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Workplace air quality — Determination of total organic isocyanate groups in air using 1-(2-methoxyphenyl)piperazine and liquid chromatography

Qualité de l'air des lieux de travail — Dosage des groupements isocyanates organiques totaux dans l'air par dérivatisation avec la 1-(2-méthoxyphényl)pipérazine et par chromatographie en phase liquide

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Foreword

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International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 16702 was prepared by Technical Committee ISO/TC 146, *Air quality*, Subcommittee SC 2, *Workplace atmospheres*.

This second edition cancels and replaces the first edition (ISO 16702:2001), which has been technically revised.

Introduction

Isocyanates (molecules containing the NCO functional group) are highly reactive molecules widely used in industry in paints, polyurethane foams, plastics, and adhesives. They are known respiratory sensitisers and are the major cause of chemically induced occupational asthma. Exposure to isocyanates can occur by inhalation and possibly by contact. Australia, Ireland, and the United Kingdom have set long-term occupational exposure limits (8 h time-weighted average) of 20 µg/m^3 [total isocyanate (NCO) group] and short-term limits (15 min) of 70 µg/m^3 for workplace air. In addition, Finland has set a short term limit (15 min) of 35 µg/m^3 and Sweden has set long-term occupational exposure limits (8 h time-weighted average) of 5 ppb[1)] [total isocyanate (NCO) group] and short-term limits (15 min) of 10 ppb for workplace air. These limits are for total isocyanate, i.e. monomeric and all polymeric (also called oligomeric, polyisocyanates, oligo-isocyanates or prepolymeric) isocyanates.

Sampling and analysis of airborne isocyanates is not easy. Isocyanates occur in a variety of chemical forms, such as monomers, oligomers, larger and more structurally complex polymers, and mixtures of all these forms. Isocyanate oligomers and polymers are commonly used in industry as they are less volatile than the monomers and so pose less of a vapour hazard. Isocyanates occur in a variety of physical forms, e.g. vapours, aerosols, and liquids. A sampling method that is suitable for one physical form of isocyanates is not automatically suitable for another. In the workplace, other substances are also present in the air, such as water vapour, dust, amines and alcohols, depending on the product and process that is being used, and these can interfere with the liquid chromatography (LC) analysis. Polymeric isocyanate standards are not available, yet these species must be quantified to give a total isocyanate result.

Due to the reactive nature of the isocyanate group, analysis in the workplace is commonly carried out by trapping isocyanates with a derivatisation reagent to produce a stable derivative. This International Standard method is based upon the UK method for isocyanate determination, MDHS25/3[1].

The method traps the isocyanate with 1-(2-methoxyphenyl)piperazine (MP) to form a stable urea derivative. The urea derivative is analysed by LC with electrochemical (EC) and ultraviolet/visible (UV/vis) detection. Isocyanates for which a standard exists or can be prepared can be quantified using a UV/vis detector. This has the advantage that a UV/vis detector is more stable than an EC detector. However, for the majority of industrially used polymeric isocyanates, no standards exist and these compounds are quantified using the EC detector, which oxidises the methoxy group on the MP derivatisation reagent. As this group is common to all MP derivatised isocyanates, the polymeric species can be calibrated using the corresponding isocyanate monomer.

The procedure used for sampling of workplace isocyanates depends upon their physical form. Filters have been found to sample vapour effectively. An impinger/filter combination is recommended for aerosol sampling. This method has been found to be suitable for the commonly occurring mono- and diisocyanates i.e. methylenebis(phenylisocyanate) (MDI), phenylisocyanate (PI), toluene-2,6-diisocyanate and toluene-2,4-diisocyanate (TDI), 1,6-(diisocyanato)hexane (HDI), isophoronediisocyanate (IPDI), naphthyldiisocyanate (NDI), methylenebis(cyclohexylisocyanate) (hydrogenated MDI) and butylisocyanate as well as polymeric isocyanates based on these monomers.

1) Parts per billion (thousand million).

Workplace air quality — Determination of total organic isocyanate groups in air using 1-(2-methoxyphenyl)piperazine and liquid chromatography

1 Scope

This International Standard gives general guidance for the sampling and analysis of airborne organic isocyanate (NCO) compounds in workplace air.

This International Standard is appropriate for a wide range of organic compounds containing isocyanate functional groups, including isocyanate monomers and prepolymers. Examples of aromatic monomers include toluene diisocyanate (TDI) (both 2,4- and 2,6-diisocyanatotoluene), naphthyl diisocyanate (NDI) (1,5-diisocyanatonaphthalene) and methylenebis(4-phenylisocyanate) [MDI, systematically named as di-(4-isocyanatophenyl)methane]. Examples of aliphatic monomers include isophorone diisocyanate (IPDI, systematically named as 1-isocyanato-3-isocyanatomethyl-3,5,5-trimethylcyclohexane), methylenebis(cyclohexylisocyanate) (hydrogenated MDI, HMDI) and 1,6-diisocyanatohexane (HDI) (also known as 1,6-hexamethylenediisocyanate). Monomers containing a single isocyanate moiety (e.g. methyl isocyanate, ethyl isocyanate, phenyl isocyanate, hexyl isocyanate) are produced during thermal degradation of polyurethanes, i.e. flame bonding and laser cutting. Isocyanate polymers, also called polyisocyanates, homopolymers, oligomers or prepolymers, are derived from the diisocyanate monomers by self-condensation or reaction with polyols. Polymeric diisocyanates are widely used in the polyurethanes, paints and coatings, and adhesives industries.

This International Standard is appropriate for measuring any product containing free isocyanate groups. It was developed primarily for the commonly used MDI, HDI, and TDI, and their oligomers and polymers[1]. It has also been used for IPDI, HMDI, and NDI, and their oligomers and polymers. The exposure limit for isocyanates in the UK requires measurement of total isocyanate groups, i.e. monomeric diisocyanates, oligomeric, prepolymeric and polymeric diisocyanates and monoisocyanates. Because there are a wide range of isocyanate structures and molecular masses, the chromatographic conditions used will need to be varied according to the isocyanate formulation being determined. If both isocyanates and amines are believed to be present, and both need to be determined, a standard which enables the simultaneous determination of both amines and isocyanates may be more appropriate[2]. This method has also been modified to allow determination of mono-isocyanates produced during thermal degradation[3], the use of mass spectrometric detection[4] and other sampling equipment, e.g. 37 mm filters and other filter cassettes, but these modifications are not covered in this International Standard. If a modified version of this method is being used, it is the responsibility of the user to demonstrate that the modifications are valid.

The method is used to determine time-weighted average concentrations of organic isocyanates in workplace atmospheres, and is suitable for sampling over periods in the range 0,5 min to 8 h. The method is designed for personal monitoring, but can also be used for fixed location monitoring by suitable modification.

NOTE The objective of air monitoring is usually to determine worker exposure and, therefore, the procedures described in this method are for personal sampling in the breathing zone. The method can be used for background or fixed location sampling. However, it should be recognised that, due to aerodynamic effects, samplers designed for personal sampling do not necessarily exhibit the same collection characteristics when used for other purposes.

