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Workplace air quality — Determination of isocyanate in air using a double-filter sampling device and analysis by high pressure liquid chromatography

Qualité de l'air des lieux de travail — Dosage des isocyanates dans l'air au moyen d'un dispositif d'échantillonnage à filtre double et par analyse par chromatographie liquide à haute performance

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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 17736 was prepared by Technical Committee ISO/TC 146, *Air quality*, Subcommittee SC 2, *Workplace atmospheres*.

Introduction

Isocyanates are commercially available chemicals used in the polyurethane industry. They are known to cause health problems, such as asthma, contact dermatitis and hypersensitivity pneumonitis, in workers even at very low levels in occupational environments.

Since isocyanates are highly reactive compounds and exposure limits are very low, the sampling and the analysis of these substances are critical.

This method is based on the standard method developed by the Institut de Recherche en Santé et en Sécurité du Travail [Occupational Health and Safety Research Institute] (IRSST) of Quebec. It has been in use for more than 18 years as the standard government method in that province of Canada. Since 1996, it has been introduced into the marketplace in the USA, Brazil, and the UK. After a year's study (Reference [10]), the method was adopted in 1998-11 by the US Air Force as an acceptable alternative to NIOSH Method 5521 for monomeric isocyanates (now withdrawn).

The method is now routinely used in the Canadian provinces of Alberta, British Columbia, and Ontario, and in the US state of Washington, which has validated the method for TDI. Thirteen laboratories have been schooled in this analytical method, three in Canada, eight in the USA and Mexico, one in Brazil, and one in the UK. This method has been in use in several countries for many years and 13 laboratories participate in round robin testing on a regular basis in order to maintain their proficiency.

The double-filter method has been validated for different applications of isocyanates such as spray-painting (Reference [11]) and foam manufacturing. It has also been compared with other established methods and demonstrated equivalent results (Reference [10]).

Double-filter methods are also available in ASTM D6561[7] and ASTM D6562[8] for HDI, and ASTM D5932[9] for TDI.

ISO draws attention to the fact that it is claimed that compliance with this document may involve the use of a patent concerning the double-filter sampling device for isocyanates.

Workplace air quality — Determination of isocyanate in air using a double-filter sampling device and analysis by high pressure liquid chromatography

1 Scope

This International Standard gives general guidelines for the sampling and analysis of airborne isocyanates in workplace air. This International Standard is appropriate for organic compounds containing free isocyanate functional groups and is specific for the quantification of monomers, polymers and prepolymers, vapours and aerosols. Differential air sampling is performed with a segregating device which can show the physical state of the isocyanates analysed as found in the field. This capacity, however, may show limitations for given situations, e.g. when aerosols collected on the first filter contain free monomer that migrates to the second filter and is then quantified as vapour phase isocyanate. The determination of aromatic monomers includes toluene diisocyanate (TDI) and 4,4'-diisocyanato-diphenylmethane (MDI). Aliphatic monomers include isophorone diisocyanate (IPDI), 4,4'-methylene bis-(cyclohexyl isocyanate) (HMDI) and 1,6-hexamethylene diisocyanate (HDI). Isocyanate oligomers and prepolymers can also be determined using this method.

The double-filter method is designed to determine short-term (15 min) exposure concentrations of organic isocyanates in a workplace environment by personal monitoring or by fixed location monitoring. However, if the exposure is expected to be in vapour form only, then sampling time can be extended to 8 h. Since the filter is derivatized in the field immediately after sampling, loss of isocyanate aerosol because of its reaction with other chemicals is negligible except for very fast-reacting isocyanate systems such as foam spraying of MDI in polyurethane applications. The method is suitable for the measurement of airborne organic isocyanates in the NCO equivalent concentration range of 0,01 µg/sample to 2,1 µg/sample, corresponding to approximately 0,67 µg/m^3 to 140 µg/m^3 for a 15 l sample volume. This range brackets about eight times the current established threshold limit value (TLV) of 5 ppb for monomers set by many national authorities.

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 Principle

A measured volume of air is drawn through a double-filter sampling device in which the first filter made of polytetrafluoroethylene (PTFE) collects the aerosols and then the isocyanate vapour is absorbed on a glass fibre (GF) filter impregnated with 9-(methylaminomethyl)anthracene (MAMA). The isocyanate present as an aerosol is collected on the PTFE filter and derivatized immediately after sampling, in a 5 ml solution of 1-(2-methoxyphenyl)piperazine (MP), 0,1 mg/ml in toluene.

Both isocyanate monomer and oligomer urea derivatives solutions are separated using reversed phase high performance liquid chromatography (HPLC). Vapour monomers are analysed by HPLC using an ultraviolet (UV) and fluorescence (FL) detector. Fluorescence detection is used when concentrations are less than 25 % of the TLV. Monomeric and oligomeric aerosols are analysed by HPLC with a UV detector for quantification and a diode array detector (DAD) for identification. Quantification of the monomeric aerosols is made by comparison with the relevant isocyanate monomer standard. The total isocyanate-in-air concentration is calculated from the sum of all the isocyanate-derived peaks calculated as NCO function. In some cases, a bulk sample is used for calibration and results are reported as mass of base per volume.

