minute by the sampling time in minutes.

Total isocyanate in air

94 Calculate the total isocyanate in air concentration (µg $NCO.m^{-3}$) using Equation 3:

$$\mu g\ NCO.m^{-3} = ((C_S - C_B) \times 1000 \times V_d) / (SE \times V_S) \quad \text{(Equation 3)}$$

Where:

C_S = concentration of isocyanates in the sample (µg $NCO.ml^{-1}$)

C_B = concentration of isocyanates in the blank (µg $NCO.ml^{-1}$)

SE = sampling efficiency

V_S = volume of air sampled (l)

V_d = desorption volume (ml)

Detection limits

95 The qualitative and quantitative detection limits for isocyanate, defined as three times and ten times the standard deviation of six blank determinations, have been found to be typically around 0.001 and 0.004 µg NCO per sample respectively (EC detection). For a 15 l air sample, these figures correspond to qualitative and quantitative detection limits of 0.07 $\mu g.m^{-3}$ and 0.27 $\mu g.m^{-3}$ respectively.

Expanded uncertainty

96 The combined expanded uncertainty[16] for a range of isocyanate formulations spiked at four concentration levels onto filters and impinger backed 1,2-MP impregnated filter samplers was 54%.[4] No significant difference was observed between the filter only and impinger-filter samplers in these tests.

Appendix 1

Supply restrictions for the derivatising agent

1 The derivatising agent 1-(2-methoxyphenyl) piperazine (1,2-MP) as used in this MDHS has recently become a controlled substance under the UK's misuse of drugs legislation. It has been placed on the controlled drug list by the Home Office (HO) as a Schedule 1 substance, the highest category. Although only the 1,4 isomer is actually listed, it has been stated that the 1,2 isomer is also included.

2 The HO position, as communicated to the Health and Safety Executive (HSE), is that those handling filters containing 1,2 MP would require the appropriate HO licence to lawfully handle these products in the course of their work unless any licensing 'exemptions' afforded by the Misuse of Drugs Regulations 2001 would apply. Therefore licence holders can only supply 1,2-MP, in any form (neat, solution, impregnated filter etc), to another licence holder. Details can be found on the UK Government website at: https://www.gov.uk/controlled-drugs-licences-fees-and-returns.

Appendix 2

Limitations of the impinger with filter in series sampler and possible alternative sampler

1 The use of an impinger backed with a filter is the most efficient way of sampling isocyanate aerosols in workplace air. A drawback of the impinger is that it is typically made of glass and filled with toluene. This makes it both fragile and flammable and therefore more suitable for static sampling rather than for personal sampling. An alternative sampling device to the impinger uses a GF/B filter (or two GF/A filters).[17–22] These are impregnated with twice the amount of 1,2-MP used for the preparation of 1,2-MP-dosed GF/A filters described in MDHS25. The filter is mounted in an IOM sampler and pumped at 2 $l.min^{-1}$. This method has been shown to give results comparable with using an impinger.[23]

2 It has been reported that in certain circumstances the use of the GF/B sampler can lead to under-reporting of the isocyanate concentration.[20, 22–24] As such, the use of an impinger is recommended in the following circumstances:

- long-term sampling of aerosols;
- heavy loading that may deplete the reagent in the filter and/or physically clog up the filter;
- aerosols of fast reacting mixes (generally aromatic isocyanates and possibly some catalysed aliphatic isocyanates).

3 As stated above, it is recognised that it may not always be practical to use an impinger. In such cases, it is suggested[23] that paired static samples are taken, ie a GF/B and an impinger/GF/A sampler in addition to other samples. A correction

factor can then be obtained should the GF/B sampler be shown to be under sampling.

Appendix 3

Analytical benefits in the use of HPLC with tandem mass spectrometric detection to augment the recommended analytical procedures

1 Analysis using HPLC with tandem mass spectrometric detection (LC/MS/MS) allows for increased sensitivity and improved identification of isocyanates. A disadvantage of LC/MS/MS in comparison to LC/EC/UV is that some prior knowledge of the composition is required before the MS quantification parameters are set. It is therefore good practice, where possible, to sample and qualitatively analyse the bulk isocyanate formulation. Using an LC/MS/MS in scan or precursor ion scan mode[25] can ensure that all isocyanate species are identified. This can be in addition to qualitative analysis using LC/UV/EC.[26]