The method is suitable for the measurement of airborne organic isocyanates in the concentration range from approximately 0,1 µg/m^3 to 140 µg/m^3 for a 15 l sample volume. The qualitative and quantitative detection limits for isocyanate, defined as three times and 10 times the standard deviation of six blank determinations, have been found to be typically between 0,001 µg and 0,004 µg of isocyanate per sample, respectively (EC detection). For a 15 l air sample, these values correspond to qualitative and quantitative detection limits of 0,07 µg/m^3 and 0,3 µg/m^3, respectively.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 5725-2, *Accuracy (trueness and precision) of measurement methods and results — Part 2: Basic method for the determination of repeatability and reproducibility of a standard measurement method*

EN 1232, *Workplace atmospheres — Pumps for personal sampling of chemical agents — Requirements and test methods*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1 Isocyanate chemical species

3.1.1
isocyanate
a chemical compound with one or more isocyanate (nitrogen carbon oxygen) functional groups

3.1.2
monomer
a chemical compound that joins with other identical compounds to form dimers, trimers, oligomers or polymers

EXAMPLE Classes of isocyanate monomers include: monoisocyanates, containing one isocyanate functional group, e.g. methyl isocyanate; diisocyanates, e.g. di(4-isocyanatophenyl)methane (MDI); and triisocyanates, e.g. tri(4-isocyanatophenyl)methane.

3.1.3
diisocyanate
a chemical compound with two isocyanate functional groups

3.1.4
oligomer
a compound of low relative molecular mass with multiple isocyanate functional groups, formed by the combination of isocyanate monomers

3.1.5
polyisocyanate
oligo-isocyanate
an isocyanate compound with multiple isocyanate functional groups

3.1.6
prepolymer
the isocyanato-terminated reaction product of a di- or poly-isocyanate with a stochiometric deficiency for a hydroxyl-terminated polyol; these compounds are then further reacted to form polyurethanes or similar compounds

3.2 Analytical definitions

3.2.1
time-weighted average concentration
concentration of a chemical agent in the atmosphere, averaged over the reference period

3.2.2
field blank
sampler that is taken through the same handling procedure as a sample, except that it is not used for sampling, i.e. sampling media is loaded into a sampler, transported to the sampling site, derivatised when field samples are derivatised, and analysed with field samples

3.3 Statisitical definition

uncertainty
⟨of measurement⟩ parameter, associated with the result of a measurement, that characterises the dispersion of the values that could reasonably be attributed to the measurand

[ISO/IEC Guide 98:1995[5], 2.2.3]

NOTE 1 The parameter can be, for example, a standard deviation (or a given multiple of it), or the width of a confidence interval.

NOTE 2 Uncertainty of measurement comprises, in general, many components. Some of these components can be evaluated from the statistical distribution of the results of series of measurements and can be characterised by standard deviations. The other components, which can also be characterised by standard deviations, are evaluated from assumed probability distributions based on experience or other information. This is often referred to as type A and type B evaluations of uncertainty, respectively.

4 Principle

The choice of sampling device used in this method depends upon the physical form of the isocyanate being sampled. For an isocyanate aerosol, a glass impinger containing 1-(2-methoxyphenyl)piperazine (MP) solution backed by a filter impregnated with the MP reagent is used. For an isocyanate vapour, then an MP impregnated filter may be used on its own.

A measured volume of air is drawn through a glass impinger containing 1-(2-methoxyphenyl)piperazine (MP) solution backed by a filter impregnated with the MP reagent (isocyanate aerosol) or a filter impregnated with the MP reagent (isocyanate vapour). Any organic isocyanates present will react to form non-volatile urea derivatives. The resultant solution is concentrated and analysed by high-performance liquid chromatography (HPLC) with ultraviolet/visible (UV) and electrochemical (EC) detection. Isocyanate-derived peaks are identified on the basis of their EC and UV responses and also by diode array detection (DAD) spectral library matching, mass spectrometry (where available), and comparison with derivatising bulk[6]. For isocyanates for which a standard MP derivative is available, e.g. HDI, MDI, TDI isomers, UV can be used for quantification. If no suitable standard is available, i.e. for isocyanate oligomers, prepolymers and polymers, quantification is by EC, using the relevant isocyanate monomer standard for calibration. The total isocyanate-in-air concentration is calculated from the sum of all the isocyanate-derived peaks.

5 Reagents and materials

Use only reagents of recognised analytical grade and only distilled water or water of equivalent purity.

5.1 MP reagent [1-(2-methoxyphenyl)piperazine]

This reagent is commercially available at appropriate (> 98 % by mass) purity.

5.2 Reagent solvent

The reagent solvent, commonly toluene, should be of chromatographic quality. It must be free from compounds co-eluting with the substances of interest. Before use for the preparation of impregnated filters or for preparation of monomer standards, it is advisable to dry the solvent with anhydrous calcium chloride or

magnesium sulfate. This step may be omitted for preparation of the absorbing solution as it will pick up atmospheric moisture during sampling.

5.3 Reagent solutions

5.3.1 Absorbing solution

Accurately weigh approximately 50 mg of MP and transfer to a dry 100 ml volumetric flask. Dissolve and make up to the mark with reagent solvent, and mix thoroughly. Dilute 10 ml of this stock solution to 100 ml with reagent solvent in a second volumetric flask to give a 260 µM absorbing solution.

5.3.2 Preparation of solution for impregnating filters (solution A)

Accurately weigh out approximately 0,25 g of MP and transfer to a 25 ml volumetric flask. Make up to the mark with anhydrous reagent solvent and shake to mix.

5.3.3 Stability of reagent solutions

Prepare fresh solutions weekly.

5.4 Calibration standards

5.4.1. Preparation of monomer derivatives

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 MP dissolved in dry toluene (10 ml) and leave to stand for 1 h. A white crystalline urea is precipitated. Collect this on a filter paper (e.g. Whatman No 1[2)]) and wash several times with dry toluene to remove excess reagent. Recrystallise the urea from toluene, by warming to about 60 °C and slowly adding methanol to dissolve the urea. Allow to cool and then filter the resulting crystals, washing with cold, dry toluene. Dry the solid in air. The urea derivatives of the mono- and most diisocyanates are only slightly soluble in toluene but readily soluble in methanol or acetonitrile.

5.4.2 Alternative procedure for the less soluble isocyanate derivatives

MDI and HMDI are rather insoluble in toluene and the alternative method of preparation given below may be more suitable for these compounds. Slowly add a solution of the appropriate isocyanate (0,25 g, ~2 mmol NCO for MDI and HMDI) in dichloromethane (25 ml) to a solution of 1-(2-methoxyphenyl)piperazine (1 g, ~5 mmol) in dichloromethane (50 ml). A white suspension will form. Add this dropwise to a beaker of hexane (500 ml) while stirring. Filter the resultant precipitate and redissolve it in a minimum volume of dichloromethane. Add hexane to reprecipitate the solid, filter this and wash with hexane. Dry the urea derivative in air.

NOTE This second method may also be used for isocyanate oligomers, polymers and prepolymers.

5.4.3 Preparation of standard solutions of recrystallised isocyanate monomer derivatives

5.4.3.1 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. Take aliquots of this solution and dilute volumetrically in acetonitrile or HPLC mobile phase to create a series of standard solutions over the NCO concentration range 0,01 µg/ml to 1,0 µg/ml.

5.4.3.2 Prepare further standard solutions if the concentration range of the samples exceeds that of the standards.

2) Example of a suitable product available commercially. This information is given for the convenience of users of this International Standard and does not constitute an endorsement by ISO of this product.

5.4.3.3 The concentration of isocyanate in the standard, ρ_{NCO}, in micrograms per millilitre, is given by Equation (1):

$$\rho_{NCO} = \frac{\rho_U M_{NCO} n}{M_U} \quad (1)$$

where

ρ_U is the concentration, in micrograms per millilitre, of the urea derivative in the standard;

M_{NCO} is the relative molecular mass of NCO;

n is the number of isocyanate groups per molecule;

M_U is the relative molecular mass of the urea derivative.