The quantitative detection limits for isocyanate, defined as $10s$, where s is the standard deviation obtained from 10 measurements carried out on a standard solution whose concentration is close to the expected detection limit, has been estimated to be approximately 0,026 µg/sample, 0,029 µg/sample, and 0,036 µg/sample for vapour phase HDI, TDI, and MDI, respectively. The quantitative detection limit for aerosol phase HDI, TDI, and MDI is 0,031 µg/sample.

NOTE The calculation of oligomeric isocyanates by this method is expressed as the total NCO function equivalent, utilizing the response factor of the corresponding monomer for the oligomer calculation.

4 Reagents and materials

During the analysis, unless otherwise stated, use only reagents of recognized analytical grade and distilled or demineralized water or water of equivalent purity.

4.1 Water, HPLC grade or equivalent.

4.2 1-(2-Methoxyphenyl)piperazine (MP) [CAS No. 35386-24-4], >98 % mass fraction.

4.3 9-(Methylaminomethyl)anthracene (MAMA) [CAS No. 73356-19-1], >99 % mass fraction.

4.4 Acetic acid, glacial [CAS No. 64-19-7], HPLC grade.

4.5 Acetic anhydride [CAS No. 108-24-7], certified ACS.

4.6 Triethylamine [CAS No. 121-44-8], >98 % mass fraction assay by GC.

4.7 Phosphoric acid [CAS No. 7664-38-2], certified ACS.

4.8 Reagent solvents, commonly toluene [CAS No. 108-88-3], dimethylformamide [CAS No. 68-12-2], and acetonitrile [CAS No. 75-05-8], should be HPLC grade. They shall be free from compounds co-eluting with the substance(s) of interest. To avoid any interference from the solvent, perform quality controls on each different lot of solvent.

4.9 Buffer solution and HPLC mobile phase.

4.9.1 Triethylamine buffer — vapour analysis. In a 1 l volumetric flask, dilute 30 ml triethylamine (4.6) in water, and make up to the mark with water. Adjust the pH of this solution to 3 using phosphoric acid (4.7). Filter the solution under vacuum with a 0,22 µm filter.

4.9.2 Sodium acetate buffer — aerosol analysis. Weigh approximately 12,5 g of sodium acetate in 1 l HPLC grade water (4.1). Adjust the pH of this solution to 6 with glacial acetic acid (4.4). Filter the resulting solution under vacuum with a 0,22 µm filter.

4.9.3 Mobile phase — vapour analysis. A solvent mixture of acetonitrile (4.8) and triethylamine buffer (4.9.1). The appropriate proportion of each solvent depends on the isocyanate analysed, see Table 1.

4.9.4 Mobile phase — aerosol analysis. A solvent mixture of acetonitrile (4.8) and sodium acetate buffer (4.9.2). The appropriate proportion of each solvent depends on the isocyanate analysed, see Table 2.

4.10 Reagent solutions.

4.10.1 Desorption solution — vapour analysis. A solvent mixture of 67 % volume fraction of dimethylformamide (4.8) and 33 % volume fraction mobile phase.

4.10.2 Derivatization solution — aerosol analysis. Weigh 10 mg MP (4.2) and transfer it to a 100 ml volumetric flask. Dissolve and make up to the mark with toluene (4.8). The final concentration of this MP solution is equivalent to 0,1 mg/ml.

5 Apparatus

5.1 Sampling system. A three-piece, closed face, 37 mm cassette is used. The sampling train consists of a 37 mm PTFE filter of porosity 5 µm followed by a binder free 37 mm glass fibre (GF) filter impregnated with MAMA (4.3) and supported by a cellulose back-up pad (see Figure 1).

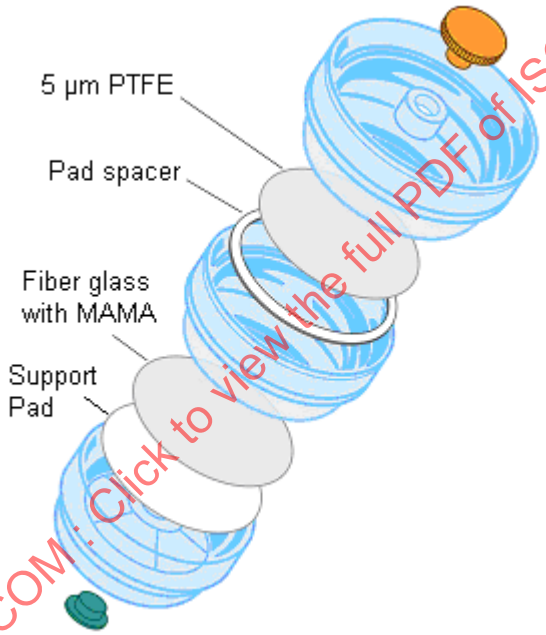


Figure 1 — Three-piece cassette 37 mm

This sampling train is commercially available as ISO-CHEK®[1)].

5.2 Sampling pump. The pump shall fulfil the requirements of EN 1232 or equivalent.

The pump should also be in accordance with local safety regulations.

5.3 Tubing, of plastic, rubber or other suitable material, about 900 mm long, of appropriate diameter to ensure a leakproof fit to both pump (5.2) and double-filter sampling cassette (5.1). Clips shall be provided to hold the cassette and connecting tubing to the worker's lapel within 300 mm of their breathing zone.