2 Characterisation, qualitative and quantitative analysis of 1,2-MP derivatised isocyanate formulations by LC/UV/EC and LC/MS/MS can provide a calibration mix for oligomeric isocyanate species. This can then be applied to quantitative analysis of samples containing oligomeric and polymeric isocyanates using LC/MS/MS. By using the isocyanate formulation for calibration, a pseudo-total isocyanate method is achievable that can account for almost all of the isocyanate content in the majority of workplace air samples.[23]

Appendix 4

Determination of sampling efficiency using standard vapour atmospheres

1 If a single impinger is used, the sampling efficiency (SE) for each isocyanate of interest should be determined over a suitable analyte concentration range. This can be done by using a standard vapour atmosphere generator to generate the isocyanates of interest at appropriate concentration, temperature, humidity, sampling time and flow rate. The SE can be determined from the mass recovered from the impinger divided by the mass applied. If the SE under the conditions is less than 0.75 (75%), the result should be discarded.

2 For isocyanate prepolymers, it is impractical to use a standard vapour atmosphere generator, as these preparations exist largely as mixtures of airborne particles and vapours at the concentrations of interest. It is also difficult to prepare accurate, stable, standard vapour atmospheres for monomers. Typically, actual concentrations are 20–30% below calculated values, due to adsorption of the monomers onto the surface of the equipment. Therefore, SE is taken to be 100% for both monomers and polymers, for most practical purposes.

Appendix 5

Interferences

1 The sampled atmosphere may contain compounds that result in co-elution with isocyanate peaks under the chosen analytical conditions. In particular, aromatic amines frequently occur in association with isocyanates. The method of identification described above using detector response ratio, DAD detection and, if necessary, FT-IR or MS detection should enable an accurate identification to be made. If interfering compounds are known or suspected, the identity of the interfering compounds should be communicated to the analyst.

Appendix 6

Stability

1 Isocyanate ureas (1,2-MP) derivatives have been found to be stable for several years on storage in a freezer.

2 Stock solutions of isocyanate monomer derivatives have been found to be stable for over six months if kept in a freezer. Isocyanate monomers (TDI) on filters and in toluene solution have been found to be stable for up to 90 days (73% and 81% recoveries respectively).

3 MDI spiked on to filters has been found to be stable for at least 6 months.

4 An isocyanate prepolymer (Desmodur N 3390, HDI isocyanurate) spiked onto 1,2-MP filters was found to be stable for 27 days (average recovery 91 ±11%, spiked at three levels, 0.1, 1 and 2 µg/filter).[14]

References

1 Hext PM et al 'A comparison of the sampling efficiency of a range of atmospheric samplers when collecting polymeric MDI aerosols' *Appl. Occup. Environ. Hyg.* 2003 **18** (5) 346-56

2 Monitoring strategies for toxic substances HSG173 HSE Books 2006 (Second edition) ISBN 978 0 7176 6188 6 www.hse.gov.uk/pubns/books/hsg173.htm

3 ISO/TR 17737:2007 *Workplace air: Guidelines for selecting analytical methods for sampling and analysing isocyanates in air* British Standards Institution

4 BS ISO 16702:2007 *Workplace air quality: Determination of total organic isocyanate groups in air using 1-(2-methoxyphenyl)piperazine and liquid chromatography* British Standards Institution

5 General methods for sampling and gravimetric analysis of respirable and inhalable dust MDHS14/4 (Fourth edition) HSE 2014 www.hse.gov.uk/pubns/mdhs

6 BS EN ISO 13137:2013 *Workplace atmospheres: Pumps for personal sampling of chemical and biological agents. Requirements and test methods* British Standards Institution

7 BS EN ISO 1042:2000 *Laboratory glassware. One-mark volumetric flasks* British Standards Institution

8 BS EN ISO 8655-6:2002 *Piston-operated volumetric apparatus. Gravimetric methods for the determination of measurement error* British Standards Institution

9 White J et al *Development of MDHS 25/2: Organic isocyanates in air.* Health and Safety Laboratory internal report IACS 97/2, 1997

10 White J *Isocyanate call-off contract,* Health and Safety Laboratory internal report OMS/2003/12, 2003

11 White J. *International Organization for Standardization, Intercomparison of methods for isocyanates in Air, Phase 1, Results for MDHS 25/3,* Health and Safety Laboratory internal report OMS/2004/07 2004

12 Vangronsveld E, Mandel F 'Workplace monitoring of isocyanates using ion trap liquid chromatography/tandem mass spectrometry' *Rapid Commun Mass Spectrom* 2003 **17** 1685–90