5.5 Stability of isocyanate ureas and their solutions

Stock solutions of isocyanate monomer derivatives have been found to be stable for ~ 6 months if kept in a freezer[7]. A mixture of 2,4-TDI and 2,6-TDI on filters and in toluene solution has been found to be stable for up to 90 days (73 %, filter, and 81 %, toluene solution, recoveries, respectively)[8]. MDI on filters has been found to be stable for at least 6 months [HSE Workplace Analysis Scheme for Proficiency (WASP)[1] data]. An isocyanate prepolymer [Desmodur N 3390[3)]] spiked onto 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)[9].

5.6 HPLC mobile phase

The exact composition of the mobile phase used depends on the isocyanate formulation being determined. The more acetonitrile in the mobile phase, the faster the peaks will elute. A “slow” mobile phase can be used for monomeric diisocyanates and monoisocyanate MP derivatives. For the polymeric isocyanate MP derivatives, a “fast” mobile phase is more suitable. Care must be taken to elute all the polymeric MP derivatives and not to lose any monomeric species under the acetylated MP reagent peak at the start of the chromatogram.

5.6.1 Preparation of “slow” mobile phase

A “slow” mobile phase, suitable for the determination of monomeric diisocyanates and mono-isocyanates, is prepared as follows. 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 550 ml of this solution to acetonitrile (450 ml) and degas this solution by filtering under vacuum or by bubbling a stream of helium through it to give a volume mixture of 45 % acetonitrile and 55 % sodium acetate buffer.

5.6.2 Preparation of “fast” mobile phase

A “fast” mobile phase, suitable for the determination of polymeric diisocyanates, is prepared as follows. 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) and degas this solution by filtering under vacuum or by bubbling a stream of helium through it to give a volume mixture of 60 % acetonitrile and 40 % sodium acetate buffer.

3) Example of a suitable product available commercially. This information is given for the convenience of users of this International Standard and does not constitute an endorsement by ISO of this product.

5.7 Calibration blend atmosphere

Prepare an atmosphere of a known concentration of the substance or substances of interest in air by a recognised method. Methods described in ISO 6145 (all parts) are suitable. Confirm the delivered atmosphere concentration using an independent method.

6 Apparatus

Before sampling and analysis, clean all glassware, including impingers (8.2).

Usual laboratory apparatus and, in particular, the following.

6.1 Sampler

The choice of sampler used depends on the form in which the isocyanate is present. For vapour phase isocyanates, sampling can be carried out using an impregnated filter only. For mixtures of airborne particles and vapour, the use of an impinger backed by an impregnated filter is recommended. Details of alternative sampling procedures are given below.

6.2 Filter

Filters of diameter 25 mm are suitable for use in the selected sampler. The chosen filter type should have a capture efficiency of not less than 95 % and be suitable for collection of stable samples of isocyanate. MP-impregnated glass fibre [GF/A[4])] filters have been found to be suitable.

6.3 Filter holder

Details of suitable sampling heads are given in MDHS14/3[10]. A 25 mm Institute of Occupational Medicine head fitted with a stainless steel cassette is recommended for filter samples. For aerosol sampling using the impinger/filter combination, it has been found to be more convenient to use the 25 mm Swinnex[5)] filter holder.

6.4 Midget impinger

A number of designs of bubblers and impingers are available[11],[12]. A midget impinger consists of a graduated receiver and a tapered inlet tube.

NOTE “Non-spill” impingers are commercially available.

6.5 Sampling pump

The pump shall fulfil the requirements of EN 1232 or equivalent. The sampling pump should be in accordance with prevailing safety regulations.

6.6 Tubing

Plastic, rubber or other suitable tubing about 900 mm long of appropriate diameter to ensure a leak-proof fit to both pump and sample tube or tube holder, if used. Fluoroelastomer or similar tubing has been found to have fewer problems due to extraction of contaminants associated with it. It is not recommended to use any tubing upstream of the first collection element (filter or impinger) as sample losses may occur.

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4) Example of a suitable product available commercially. This information is given for the convenience of users of this International Standard and does not constitute an endorsement by ISO of this product.

5) Example of a suitable product available commercially. This information is given for the convenience of users of this International Standard and does not constitute an endorsement by ISO of this product.

6.7 Flowmeter

Flowmeter, portable, capable of measuring the appropriate flow rate to within ± 5 %, and calibrated against a primary standard[10]. Flowmeters incorporated in sampling pumps are not suitable for accurate measurement of the flow rate. However, they can be useful for monitoring the performance of samplers, provided they have adequate sensitivity.

6.8 Filtration equipment

A solvent resistant filter unit of < 0,5 µm pore size for filtration of LC solvents. Syringeless filters or < 0,5 µm syringe filters for filtration of the desorbed samples prior to LC analysis.

6.9 Ancillary equipment

Belts or harnesses, to which the sampling pump may be conveniently fixed, unless the pump is sufficiently small to fit into a worker's pocket.

Flat tipped tweezers for handling the filters.

Protective holder for impinger.

Charcoal trap to protect the sampling pumps from toluene vapour (if plastic pumps are being used).

6.10 Liquid chromatograph

An HPLC linked to ultraviolet (UV) and electrochemical (EC) detectors is required. The EC detector should be used in the oxidation mode. A diode array detector (DAD) is also advisable for confirmation of identification. Temperature fluctuations must be avoided in order to obtain the sensitivity required in this method. 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.

6.11 Autosampler

These are commercially available.

7 Sampling

NOTE The existing analytical methods for the sampling of isocyanates exhibit an as yet unknown bias relative to each other.

7.1 Calibration of pump

Calibrate the pump with a representative impinger and/or filter assembly in line, using an appropriate external calibrated meter. If an impinger is used, it shall contain absorbing solution (or toluene).

7.2 General

For long-term samples, select a sampling period of an appropriate duration, such that the filter does not become overloaded with particulate material.

NOTE An 8 h time-weighted average concentration may be derived from the results of two or more consecutive samples.

7.3 Preparation of sampling equipment (general)

Clean the samplers (filter cassette and/or impingers) before use. Dismantle the samplers, soak in laboratory detergent solution, rinse thoroughly with water, wipe with absorptive tissue, and allow to dry thoroughly before reassembly. Alternatively, use a laboratory washing machine.

7.4 Preparation of sampling equipment (filters)

7.4.1 Preparation of impregnated filters

Accurately weigh out approximately 0,25 g of 1-(2-methoxyphenyl)piperazine and transfer to a 25 ml volumetric flask. Make up to the mark with anhydrous toluene and shake to mix. This is solution A (see 5.3.2). In an area free from dust and isocyanates, and using blunt tweezers, place a number of 25 mm glass-fibre filters on a clean glass plate so that no filters touch. Using a suitable microlitre syringe, dispense 200 µl of solution A onto the surface of each filter, ensuring that the reagent impregnates the whole filter. Allow the filters to dry in air for several hours. When completely dry, transfer the filters from the glass plate to a screw-cap brown bottle using blunt tweezers. Label the bottle with the preparation and "use by" date. Store until required in a dark cupboard or refrigerator for up to 6 months after preparation.

7.4.2 Preparation of sampling devices (filters)

In an area free from isocyanates, load the filters into clean, dry samplers using clean flat-tipped tweezers. Connect each loaded sampling head to a sampling pump using plastic tubing ensuring that no leaks can occur. Switch on the pump, allow to stabilise, and attach the calibrated flowmeter to the sampling head so that it measures the flow through the sampler inlet orifice, and set the appropriate flow rate with an accuracy of ± 5 %. Switch off the pump and seal the sampler with a protective cover to prevent contamination during transport to the sampling position.