5.4 Flow meter, portable, capable of measuring the appropriate flow rate to within ±5 %, and calibrated against a primary standard.

1) ISO-CHEK is the trade name of a product supplied by SKC. This information is given for the convenience of users of this document and does not constitute an endorsement by ISO of the product named. Equivalent products may be used if they can be shown to lead to the same results.

5.5 Glass jar, consisting of a 30 ml glass container equipped with a PTFE lined screw cap, capable of receiving 37 mm filters.

5.6 Liquid chromatographic system. An HPLC linked to UV and FL detectors is required. The FL detector should be used for the quantification of monomeric vapours when they are present at less than 0,180 µg/sample of isocyanate. A diode array detector (DAD) is also suitable for confirmation of identification.

5.7 Autosampler, commercially available, with a sampling loop within the range 10 µl to 100 µl.

5.8 HPLC column, of stainless steel, C-18 type, capable of separating the urea derivatives of interest.

6 Air sampling

6.1 Calibration of sampling system

Calibrate the sampling system (5.1) with a representative sampling device assembly in line, using an appropriate external calibrated meter. One end of the calibrated flow meter (5.4) should be at atmospheric pressure to ensure proper operation.

6.2 Preparation of sampling equipment

A glass jar (5.5) containing 5 ml MP derivatization solution (4.10.2) should be prepared in the laboratory before sampling. Prepare one jar for each sample to be used.

6.3 Preparation of MAMA-impregnated filter

Approximately 100 GF filters are put in a beaker containing 25 mg MAMA (4.3) dissolved in 250 ml toluene (4.8) for a period of 30 min. Remove the filters from the beaker with tweezers and transfer them to dry on a sheet of aluminium foil placed in a compartment away from light for 12 h. The volume of solution absorbed by one filter is evaluated to be 500 µl, equivalent to a mass of approximately 50 µg of MAMA on each filter. This quantity corresponds to approximately 0,11 µmol and is 36 times the amount that would be required during sampling before the reagent is exhausted (reacts) at a concentration of 5 ppb sampled at 1 l/min for 15 min.

6.4 Collection of samples

The recommended sampling volume for the double-filter sampling system (5.1) is 15 l (1 l/min for a period of 15 min). This sampling volume is used for short-term exposure and for mixtures of airborne particles and vapour. The sampling time can be extended to 8 h if all the expected exposure is in a vapour form.

In accordance with EN 1232, adjust the pump (5.2) flow rate to approximately 1 l/min. To compensate for any pressure drop due to the cassette, make sure the flow rate is adjusted with a sampling device in place. Turn off the pump and use a new sampler. Record the sample identity and all relevant sampling data.

NOTE Keep a sampling device as a calibrator for further pump calibration.

Fix the sampler to the worker's lapel and position the sample as close to the breathing zone as possible. Place the sampling pump in a convenient pocket (ensure the pump exhaust is not restricted) or fix to a belt around the waist. Turn on the pump and write down the time of the beginning sampling period. At the end of the sampling period, check and make a note of the sample flow rate before removing the cassette. The flow rate of the pump should be within the ±5 % variation of the nominal value; if greater, discard the sample.

Calculate the mean flow rate, in litres per minute, by averaging the flow rate measurements throughout the sampling period and calculate the volume of air sampled, in litres, by multiplying the mean flow rate by the sampling time, in minutes.

As soon as the sampling period is over, using tweezers, immediately remove the PTFE filter from the sampling device and place the filter in a glass jar (5.5) containing 5 ml MP derivatization solution (4.10.2).

Take care to avoid contact with the GF filter when removing the PTFE filter from the sampling device. Identify the jar with the corresponding sampler's identification number. Losses of isocyanate aerosol because of their reaction with other chemicals are negligible except for very fast-reacting isocyanate systems such as foam spraying of MDI polyurethane applications (Reference [12]).

6.5 Blanks

Field blanks should be prepared by using cassettes identical to those used for sampling and subjecting them to the same handling procedures as the samples except for the actual period of sampling. Label these as field blanks. Provide a blank for every 10 samples or when changing sampler batch.

7 Procedure

7.1 Safety precautions

Wear safety glasses and appropriate disposable gloves during analysis to protect the eyes and hands from harmful solvents and reagents, and to reduce the possibility of contamination.

WARNING — This International Standard does not purport to address all the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate health and safety practices and to ensure compliance with any national regulatory conditions.

7.2 Calibration standard

7.2.1 Preparation of monomer derivatives

Slowly add the appropriate diisocyanate to a MAMA solution in a ratio 1 mmol diisocyanate +2 mmol MAMA or 1 mmol monoisocyanate +1 mmol MAMA; a slight excess of MAMA may be used. The choice of solvent may vary from one isocyanate to another; usually dichloromethane is suitable, but some reactions have shown better performance using diethyl ether. Most reactions are exothermic and so an ice bath may be used to cool down the resulting mixture.

Collection of the white crystalline urea precipitate is performed using a paper filter [e.g. Whatman No. 42[2)]]. The resulting precipitate is washed with toluene (4.8) to remove the excess of MAMA. The urea derivatives are slightly soluble in toluene. If needed, purification of the precipitate may be performed by dissolving in warm methanol and then using an ice bath to cool down the solution to re-precipitate the solid, filter and dry the purified urea derivative. The purity of the derivative is determined by the melting point and HPLC analysis.