13 White J.et al. 'Particle beam liquid chromatography: Mass spectrometry analysis of hazardous agricultural and industrial chemicals' *Rapid Commun Mass Spectrom* 1997 **11** 618–23

14 White J *Evaluation of MDHS 25/2: The determination of isocyanates in a reacting paint mix* Health and Safety Laboratory internal report IACS 97/19 1997

15 White J 'MDHS 25 revisited: Development of MDHS 25/3, the determination of organic isocyanates in air' *Ann. Occup. Hyg.* 2006 50(1) 15–27

16 BS EN 482:2012 *Workplace exposure: General requirements for the performance of procedures for the measurement of chemical agents* British Standards Institution

17 Henriks-Eckerman M-L, Välimaa J, Rosenberg C 'Determination of airborne methyl isocyanate as dibutylamine or 1-(2-methoxyphenyl)piperazine derivatives by liquid and gas chromatography' *Analyst* 2000 **125** 1949–54

18 Kääriä K, Hirvonen A, Norppa H et al 'Exposure to 2,4- and 2,6- toluene diisocyanate during production of flexible foam: determination of airborne TDI and urinary 2,4- and 2,6- toluenediamine' *Analyst* 2001 **126** 1025–31

19 Kääriä K, Hirvonen A, Norppa H et al 'Exposure to 4,4'-methylenediphenyl diisocyanate during moulding of rigid polyurethane foam: determination of airborne 4,49- methylenediphenyl diisocyanate and urinary 4,49-methylenedianiline' *Analyst* 2001 **126** 476–9

20 Sennbro CJ, Ekman J, Lindh CH et al 'Determination of isocyanates in air using 1,2-methoxyphenyl piperazine impregnated filters: long-term sampling performance and field comparison with impingers with dibutylamine' *Ann Occup Hyg* 2004 **5** 415–24

21 Sennbro CJ, Lindh CH, Östin A et al 'A survey of airborne isocyanate exposure in 13 Swedish polyurethane industries' *Ann Occup Hyg* 2004 **5** 405–14

22 Mattsson C, Lindh CH, Tinnerberg H 'Underestimation of toluene diisocyanate

concentration using long-term sampling with 1-(2-methoxyphenyl)piperazine impregnated filters' *Int J Hyg Environ Health* 2008 2**11** 458–63

23 White J, Johnson P, Pengelly I, Keen C and Coldwell M 'MDHS 25 Revisited: Part 2, Modified Sampling and Analytical Procedures Applied to HDI-Based Isocyanates' *Ann Occup Hyg* 2012 **56** (4) 466–480

24 Lesage J, Stanley J, Karoly MJ et al 'Airborne methylene diphenyl diisocyanate (MDI) concentrations associated with the application of polyurethane spray foam in residential construction' *J Occup Environ Hyg* 2007 4: 145–55.

25 White J, Corns H, Jones K et al *New instrumental techniques for toxic and harmful substances—call off contract 2003–2005* Report HSL/2007/18 Health and Safety Executive 2007 www.hse.gov.uk/research/hsl_pdf/2007/hsl0718.pdf. Accessed 17 December 2013

26 White J, Coldwell M, Davies T et al *Isocyanate exposure, emission and control in small motor vehicle repair premises using spray room—phase 1,* Report RR496 Health and Safety Executive 2006 www.hse.gov.uk/research/rrpdf/rr496.pdf

You should use the most current edition of any standards listed.

Further information

For information about health and safety, or to report inconsistencies or inaccuracies in this guidance, visit www.hse.gov.uk/. You can view HSE guidance online and order priced publications from the website. HSE priced publications are also available from bookshops.

British Standards can be obtained in PDF or hard copy formats from BSI: http://shop.bsigroup.com or by contacting BSI Customer Services for hard copies only Tel: 020 8996 9001 email: cservices@bsigroup.com.

This guidance is issued by the Health and Safety Executive. Following the guidance is not compulsory, unless specifically stated, and you are free to take other action. But if you do follow the guidance you will normally be doing enough to comply with the law. Health and safety inspectors seek to secure compliance with the law and may refer to this guidance.

This mdhs is available at: www.hse.gov.uk/pubns/mdhs

For further information about this method or other MDHS methods, please visit HSL's website: www.hsl.gov.uk or email: hslinfo@hsl.gov.uk

© *Crown copyright* If you wish to reuse this information visit www.hse.gov.uk/copyright.htm for details. First published 12/14.