7.5 Preparation of sampling equipment (impingers)

In an area free from isocyanates and immediately before sampling, transfer 10 ml of the absorbing solution into an impinger and assemble it. Place the impinger in a protective holder and connect to the sampling pump with suitable tubing. Ensure that all connections are free from leaks.

7.6 Collection of filter samples (vapour phase samples)

7.6.1 Set-up of filter samplers

In an area free from isocyanates, fix the sampler to the worker, on their lapel, within the breathing zone. Place the sampling pump in a convenient pocket or attach it to the worker in a manner that causes the minimum inconvenience, e.g. to a belt around the waist. When ready to begin sampling, remove the protective cover from the sampler and switch on the pump. 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.

7.6.2 Collection of filter samples

Draw a measured volume of air through the sampler at a rate of 2,0 l/min. The recommended air volume is within the range 20 l to 900 l. Since it is possible for a filter to become clogged, monitor the performance of the sample periodically, a minimum of every 2 hs (or more frequently if heavy filter loadings are suspected) and at the end of the sampling period. It is preferable to take several short time period samples instead of one long time period sample if a heavy filter loading is expected. Measure the flow rate with the calibrated flowmeter and record the measured value. Terminate sampling and consider the sample to be invalid if the flow rate is not maintained to within ± 5 % of the nominal value throughout the sampling period. Regular observation of the flow fault indicator is an acceptable means of ensuring that the flow rate of flow-stabilised pumps is maintained satisfactorily, provided that the flow fault indicator indicates malfunction when the flow rate is outside ± 5 % of the nominal value.

7.7 Collection of impinger backed by filter samples (isocyanate aerosols)

7.7.1 Rationale for impinger backed by filter sampling

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 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. 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 followed by a reagent-coated filter should collect both isocyanate aerosols and vapours satisfactorily (Reference [13]).

7.7.2 Recommended sampling rate for impinger backed by filter

For the impinger backed by filter combination a sampling rate of 1 l/min is suggested. When using an impinger/filter combination the filter must be placed after the impinger; otherwise the filter will clog with large particles that may not be efficiently derivatised on the filter; i.e. the sampling train is impinger-filter-pump. The purpose of the filter is to derivatise any fine particles that may pass through the impinger.

7.8 Measurements to be made at the end of the sampling period

At the end of the sampling period, measure the flow rate with an accuracy of ± 5 % using a calibrated flowmeter, switch off the sampling pump, and record the flow rate and the time. Also observe the reading on the elapsed time indicator, where fitted, and consider the sample to be invalid if the reading on the elapsed time indicator and the timed interval between switching on and switching off the sampling pump do not agree to within ± 5 %, since this suggests that the sampling pump has not been operating throughout the sampling period. Calculate the mean flow rate by averaging the flow rate measurements throughout the sampling period and calculate the volume of air sampled, in litres, by multiplying the flow rate, in litres per minute, by the sampling time, in minutes.

7.9 Sample logging and field desorption of samples

Reseal the sampler with its protective cover and disconnect it from the sampling pump. Carefully record the sample identity and all relevant sampling data. Isocyanate species present in large particles (>10 µm) and collected on reagent-coated filters may not be efficiently derivatised. For this reason, it is advisable to field-desorb the filter immediately after sampling with MP absorbing solution (5.3.1).

7.10 Transportation

7.10.1 Transportation of filter samples

For transport to the laboratory, remove each filter from the sampler, place in a 50 mm × 35 mm glass vial containing 2 ml MP absorbing solution (5.3.1) and cap the vial. If deposition from aerosols is suspected, rinse the inlet of the sampler head with a little MP absorbing solution.

7.10.2 Transportation of impinger samples

For impingers, transfer the contents to a glass vial and seal with a poly(tetrafluoroethylene)-lined screw-cap. Rinse the impinger and its inlet tube with a small volume of reagent solvent and add the washings to the vial. It is not necessary to note the final volume of the solution or to make it up to its original volume.

7.11 Field Blanks

Field blanks (3.2.2) 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. Label these as field blanks.

8 Procedure

8.1 Safety precautions

WARNING — Wear disposable gloves during analysis to reduce the possibility of contamination and to protect the hands from harmful solvents and/or reagents. This International Standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this International Standard to establish appropriate health and safety practices and determine the applicability of regulatory limitations prior to use.

8.2 Cleaning of glassware

Before use, clean all glassware including sampling devices, e.g. impingers, to remove any residual grease or chemicals.

8.3 Prereaction of impinger samples before HPLC analysis

Acetylation of unreacted MP reagent improves the chromatographic separation of isocyanate derivatives. After sampling, transfer the contents of the impinger to a screw-cap vial as described above. Allow at least 24 h to elapse from the time of sampling to ensure complete reaction of the isocyanate prepolymers. Pipette 100 µl acetic anhydride into the vial and mix well. Evaporate to dryness, redissolve the residue in 2 ml acetonitrile or mobile phase and transfer to a glass vial. Analyse using LC as described below.

8.4 Prereaction of filter samples before HPLC analysis

Pipette 100 µl acetic anhydride into each glass vial containing the MP absorbing solution (5.3.1) and filter paper and mix well. Evaporate to dryness and redissolve the residue in 2 ml acetonitrile or mobile phase. Filter this solution into an autosampler vial, using a syringeless filter or < 0,5 µm syringe filter. Analyse using LC as described below.

8.5 HPLC conditions

8.5.1 Choice of HPLC conditions

A variety of chromatographic conditions may be used for the analysis of organic isocyanates in solution. The choice will depend largely on the nature of interfering compounds, which may affect the chromatographic analysis and the nature of the isocyanate formulation being determined. Typical instrumental conditions are:

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
UV detector	242 nm and/or DAD
EC detector	porous graphite electrode, operating at a potential of + 0,8 V

8.5.1.1 Typical retention time data using the “slow” conditions described in 5.6.1 are given in Table 1.

Table 1 — Typical retention times using "slow" conditions

Isocyanate	Retention time min
HDI	6,0
MDI	11,5
2,6-TDI	5,0
2,4-TDI	6,7

8.5.2 Optimising the HPLC analysis

8.5.2.1 The reagent peak may mask the isocyanate monomer peak. To improve the separation, decrease the acetonitrile concentration of the mobile phase and acetylate the sample by adding acetic anhydride as described in 8.3 prior to analysis. If the LC backpressure is high, then using a less concentrated buffer should improve this.

8.5.2.2 For a more rapid analysis of MDI, modify the mobile phase by increasing acetonitrile concentration, e.g. with the above system 56 % acetonitrile gave an MDI retention time of 7,0 min. Where high concentrations are found, dilute the sample solutions with acetonitrile to bring the concentration back within the calibration range. Repeat the analysis and record the dilution factor.

8.5.2.3 Retention times of prepolymer peaks vary depending on the source of the prepolymer. The “fast” conditions described in 5.6.2 give the typical retention times listed in Table 2.

Table 2 — Typical retention times using "fast" conditions

Isocyanate	Retention time min
HDI	3,0
MDI	4,5
HDI (polymers)	6 to 45
MDI (polymers)	6 to 45

8.6 Determination of airborne isocyanate for monomeric isocyanates (UV detection)

Prereact the samples, field blanks and the samples used to determine sampling efficiency as described in 8.3 and 8.4. Analyse by injecting a known fixed volume (10 µl to 20 µl) of each standard solution into the liquid chromatograph and using UV detection, at a given wavelength, as described above. A standardised injection technique is required to obtain reproducible peak heights/areas. Prepare a calibration graph of UV response (height or area) versus analyte concentration in the standard solutions.