7.2.2 Preparation of standard solutions from the isocyanate monomer-urea derivatives (MAMA)

Weigh out precisely about 25 mg of the urea derivative in a 100 ml volumetric flask and make up to the mark with dimethylformamide (4.8). Take aliquots of this solution and dilute volumetrically with the desorption solution to create a series of working standard solutions over an NCO concentration range of 0,01 µg/ml to 2,1 µg/ml. Prepare further standard solutions, if the concentration range of the samples exceeds that of the standards.

The isocyanate concentration in the standard, $\rho_{NCO,std}$, in micrograms per millilitre, is given by Equation (1):

$$\rho_{NCO,std} = \frac{\rho_{ud,std} \; M_{NCO} \; N}{M_{ud}} \qquad (1)$$

2) Whatman No. 42 is the trade name of a product supplied by Whatman. This information is given for the convenience of users of this document and does not constitute an endorsement by ISO of the product named. Equivalent products may be used if they can be shown to lead to the same results.

where

$\rho_{ud,std}$ is the concentration, in micrograms per millilitre, of urea derivative in the standard;

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

N is the number of isocyanate groups (functions) per molecule;

M_{ud} is the relative molecular mass of the urea derivative.

7.2.3 Stability of isocyanate-ureas in solutions

Stock solutions of isocyanate monomer-urea derivatives have been found to be stable over a period of 1 year if kept in a refrigerator. Isocyanate monomer-urea working solutions have been found to be stable for up to 90 days.

7.2.4 Preparation of standard solution for the aerosol isocyanates analysis

For each isocyanate to be analysed, produce a stock solution from the monomeric isocyanate by dissolving in a known volume of toluene (4.8) in order to obtain a concentration of approximately 10 mg/l. Working standards are made by further diluting with toluene to generate a working range from 0,1 µg/ml to 1,0 µg/ml.

When kept in a refrigerator, the stock solutions have been found to be stable for several months. However, working standard solution should be made weekly.

8 Sample processing

8.1 Vapour analysis

The samples, quality controls, and blanks should receive the same treatment.

Remove the GF filter from the cassette and place it in a 30 ml glass jar (5.5). Add 2 ml desorption solution (see 4.10.1) to the jar. Close the jar and shake for 30 min on a reciprocating shaker. Filter the solution into an autosampler (5.7) vial, using a 0,22 µm syringe filter. Analyse using the HPLC vapour conditions specified in 9.2.

8.2 Aerosol analysis

The samples, quality controls and blanks should receive the same treatment.

Transfer the solution from the sampling jar (see 6.2) to an evaporator vial. Rinse the sampling jar and the filter three times with 1 ml toluene (4.8).

For the standard solution, place 5 ml MP derivatization solution (4.10.2) in an evaporator vial. Add 1 ml working standard solution (7.2.4) to the vial and mix gently to produce the monomer-urea.

The samples, blanks and standard are then processed as follows.

Place all the vials in a 50 °C pre-heated vacuum evaporator and evaporate to dryness. Allow the vials to cool to ambient temperature. Dissolve the residue in 1 ml acetic anhydride (4.5) 0,5 % volume fraction in acetonitrile (4.8). Filter the solution into an autosampler (5.7) vial, using a 0,22 µm syringe filter. Analyse using the HPLC conditions for NCO oligomers specified in 9.3.

9 HPLC conditions

9.1 General

A variety of chromatographic conditions may be used for the analysis of organic isocyanates in solution. The choice depends largely on the nature of interfering compounds, which may affect the chromatographic analysis.

9.2 HPLC conditions — vapour isocyanates

Typical conditions for the analysis of the vapour isocyanates are:

Column type Stationary phase C-18 (ODS – octadecylsilica, e.g. ODS-1), 3 µm, 150 mm × 3,2 mm

Column temperature Ambient

Flow rate 0,6 ml/min

Injection volume 15 µl

UV detector 254 nm

Fluorescence detector emission: 412 nm
excitation: 254 nm

NOTE A column oven can be used to obtain more consistent retention times by stabilizing the column temperature.

Mobile phase and expected retention times for the most common monomeric isocyanates are given in Table 1.

Table 1 — Mobile phase and expected retention times for the most common monomeric isocyanates

Method	Isocyanate					
	HDI	MDI	2,4-TDI	2,6-TDI	IPDI[a]	HMDI
Mobile phase (4.9.3) Triethylamine buffer (4.9.1) + acetonitrile (4.8)	25 + 75	30 + 70	35 + 65	35 + 65	25 + 75	20 + 80
Expected retention time, min	4,6	6,0	6,8	9,0	6,7	12,2[b]

[a] One isomer has been validated for IPDI.

[b] Retention time of the major HMDI isomer.

9.3 HPLC conditions — aerosol isocyanates

Typical conditions for the analysis of the aerosol isocyanates are:

Fluorescence detector ODS-1, stationary phase C18, 3 µm, 150 mm × 3,20 mm (HDI, TDI, IPDI, and HDMI)
ODS-2, stationary phase C18, 3 µm, 150 mm × 3,20 mm (MDI)

Column temperature Ambient

Flow rate 0,6 ml/min

Injection volume 30 µl to 40 µl

UV detector 242 nm

Mobile phase and expected retention times for the most common monomeric and oligomeric isocyanates are given in Table 2.

Table 2 — Mobile phase and expected retention times for the most common monomeric and oligomeric isocyanates

Method	Isocyanate						
	HDI	HDI oligomers	MDI	MDI oligomers	2,4-TDI	2,6-TDI	IPDI
Mobile phase (4.9.3) Sodium acetate buffer (4.9.2) + acetonitrile (4.8)	45 + 55	45 + 55	40 + 60	40 + 60	50 + 50	50 + 50	40 + 60
Expected retention time, min	5,7	6 to 35	4,7	7 to 45	6,5	6,0	4,7

10 Analysis

10.1 Calibration curve

For each sequence of analyses, prepare a calibration curve by injecting at least three working standard solutions as prepared in 7.2 and processed in Clause 8. The signal from the monomer-urea derivative of the isocyanate of interest is plotted against the concentration of NCO equivalent. The coefficient of correlation should be greater than or equal to 0,99. A working standard is injected every 10 injections to verify the response stability of the detectors throughout the sequence.

Although not specified in the method, the use of an internal standard is likely to improve the performance of the method. The internal standard can identify or correct such things as variability in injection volume and retention time drift. Ensure that internal standards are not naturally present in the sample and that they elute in regions of the chromatogram where no analytes elute.

10.2 Quality control

10.2.1 Vapour isocyanates

For the UV detector, spike an impregnated GF filter with 15 µl of the stock solution prepared in 7.2.2. Transfer the GF filter to a glass jar (5.5); allow to dry with the cap open and process as a sample (see 8.1). For the fluorescence detector, proceed in the same manner, except that the stock solution is diluted 1→10 with the desorption solution (see 4.10.1).

10.2.2 Aerosol isocyanates

Prepare a quality control sample by repeating the procedures specified in 7.2.4 using a monomeric isocyanate from a different lot number. The concentration of the control sample should be the midpoint of the working range.

10.3 Sample quantification

10.3.1 Calculation of vapour isocyanates

The final isocyanate concentration in air, $\rho_{v,air}$, in micrograms per cubic metre, is determined by Equation (2):

$$\rho_{v,air} = \frac{m_{mono}}{V} \quad (2)$$

where

m_{mono} is the mass, in micrograms, of isocyanate monomer in the extract obtained from the calibration curve;

V is the volume, in cubic metres, of air sampled.

10.3.2 Calculation of aerosol isocyanates

The concentration for the aerosol isocyanates is calculated using the calibration curve obtained from the monomer-urea derivative (see 7.2.4) and is expressed in mass of monomeric isocyanate equivalent per unit of volume. The total NCO concentration in monomer equivalent is obtained by summing the signals from all the oligomeric peaks on the chromatogram and entering it into the calibration curve equation (see 7.2.2). The diode array detector spectrum provides the identification and confirmation of which eluted peak to consider as a related isocyanate oligomer. In order to obtain the final mass, in micrograms of NCO equivalent, an equation involving the molar mass of the NCO function (42 g/mol), the number of NCO groups in the monomer (usually two) and the molar mass of the isocyanate involved in the analysis (e.g. TDI, 174 g/mol) is used. The final aerosol isocyanate concentration in air, $\rho_{a,air}$, in micrograms of NCO equivalent per cubic metre, is determined by Equations (3) and (4):

$$m_{NCO} = \frac{m_{mono,eq}\ M_{NCO}\ N}{M_i} \tag{3}$$

$$\rho_{a,air} = \frac{m_{NCO}}{V} \tag{4}$$

where

m_{NCO} is the mass, in micrograms of NCO equivalent, of oligomer isocyanate;

$m_{mono,eq}$ is the mass, in micrograms of NCO monomer equivalent, of isocyanate oligomers obtained by summing all oligomeric peaks;

M_{NCO} is the molar mass of NCO function (42 g/mol);

N is the number of isocyanate groups (functions) in the monomeric isocyanate involved in the analysis;

M_i is the molar mass, in grams per mole, of the monomeric isocyanate involved in the analysis;

V is the volume, in cubic metres, of air sampled.

11 Interference

The atmosphere sampled may contain compounds that result in chromatographic peaks that interfere with the sample under the HPLC conditions chosen for the method. In particular, aliphatic and aromatic amines frequently occur in association with isocyanates. However, using a diode array detector, fluorescence or a mass spectrometer should enable interfering peaks in the chromatogram to be rejected. If interfering substances are known to be present in the sampling environment, their possible presence should be made known to the analyst.

12 Determination of performance characteristics

12.1 Introduction

The measurement of the concentration of isocyanates in workplace air is associated with an uncertainty that may be expressed as overall uncertainty (EN 482[6]) or expanded uncertainty (ISO/IEC Guide 98-3[5]). Thus, an uncertainty assessment has to 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 may then be compared with preset criteria, e.g. those in EN 482[6], or defined in national or international legislation.

This section on determination of performance characteristics is taken from ISO 17734-1[4] with relatively few changes. Most of the factors that contribute to uncertainty are similar, so the changes are due to disparities between ISO 17734-1[4] and this method.