Inject the same fixed volume of the prereacted sample solution into the liquid chromatograph. Determine the UV response at a given wavelength, e.g. 242 nm, and read the concentration of the analyte in the prereacted sample from the calibration graph. Analyse the sample blank and any samples used to determine sampling efficiency (see Annex A) in the same way.

8.7 Identification of polymeric isocyanates: EC/UV ratio approach

Standards of the polymeric isocyanate 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 derived.

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. Normally, the monomer is present in the prepolymer chromatogram, but this may be at very low levels compared to the polymer peaks, e.g. typically < 1 % monomeric HDI in poly-HDI-based paints used in the motor vehicle repair industry.

The ratio of the peak responses in the two detectors is calculated as follows. The polymer peak response ratio, y, is given by Equation (2):

$$y = \frac{E_{\text{poly}}}{U_{\text{poly}}} \tag{2}$$

where

E_{poly} is the polymer peak response of the EC detector;

U_{poly} is the polymer peak response of the UV detector.

The monomer peak response ratio, x, is given by Equation (3):

$$x = \frac{E_{\text{mono}}}{U_{\text{mono}}} \tag{3}$$

where

E_{mono} is the monomer peak response of the EC detector;

U_{mono} is the monomer peak response of the UV detector.

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.

With some prepolymer preparations, it can take over 40 min to elute all the components. In such cases, it is advisable to modify the mobile phase 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.

NOTE 1 Ideally, y/x would be 1, i.e. 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[14].

NOTE 2 The detector response ratio varies with isocyanate type and from day to day, depending on the condition of the EC detector. 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 approximately constant for a given isocyanate monomer and its derived prepolymers.

NOTE 3 The E/U ratio is a guide to identification only. It is the responsibility of the analyst to correctly identify the major peaks in a chromatogram. Typical EC and UV chromatograms are given in Annex D.

8.8 Confirmation of identification for polymeric isocyanates (prepolymers)

8.8.1 Analysis of a bulk sample

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 MP-derivatised material. This

approach will not be successful for end-capped or stoved isocyanates. In principle, 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, e.g. by partial reaction with atmospheric polyol compounds. In practice, additional peaks have not been found in the samples routinely analysed (at the UK Health and Safety Laboratory)[6,7,14]. If partially reacted species exist, the EC response of the prepolymer 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.

8.8.2 Confirmation of identity using a diode array detector

A DAD is also of use for confirmation that a peak derives from isocyanate[14]. DAD detection 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 and library matching carried out to aid identification. It has been found that isocyanate prepolymers give DAD spectra that closely match that of the parent monomer[7,14]. The use of a DAD also allows the use of gradient elution to decrease run times and improve peak shapes for any late eluting peaks. Running a gradient up to 100 % acetonitrile should remove any highly polymerised isocyanates if these compounds are suspected to be present. Gradient elution is not suitable for EC detection, as the response factors of the EC are dependent on mobile phase composition.

8.8.3 Confirmation of identity using other techniques

Other techniques can also be used for confirmation of identity. Liquid chromatography with mass spectroscopic detection has also been used to confirm peak identity[4,6,15]. Titration or Fourier transform infrared (FT-IR) spectrometry can be used to determine isocyanate content if an underivatised bulk sample is available[6,7,9]. Other useful sources of information for underivatised bulks are safety data sheets or manufacturer's information.

8.9 Quantification of airborne isocyanate for polymeric isocyanates (EC detection)

For routine analysis of monomers, as described above, only UV detection need be used as standards of 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 oxidises the methoxy group on the MP derivatisation reagent. As this group is common to all MP-derivatised isocyanates, the polymeric species may be calibrated using the corresponding isocyanate monomer[16]. After identification of the isocyanate-derived peaks, as described in 8.7 and 8.8, the peaks of interest are quantified using the EC response factor for the relevant isocyanate monomer MP derivative, in a similar manner to that described in 8.6 for UV detection. As mentioned in the introduction, the EC detector, used to quantify polymeric isocyanates, is more variable and less 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[16].

NOTE It is a requirement under UK law to quantify polymeric as well as monomeric isocyanates.

8.10 Sampling efficiency

Sampling efficiency, E_{sam}, may be less than 1,0 (100%) due to incomplete reaction of the isocyanate with the MP reagent on the filter or in the impinger, e.g. if a large air volume is taken or the sampling rate is too high. Low sampling efficiency can also occur if the local concentration of MP reagent is depleted, e.g. because of large droplets with a high isocyanate content. See Annex A for a method of determining sampling efficiency. Alternatively, use two samplers in series and add together the results of the isocyanate determination for each. Normally, sampling efficiencies fall between 0,95 and 1,05. Correct for incomplete absorption if E_{sam} falls below 0,95 under the sampling conditions used.

9 Calculations

Correct for blanks and sampling efficiency as follows.

The total concentration, in micrograms per cubic metre, of isocyanate in the air sampled, ρ_{sam}, is given by Equation (4):

$$\rho_{sam} = \frac{1\,000 D_f (\rho - \rho_{blank})}{E_{sam} V_{sam}} \quad (4)$$

where:

D_f is the dilution factor of the sample, i.e. the desorption volume, in millilitres;

ρ is the concentration, in micrograms per millilitre, of isocyanate in the sample, obtained by comparison with the standard solutions;

ρ_{blank} is the concentration, in micrograms per millilitre, of isocyanate in the blank;

E_{sam} is the sampling efficiency;

V_{sam} is the volume, in litres, of air sampled.

To express concentrations under specified conditions, e.g. 25 °C and 101 kPa, then the concentration, in micrograms per cubic metre, of isocyanate in the air sampled, ρ_c is given by Equation (5):

$$\rho_c = \rho_{sam} \left(\frac{101}{p} \right) \left(\frac{\theta + 273}{298} \right) \quad (5)$$

where:

p is the actual pressure, in kilopascals, of the air sampled;

θ is the temperature, in degrees Celsius, of the air sampled.

10 Interferences

The sampled atmosphere may contain compounds that give chromatographic peaks under the conditions chosen for LC analysis. 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.

11 Uncertainty of measurement

11.1 Introduction

Isocyanate concentration measurement in workplace air has associated with it an uncertainty that shall be expressed as expanded uncertainty (EN 482 or ISO/IEC Guide 98:1995). Thus, an uncertainty assessment shall be performed according to one or other of these definitions of uncertainty. In both cases, this consists of the determination of uncertainty contributions evaluated by means of laboratory and simulated field tests or from existing information. The values obtained of the measurement uncertainty shall then be compared with preset criteria, for example those in EN 482, or defined in national or international legislation.

NOTE The calculations were based on the approach used in ISO 17734-2.

11.1.1 Summary of approach

The “uncertainty budget” approach sums the contributions for each individual source of uncertainty for an analytical method. For the results of isocyanate concentration measurement in workplace air determined by the method specified in this International Standard, the square of the combined uncertainty, u_c, is given by Equation (6):

$$u_c^2 = u_{V\text{sam}}^2 + u_{\rho\text{sam}}^2 + u_{\rho\text{blank}}^2 + u_{bL}^2 \quad (6)$$

where

$u_{V\text{sam}}$ is the uncertainty in the volume sampled;

$u_{\rho\text{sam}}$ is the uncertainty in the isocyanate concentration determined;

$u_{\rho\text{blank}}$ is the uncertainty in the isocyanate concentration in the blank;

u_{bL} is the between laboratories uncertainty.