12.2 Relevant uncertainty contributions and criteria

See Table 3.

Table 3 — Relevant uncertainty contributions and criteria

Uncertainty contribution	Symbol or abbreviation	Section	Criterion
Sample volume	V_{sam}	12.3.2	
Sample flow — calibration	q_{cal}		Relative uncertainty <2 %
Sample flow — variation	Δq		<5 %
Sampling time	t		Relative uncertainty 3 %
Knowledge of temperature during sampling	T		Relative uncertainty <4 %
Knowledge of pressure during sampling	p		Relative uncertainty <2 %
Analyte mass	m_{sam}	12.3.3	
Analyte stability during storage	AS		No significant difference between results of analysis of samples before and after storage
Reaction and extraction efficiency	η_{RE}		>90 % at the limit value with a relative uncertainty of <3 %
Response factor	ϕ	12.3.3.12	Relative uncertainty <20 %
Mass of isocyanate in calibration standards	m_{CS}		Relative uncertainty <2 %
Calibration lack-of-fit	LOF		Relative residuals over the calibration range <3 %; at the limit value <2 %
Response drift between calibrations	RD		<3 %
Analytical precision	r		<1 %
Selectivity	s		Resolution factor >1, diode array detector is used
Blank level	m_{BL}	12.3.4	<50 ng with a relative uncertainty of <5 %
Between-laboratory variations		12.3.5	Relative uncertainty <7,5 %

12.3 Assessment of performance characteristics, following the detailed approach in ISO/IEC Guide 98-3[5]

12.3.1 Collection efficiency — relative to particle size distribution

12.3.2 Air sampling

12.3.2.1 Sampling volume

The volume of air sampled is calculated on the basis of measuring the sample flow rate before and after sampling:

$$V_{\text{sam}} = \frac{q_0 + q_t}{2} t \tag{5}$$

where

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

q_t is the sample flow rate at the end of the sampling period;

t is the sampling time, in minutes.

The uncertainty in the volume of air sampled is built up of contributions from

a) the measurements of the flow rates before and after sampling;

b) the measurement of the sampling time;

c) variations in the flow rate during the sampling period;

and may be expressed as

$$\frac{u^2(v_{\text{sam}})}{V_{\text{sam}}^2} = \frac{u^2(q_0) + u^2(q_t)}{(q_0 + q_t)^2} + \frac{u_t^2}{t^2} + \frac{u_{\text{var,q}}^2}{\left[(q_0 + q_t)/2\right]^2} \tag{6}$$

where the last term represents the uncertainty contribution due to flow rate variations during sampling.

12.3.2.2 Sampling time

The sampling time, t, can be measured to within ±0,5 min. For a sampling time of 15 min, the relative uncertainty due to the measurement of t is 3 %.

12.3.2.3 Variations in flow rate during sampling

The flow rate during sampling is unknown. The uncertainty due to variations in the flow rate during sampling can be estimated by assuming a uniform distribution as

$$u_{\text{var},q}^2 = \frac{(q_0 - q_t)^2}{12} \tag{7}$$

12.3.2.4 Conversion of sample volume to STP

For the conversion of concentrations to STP, knowledge is required of the actual mean temperature and pressure during sampling. Uncertainties in values of T and p used for conversion may be obtained from a) and b).

a) Actual measurements, taking into account the uncertainty in the calibration of temperature and pressure sensors used as

$$u^2 = u_{\text{cal}}^2 + \frac{s_{\text{meas}}^2}{n} \tag{8}$$

where

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

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

n is the number of temperature or pressure measurements.

b) Knowledge of extremes of temperature and pressure during sampling, assuming these to be uniformly distributed.

For example, if the temperature extremes are known to be T_{min} and T_{max}, the uncertainty in T may be calculated from

$$u_T^2 = u_{\text{cal}}^2 + \frac{\left(T_{\text{max}} - T_{\text{min}}\right)^2}{12} \tag{9}$$

Generally, the first term is negligible compared to the second.

12.3.2.5 Combined uncertainty of sample volume

The above uncertainty contributions are combined to give the uncertainty in the sample volume converted to STP as

$$\frac{u^2\left(V_{\text{sam, SPT}}\right)}{V_{\text{sam, SPT}}^2} = \frac{u^2\left(V_{\text{sam}}\right)}{V_{\text{sam}}^2} + \frac{u^2(T)}{\overline{T}^2} + \frac{u^2(p)}{\overline{p}^2} \tag{10}$$

12.3.3 Analysis

12.3.3.1 Sampled mass

The mass of isocyanate in the air samples may be expressed as

$$m_{\text{sam}} = \frac{m_{\text{anal}}}{\eta_{\text{coll}}\ \Delta S\ k_{\text{AS}}\ \eta_{\text{RE}}} \tag{11}$$

where

η_{coll} is the collection efficiency;

ΔS is the sampler variability;

k_{AS} is the analyte stability in the sample;

η_{RE} is the reaction and extraction efficiency;

m_{anal} is the uncorrected analytical mass of isocyanate in the analytical sample.