The full breakdown of these component uncertainties is given in EN 482 and ISO/IEC Guide:1995, and in 11.2 to 11.7. This approach was also used to calculate the uncertainty for Desmodur N 3390®, an HDI-based formulation, using data obtained previously[9]. A list of the data used to calculate the combined and expanded uncertainties is given in Table B.1. A list of the values calculated, for each level and formulation, is given in Table C.1.

11.1.2 Summary of calculated uncertainty data

Pooling the data for the formulations tested gave the following combined uncertainty: 27 % (7 formulations, 4 levels, 2 sampler types).

The corresponding expanded uncertainty (twice the combined uncertainty) was 54 %.

No significant difference was observed between the impinger/filter and filter only results (p = 0,01). For some specific formulations, expanded uncertainties are given in Table 3.

Table 3 — Expanded uncertainties for some specific formulations

Formulation[a]	Expanded uncertainty %	
	Best case	Worst case
Desmodur H	43	60
Suprasec 5030	48	77
Suprasec 2234	42	80
Aldrich 415806	43	65
Desmodur N 3300	47	87
Desmodur T80	47	50
Desmodur N 3390	46	72

[a] The Desmodur, Suprasec, and Aldrich grades are examples of products available commercially. This information is given for the convenience of users of this International Standard and does not constitute an endorsement by ISO of these products.

11.2 Assessment of performance characteristics of the method — Sampling considerations (detailed ISO/IEC Guide 98:1995 approach)

11.2.1 Collection efficiency relative to particle size distribution

For a complete description of the performance requirements and tests to be performed, see ISO 16200-1[18].

11.2.2 Sampled volume of air

The volume of air sampled, V_{sam}, is calculated from Equation (7)[19]:

$$V_{sam} = \frac{(q_0 + q_e)}{2} t \tag{7}$$

where

q_0 is the sample flow rate, in litres per minute, at the beginning of the sampling period;

q_e is the sample flow rate, in litres per minute, at the end of the sampling period;

t is the sampling time, in minutes.

The uncertainty in the volume of air sampled is given by Equation (8):

$$\frac{u^2_{V\text{sam}}}{V^2_{sam}} = \frac{u^2_{q0} + u^2_{qe}}{(q_0 + q_e)^2} + \frac{u^2_t}{t^2} + \frac{u^2_{q\text{var}}}{\left[(q_0 + q_e)/2\right]^2} \tag{8}$$

in which: the first term represents uncertainty in the measurements of the flow rates before and after sampling; the second term represents uncertainty in the measurement of the sampling time; and the third term represents uncertainty arising from any variations in the flow rate during the sampling period.

11.2.3 Sampling time

Sampling time, t, can be measured to within ± 0,1 min. For a sampling time of 8 h, the relative uncertainty due to the measurement of t is negligible, i.e. for practical purposes the second term in Equation (8) can be ignored.

11.2.4 Variations in flow rate during sampling

The flow rate during sampling is unknown. The square of the uncertainty (see ISO/IEC Guide 98:1995[5]) due to variations in the flow rate during sampling can be estimated by assuming a uniform distribution, giving a factor of 1/12 as in Equation (9):

$$u^2_{q\text{var}} = \frac{(q_0 - q_e)^2}{12} \tag{9}$$

11.2.5 Concentration conversion to other specified temperature and pressure conditions

For the conversion of concentrations to specified temperature and pressure conditions, knowledge is required of the actual mean temperature and pressure during sampling. Squares of uncertainties in temperature, θ, and pressure, p, values used for conversion may be obtained from actual measurements, taking into account the uncertainty in the calibration of the temperature and pressure sensors used as in Equation (10):

$$u^2 = u_{\text{cal}}^2 + \frac{s_{\text{meas}}^2}{n} \tag{10}$$

where

u_{cal} is the uncertainty due to calibration of the temperature or pressure sensor;

s_{meas} is the standard deviation of the end measurements of temperature or pressure;

n is the number of temperature or pressure measurements.

Knowledge is also required of extremes of temperature and pressure during sampling, assuming these to be uniformly distributed. For example, the square of the uncertainty in temperature is given by Equation (11):

$$u_\theta^2 = u_{\text{cal}}^2 + \frac{(\theta_{\text{max}} - \theta_{\text{min}})^2}{12} \tag{11}$$

where θ_{max} and θ_{min} are the temperature extremes. Generally, the first term will be negligible compared to the second.

11.2.6 Combined uncertainty of sample volume

The above uncertainty contributions are combined to give the uncertainty in the sample volume converted to specified conditions, as in Equation (12):

$$\frac{u_{V\text{sam,sp}}^2}{V_{\text{sam,sp}}^2} = \frac{u_{V\text{sam}}^2}{V_{\text{sam}}^2} + \frac{u_\theta^2}{\overline{\theta}^2} + \frac{u_p^2}{\overline{p}^2} \tag{12}$$

11.3 Assessment of performance characteristics of the method — Other considerations — (detailed ISO/IEC Guide 98:1995 approach)

11.3.1 Mass of compound in sample

The mass of compound in the air sample, m_{sam}, may be expressed as in Equation (13):

$$m_{\text{sam}} = \frac{m_{\text{uc}}}{E_{\text{coll}} v_{\text{s}} S_{\text{anal}} E_{\text{r/e}}} \tag{13}$$

where

m_{uc} is the uncorrected analytical mass of compound in the analytical sample;

E_{coll} is the collection efficiency;

v_{s} is the sampler variability;

S_{anal} is the analyte stability in the sample;

$E_{\text{r/e}}$ is the reaction/extraction efficiency.

11.3.2 Analyte stability

The analyte stability, S_{anal}, shall be experimentally established for storage under conditions (time, temperature, environment) typical to an individual laboratory. Tests shall be performed at an analyte level corresponding to a concentration equivalent to the limit value. At times $t = 0$ and $t = t$, a number, $n \geqslant 6$, of samples shall each be analysed under repeatability conditions. At both times, the samples shall be randomly picked from a batch of representative samples in order to minimise possible systematic concentration differences. As a test of (in)stability, a Student t-test shall be performed (95 % confidence, 2-sided). The uncertainty of the stability determination consists of contributions from:

a) desorption (random part of desorption efficiency);

b) calibration (random part of calibration);

c) analytical precision;

d) inhomogeneity of the sample batch.

As such, the contribution of the determination of analyte stability will already be incorporated in other contributions and needs not to be taken into account.

11.3.3 Reaction/extraction efficiency

The reaction/extraction efficiency, $E_{r/e}$, of compounds and its uncertainty are typically obtained from replicate measurements on certified reference materials (CRM) of the compound or of its reaction product(s). The uncertainty due to incomplete reaction/extraction for the compound level corresponding to the limit value can be calculated from Equation (14):

$$\frac{u^2_{Er/e}}{E^2_{r/e}} = \frac{u^2_{mCRM}}{m^2_{CRM}} + \frac{s^2_{\overline{m}det}}{\overline{m}^2_{det}} + \frac{(\overline{m}_{det} - m_{CRM})^2}{m^2_{CRM}} \qquad (14)$$

where

$u_{m\,CRM}$ is the uncertainty in the certified mass of compound in the CRM;

m_{CRM} is the certified mass of compound in the CRM;

$s_{\overline{m}det}$ is the standard deviation of the mean mass derived from the replicate measurement results;

$\overline{m}_{det}$ is the mean mass derived from the replicate measurement results.