12.3.3.2 Analyte stability

The analyte stability shall be experimentally established for storage under conditions (time, temperature, environment) typical to the individual laboratory. Tests shall be performed at an isocyanate level corresponding to a concentration equivalent to the limit value.

At times $t = 0$ and $t = t$, n samples shall each be analysed under repeatability conditions ($n \geqslant 6$). For both times, the samples shall be randomly picked from a batch of representative samples in order to minimize possible systematic concentration differences. As a test of (in)stability, a t-test shall be performed (95 % confidence, two-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 k_{AS} is already incorporated in other contributions and does not need to be taken into account.

12.3.3.3 Reaction and extraction efficiency

The reaction and extraction efficiency of isocyanate and its uncertainty are typically obtained from replicate measurements on certified reference materials (CRM) of the isocyanate or of its reaction product(s). The uncertainty due to incomplete reaction and extraction for the isocyanate level corresponding to the limit value is calculated from contributions of

a) the uncertainty in the concentration of the CRM;

b) the standard deviation of the mean recovery;

c) the bias between the mass of isocyanate in the CRM and the mean mass of isocyanate determined as

$$\frac{u_{RE}^2}{\eta_{RE}^2} = \frac{u_{CRM}^2}{m_{CRM}^2} + \frac{s^2(m_{DE})}{m_{DE}^2} + \frac{(m_{DE} - m_{CRM})^2}{m_{CRM}^2} \quad (12)$$

where

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

u_{CRM} is the uncertainty in the certified mass of isocyanate in CRM;

m_{DE} is the mean mass of isocyanate determined;

$s(m_{DE})$ is the standard deviation of the mean of the replicate measurement results.

The last term, representing the uncertainty due to a significant 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 a CRM is not available, the material with the highest metrological quality available should be used.

12.3.3.4 Response factor

Since this method quantifies isocyanate oligomers with the derivatized monomer calibration curve, the variability in response between the derivatized monomer and the derivatized oligomers contributes to the uncertainty. The relative uncertainty for the response factor (RF) is estimated at 10 %.

12.3.3.5 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 of the calibration function;

c) drift of detector response between calibrations;

d) the precision of the analysis;

e) the selectivity of the chromatographic system.

12.3.3.6 Calibration standards

The uncertainty of the concentration of isocyanate in the calibration standards used depends on the type of calibration standard used.

For calibration standards consisting of solutions in toluene or acetonitrile (4.8), the uncertainty is built up of contributions from a) and b).

a) The purity of isocyanate, which is generally known from manufacturer's specifications as a minimum purity, w, e.g. $w = 99$ % mass fraction or $w \geqslant 99$ % mass fraction. In the first case, the relative uncertainty due to impurity is given by $(100 - w)$ % mass fraction; in the second case, the relative uncertainty can be estimated assuming a uniform distribution as

$$u_{\text{pur}}^2 = \frac{(100 - w)^2}{12} \tag{13}$$

b) The uncertainties in the weighings of compounds and solutions, which arise from the uncertainty of the balance used.

The latter contribution is generally expressed for differential weighings as

$$u_{\text{weigh}}^2 = 2u_{\text{bal}}^2 \tag{14}$$

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

12.3.3.7 Lack-of-fit of calibration function

The uncertainty due to lack-of-fit of the calibration function can be calculated for the relevant concentration (corresponding to a mass of isocyanate sampled at the limit value) from residuals of a calibration function obtained by a least-squares linear regression weighted in the concentration of isocyanate in the calibration standard as

$$u_{\text{lof}}^2 = \frac{\left(m_{\text{regr}} - m_{\text{std}}\right)^2}{m_{\text{std}}^2} = \rho_{\text{rel}}^2 \tag{15}$$

where

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

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

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

NOTE The lack-of-fit of the calibration function contributes 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 a correction for incomplete reaction or extraction is applied, the uncertainty due to lack-of-fit of the calibration function does not need to be taken into account in the uncertainty assessment.

12.3.3.8 Drift in detector response

The uncertainty due to response drift can be estimated from data on the relative differences in responses between subsequent calibrations as

$$u_{\text{drift}}^2 = \frac{\left(r_n - r_{n-1}\right)^2}{12\left[(r_n - r_{n-1})/2\right]^2} \tag{16}$$

where r_n is the detector response for a calibration standard corresponding most closely to the mass of isocyanate representing a sample at the limit value.

12.3.3.9 Precision of the analysis

The uncertainty due to the precision of the analysis is determined by analysis under repeatability conditions of calibration standards of the same composition; a minimum of 6 replicate analyses shall be performed. The uncertainty is then calculated as

$$u_{\text{r}}^2 = \frac{s_{\text{anal}}^2}{n\bar{r}^2} \tag{17}$$

where

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

n is the number of replicate analyses;

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

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

12.3.3.10 Analytical selectivity

12.3.3.10.1 The separation system used (liquid chromatographic column) shall be optimized in order to minimize uncertainty due to (unnoticed) co-elution of potential interferents.

The resolution R of the liquid chromatographic system used, given by Equation (18), shall be better than 1. In that case, the maximum uncertainty due to co-elution is 2,5 %. The typical uncertainty contribution is then ±0,7 %.

$$R = \frac{\Delta t_r}{0{,}85\left(w_B + w_I\right)} \tag{18}$$

where

Δt_r is the difference, in seconds, in the retention times of isocyanate and interferent;

w_B is the peak width at half height, in seconds, of the isocyanate peak;

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

12.3.3.10.2 The detector shall be able to differentiate the analyte from the potential interferents.

The diode array detector is used to assist in the identification of derivatized isocyanate compounds.