The last term in Equation (14), representing the uncertainty due to a bias between certified and determined mass, may be ignored if the bias is statistically insignificant at the 95 % level. A correction is applied for the bias if it is statistically significant at the 95 % level.

If a CRM is not available, the material with the highest metrological quality available should be used.

11.3.4 Uncorrected analytical mass of compound

The uncertainty in the uncorrected analytical mass of a compound is determined by:

a) the uncertainty in the concentrations of the calibration standards used;

b) the lack-of-fit (LOF) of the calibration function;

c) drift of the detector response between calibrations;

d) the precision of the analysis;

e) the selectivity of the chromatographic system.

11.3.5 Calibration standards

The uncertainty of the concentration of compound in the calibration standards used will depend on the type of calibration standard used. For calibration standards consisting of solutions in toluene or acetonitrile, the uncertainty will be built up of contributions from the following.

11.3.5.1 Isocyanate purity, generally known from the manufacturer's specifications as a minimum purity expressed as a percentage by mass, w, given either as a definite figure or as a "better than" figure, i.e. $w = 99$ % or $w \geqslant 99$ %. If $w = 99$ %, the relative uncertainty due to impurity is given by $(100 - w)$ %; if $w \geqslant 99$ %, the relative uncertainty can be estimated assuming a uniform distribution as in Equation (15):

$$u_w^2 = \frac{(100 - w)^2}{12} \tag{15}$$

11.3.5.2 Uncertainties in weighings of compounds and solutions, i.e. the uncertainty of the balance used. The latter contribution is generally expressed for differential weighings as in Equation (16):

$$u_{\text{weigh}}^2 = 2u_{\text{bal}}^2 \tag{16}$$

where u_{bal} is the the uncertainty of the balance used.

11.3.6 Lack-of-fit of calibration function

The uncertainty due to LOF, u_{LOF}, of the calibration function can be calculated for the relevant concentration (corresponding to a mass of compound sampled at the limit value) from residuals of a calibration function obtained by a least-squares linear regression weighted in the concentration of compound in the calibration standard as in Equation (17):

$$u_{\text{LOF}}^2 = \frac{(m_{\text{regr}} - m_{\text{std}})^2}{m_{\text{std}}^2} = R_{\text{rel}}^2 \tag{17}$$

where

m_{regr} is the mass of compound calculated from the regression equation at the level of the calibration standard corresponding most closely to the mass of compound representing a sample at the limit value;

m_{std} is the mass of compound present in the corresponding calibration standard;

R_{rel} is the relative residual for the particular concentration level.

NOTE LOF of the calibration function will contribute to the uncertainty due to incomplete extraction or reaction if the latter's efficiency is significantly different from 1. In that case — irrespective of whether or not a correction for incomplete reaction/extraction is applied — the uncertainty due to LOF of the calibration function need not be taken into account in the uncertainty assessment.

11.3.7 Drift in detector response

The uncertainty due to detector response drift, u_{drift}, can be estimated from data on the relative differences in responses between subsequent calibrations as in Equation (18):

$$u_{drift}^2 = \frac{(r_n - r_{n-1})^2}{12[(r_n + r_{n-1})/2]^2} \quad (18)$$

where

r_n is the detector response, r, for the nth determination of a calibration standard corresponding most closely to the mass of compound representing a sample at the limit value;

r_{n-1} is the detector response, r, for the preceding, $(n-1)$th, determination of a calibration standard corresponding most closely to the mass of compound representing a sample at the limit value.

11.3.8 Precision of the analysis

The uncertainty due to the (im)precision of the analysis, u_r, is determined by analysis under repeatability conditions of calibration standards of the same composition. A minimum of six replicate analyses shall be performed. The uncertainty is then calculated as in Equation (19):

$$u_r^2 = \frac{s_{anal}^2}{\bar{r}^2} \quad (19)$$

where

s_{anal} is the standard deviation of the replicate responses;

$\bar{r}$ is the mean response.

In the uncertainty assessment, this contribution is already incorporated in contributions from the determination of desorption efficiency and need not be taken into account.

11.3.9 Analytical selectivity

The separation system used (liquid chromatographic column, gradient programme) shall be optimised in order to minimise uncertainty due to (unnoticed) co-elution of potential interferents. The resolution, R, of the liquid chromatographic system used is given by Equation (20),

$$R = \frac{\Delta t_r}{0{,}85(b_{anal} + b_i)} \quad (20)$$

where

Δt_r is the difference in retention time, in seconds, between the analyte and interferent;

b_{anal} is the peak width at half height, in seconds, of the analyte peak;

b_i is the peak width at half height, in seconds, of the interferent peak.

To comply with this International Standard, R shall be less than 1. In that case, the maximum uncertainty due to co-elution is 2,5 %. The typical uncertainty contribution will then be ± 0,7 %.

11.3.10 Combined uncertainty in the analytical mass of compound

The above contributions are combined to give the uncertainty of the analytical mass of compound, $u_{m\,\text{anal}}$, excluding the uncertainty due to imprecision, in Equation (21):

$$\frac{u^2_{m\text{anal}}}{m^2_{\text{anal}}} = \frac{u^2_{c\text{std}}}{c^2_{\text{std}}} + u^2_{\text{LOF}} + u^2_{\text{drift}} + u^2_{\text{sel}} \tag{21}$$

where

$u_{c\text{std}}$ is the uncertainty in the concentration of the calibration standards (11.3.5);

u_{LOF} is the uncertainty due to LOF of the calibration function (11.3.6);

u_{drift} is the uncertainty due to drift in detector response (11.3.7);

u_{sel} is the uncertainty in analytical selectivity (11.3.9).

11.3.11 Combined uncertainty in the sampled mass of compound

The contributions given in 11.3.2 to 11.3.9 are combined to give the uncertainty in the mass of compound in the air sample as:

$$\frac{u^2_{m\text{sam}}}{m^2_{\text{sam}}} = \frac{u^2_{m\text{anal}}}{m^2_{\text{anal}}} + \frac{u^2_{Er/e}}{E^2_{r/e}} \tag{22}$$

11.4 Mass of compound in field sample blank

The mass of compound in a field sample blank, m_{blank}, is determined by analysis under repeatability conditions of a series of sample blanks; a minimum of six replicate analyses shall be performed. The uncertainty is then calculated using the slope of the calibration function extrapolated to the blank response level as:

$$u^2_{m\text{blank}} = \frac{s^2_{\text{blank}}}{b_{\text{blank}}} \tag{23}$$

where

s_{blank} is the standard deviation of the replicate analytical results from the blank;

b_{blank} is the slope of the calibration function at the field sample blank response level.

If the blank response is below three times the noise level of the detector at the retention time of analyte, then the blank level and its uncertainty shall be calculated from the detector noise level using the slope of the calibration function extrapolated to zero response assuming a uniform distribution:

$$m_{\text{blank}} = \frac{3r_0}{2b_0} \tag{24}$$

$$u^2_{m\text{blank}} = \frac{9r_0^2}{12} \tag{25}$$

where

r_0 is the noise level;

b_0 is the slope of the calibration function at zero response.

11.5 Between-laboratory uncertainty contributions

The procedures described above are not restrictive, but allow for possible variations in approaches between laboratories. The resulting additional uncertainty contributions can be quantified by performing interlaboratory comparisons involving the complete measurement procedure inclusive of sampling, as well as the analytical part of the measurement procedure. Interlaboratory comparisons shall be organised in accordance with ISO 5725-2 using samples of sufficient homogeneity to assure that the contribution to the between-laboratory uncertainty due to inhomogeneity is negligible. In practice, an uncertainty due to inhomogeneity of < 2 % is usually sufficient.

11.6 Combined uncertainty

The combined uncertainty in the compound concentration, $u_{c\text{sam}}$, in the air sampled is obtained by combination of contributions given in Equations (12), (22), and (23) or (25), adding the between-laboratory uncertainty (if considered appropriate) as:

$$u^2_{\rho\text{sam}} = u^2_{m\text{sam}} + u^2_{m\text{blank}} + u^2_{V\text{sam,sp}} + u^2_{\text{bL}} \tag{26}$$

where u_{bL} is the between-laboratory uncertainty contribution.

11.7 Expanded uncertainty

The expanded uncertainty in ρ_{sam} at the 95% confidence level is obtained by multiplying $u_{\rho\text{sam}}$ with a coverage factor of 2.

12 Stability

Isocyanate ureas (MP derivatives) have been found to be stable for several years when stored in a freezer. Stability data for filters and solutions (toluene and acetonitrile) are given in 5.5.

13 Test report

The test report shall contain at least the following information:

f) complete identification of the sample;

g) reference to this International Standard or any supplementary International Standard;

h) the sampling location, sampling time period and volume of air sampled;

i) the barometric pressure and temperature (if appropriate);

j) the test result(s);

k) any unusual features noted during the determination;

l) any operation not included in this International Standard or in any International Standard to which reference is made or which is regarded as optional.

14 Quality control

An appropriate level of quality control should be employed when using this International Standard. It is strongly recommended that all laboratories undertaking the determination of hazardous substances in workplace air should participate in an external quality assessment scheme such as WASP[1].

Annex A
(informative)

Determination of sampling efficiency

A.1 Generation of standard vapour atmospheres

If a single impinger is used, the sampling efficiency (SE) for each isocyanate of interest should be determined over the sample concentration range. This can be done by using a standard vapour atmosphere generator to sample the isocyanates of interest at appropriate concentration, temperature, humidity, time, and sampling flow rate. Treat these SE samples in the manner described previously. The SE is the mass, in milligrams, recovered from the impinger divided by the mass, in milligrams, applied. If the SE under the conditions used during sampling is less than 0,75 (75 %), the result should be discarded.

A.2 Difficult to generate vapour atmospheres

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 1,0 for both monomers and polymers, for most practical purposes.

Annex B
(informative)

Data used for uncertainty estimates

Table B.1 — Uncertainty estimates

Isocyanate formulation[a]	Desmodur H	Suprasec 5030	Suprasec 2234	Desmodur N 3300	Aldrich 415806	Desmodur T 80	Desmodur N 3390
Uncertainty in sampled volume							
Sample volume	5% — worst case measured value						
Flowmeter calibration	HSL performance criteria for flowmeters gives a tolerance of ± 8 (HSL in-house procedure SCP-001); the flowmeters used to check the pumps were within this tolerance; this value (8%) was used as a worst case						
Flowmeter variation							
Sampling time	15 min (impinger/filter) or 8 min (filter) ± 6 s on stopwatch, gives an uncertainty of 1 % (filter) or 0,5 % (impinger/filter)						
Temperature	1 % — estimated						
Pressure	1 % estimated						
Uncertainty in analyte mass determined							
Analyte mass	Measured, used percentage RSD values, data from OMS/2004/07[7], Table 2						Data from IACS/97/19[9]
Stability	Solid MP derivatives standards are stable > 10 years 1 % — solutions (measured during HSL calibration stock procedures, ~ 6 months) 9 % — filters (27 days) – data from IACS/97/19[9]						
Reaction/extraction efficiency	Measured, used percentage recovery values from OMS/2004/07[7], Table 2						Data from IACS/97/19[9]
Isocyanate mass in calibrations	0,1 % balance performance criteria (HSL in-house procedure SCP-002); analytical standards are usually > 99 % pure						
Calibration lack of fit	5 % — worst case measured value for EC detector						
Drift	5 % — worst case measured value; a fresh calibration is obtained for each sample set, calibrations are run front and back, with check samples every 10 samples or 4 h						
Precision	12 % — calculated from HSL WASP data; six analysts, 2 LC systems: 29 rounds, 4 MDI filters/round						
Chromatographic selectivity	Negligible —– see MDHS25/3[1] for peak identification procedures						
Uncertainty in blank value							
Blank	Negligible — 10σ for blank determination ($n = 6$) isocyanate concentration ~0,004 µg/ml						
Uncertainty in between laboratory performance							
Between lab	12 % — calculated from WASP data (all participant laboratories), 19 labs/27 rounds						

[a] The Desmodur, Suprasec, and Aldrich grades are examples of products available commercially. This information is given for the convenience of users of this International Standard and does not constitute an endorsement by ISO of these products.

Annex C
(informative)

Combined uncertainties for isocyanate formulations

Table C.1 — Calculated combined uncertainties for isocyanate formulations

Isocyanate formulation [a]	Sampler	Spiking level	Combined uncertainty	Expanded uncertainty
Desmodur H	Impinger plus filter	2	23,8	47,7
		1	26,9	53,8
		0,5	21,4	42,8
		0,1	28,1	56,1
	Filter	2	24,9	49,8
		1	27,9	55,8
		0,5	23,4	46,8
		0,1	30,1	60,3
Suprasec 5030	Impinger plus filter	2	29,0	58,0
		1	38,6	77,2
		0,5	38,0	76,0
		0,1	26,3	52,6
	Filter	2	24,0	48,0
		1	24,9	49,7
		0,5	24,7	49,5
		0,1	33,1	66,3
Suprasec 2234	Impinger plus filter	2	21,1	42,2
		1	22,5	44,9
		0,5	21,5	42,9
		0,1	26,3	52,6
	Filter	2	29,7	59,5
		1	27,5	55,0
		0,5	29,3	58,6
		0,1	39,8	79,6

Table C.1 (*continued*)

Isocyanate formulation [a]	Sampler	Spiking level	Combined uncertainty	Expanded uncertainty
Desmodur N3300	Impinger plus filter	2	31,7	63,5
		1	27,7	55,5
		0,5	23,6	47,3
		0,1	43,5	87,1
	Filter	2	30,6	61,2
		1	29,1	58,1
		0,5	25,7	51,4
		0,1	27,2	54,4
Aldrich 415806	Impinger plus filter	2	23,6	47,3
		1	21,6	43,3
		0,5	30,9	61,7
		0,1	27,1	54,3
	Filter	2	24,0	48,0
		1	25,3	50,7
		0,5	26,0	52,0
		0,1	32,5	65,0
Desmodur T80	Impinger plus filter	2	24,3	48,5
		1	23,6	47,2
		0,5	24,1	48,2
		0,1	25,2	50,4
	Filter	2	23,3	46,6
		1	24,0	48,0
		0,5	23,9	47,9
		0,1	24,0	48,0
Desmodur N3390	Impinger plus filter	2	23,0	46,1
		1	24,4	48,8
		0,5	29,0	58,0
		0,1	36,0	72,0
	Filter	2	24,2	48,4
		1	27,1	54,1
		0,5	27,7	53,4
		0,1	27,6	55,2

[a] The Desmodur, Suprasec, and Aldrich grades are examples of products available commercially. This information is given for the convenience of users of this International Standard and does not constitute an endorsement by ISO of these products.