12.3.3.11 Combined uncertainty in the analytical mass of isocyanate

The above contributions are combined to give the uncertainty of the analytical mass of isocyanate excluding the uncertainty due to imprecision as

$$\frac{u^2\left(m_{anal}\right)}{m_{anal}^2} = \frac{u_{std}^2}{m_{std}^2} + u_{lof}^2 + u_{drift}^2 + u_{sel}^2 \tag{19}$$

12.3.3.12 Combined uncertainty in the sampled mass of isocyanate

The contributions given in 12.3.3.3 to 12.3.3.8, 12.3.3.10, and 12.3.3.11 are combined to give the uncertainty of the mass isocyanate in the air sample as

$$\frac{u^2\left(m_{sam}\right)}{m_{sam}^2} = \frac{u^2\left(m_{anal}\right)}{m_{anal}^2} + \frac{u_{\eta RE}^2}{\eta_{RE}^2} + \frac{u_{RF}^2}{\phi^2} \tag{20}$$

12.3.4 Mass of compound in sample blank

The mass of isocyanate in a sample 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

$$u^2\left(m_{BL}\right) = \frac{s_{BL}^2}{n b_{BL}} \tag{21}$$

where

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

n is the number of replicate analyses;

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

If the blank response is below three times the noise level of the detector at the retention time of isocyanate, 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 as

$$m_{\mathrm{BL}} = \frac{3r_0}{2b_0} \tag{22}$$

$$u^2(m_{\mathrm{BL}}) = \frac{9r_0^2}{12} \tag{23}$$

where

r_0 is the noise level;

b_0 is the slope of calibration function at zero response.

12.3.5 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

a) the complete measurement procedure inclusive of sampling;

b) the analytical part of the measurement procedure.

Interlaboratory comparisons shall be organized in accordance with ISO 5725-2 using samples of sufficient homogeneity to assure that the contribution to the interlaboratory uncertainty due to inhomogeneity is negligible. In practice, an uncertainty due to inhomogeneity of <2 % is usually sufficient.

12.3.6 Combined uncertainty

The combined uncertainty of the isocyanate concentration in the air sampled is obtained by combination of contributions given by Equations (10), (20), and (23), with the addition of the interlaboratory uncertainty (if considered appropriate) in the form

$$u_{\mathrm{c}}^2(\rho_{\mathrm{m}}) = u^2(V_{\mathrm{sam,STP}}) + u^2(m_{\mathrm{sam}}) + u^2(m_{\mathrm{BL}}) + u_{\mathrm{il}}^2 \tag{24}$$

where u_{il} is the interlaboratory uncertainty contribution.

12.3.7 Expanded uncertainty

The expanded uncertainty in the isocyanate concentration in the air sampled, ρ_{m}, at the 95 % confidence level is obtained by multiplying $u_{\mathrm{c}}(\rho_{\mathrm{m}})$ with a coverage factor of 2.

12.3.8 Uncertainty from performance criteria

When combining the uncertainties specified for the performance characteristics (12.2) a worst-case situation results. The resulting combined relative uncertainty, calculated as described in 12.3.6, is ±10 %. The expanded uncertainty is ±20 %.

Annex A
(informative)

Performance characteristics

A.1 Combined uncertainty

Based on the uncertainty values listed in Table A.1, the combined uncertainty according to Equation (24) is estimated at 25 % for isocyanate vapour and 45 % for isocyanates present as an aerosol (monomer and oligomers combined).

Table A.1 — Uncertainty estimates

Uncertainty contribution	Uncertainty %	Comments
Sample volume	4	For a 15 min air sample at a flow rate of 1 l/min
Sample flow — calibration	2	Calibration — instrument specification
Sample flow — variation	3	Estimation
Sampling time	0,2	
Knowledge of temperature during sampling	1	Estimation
Knowledge of pressure during sampling	1	Estimation
Analyte mass Monomer Oligomer	 8 13	
Analyte stability during storage	negligible	If the delay of storage is respected, Reference [8]
Reaction and extraction efficiency	6	Reference [5]
Response factor	10	Estimation, applicable on oligomer determination
Mass of isocyanate in calibration standards (weighing + dilution)	1	Estimation
Calibration lack-of-fit	4	Calculated over the calibration range
Response drift between calibrations	negligible	Instrumental drift is small and verified by injecting calibration standards at a given interval throughout sequence of analyses.
Analytical precision	2	Reference [15]
Selectivity	3	Estimation
Blank level	1	Estimation
Between-laboratory variations[a]*; vapour (MAMA)* *Monomer determination* *13 different labs; 483 samples*	24 23 23	HDI TDI (2 isomers) MDI
Between-laboratory variations[a]*; aerosol (MP)* *Monomer + oligomer determination* *10 different labs; 96 samples*	45 na 45	HDI (Desmodur N-3200)[b] TDI MDI (Mondur MR-200)[b]

[a] Ongoing interlaboratory study, the presented values include data from 2000 to 2005.

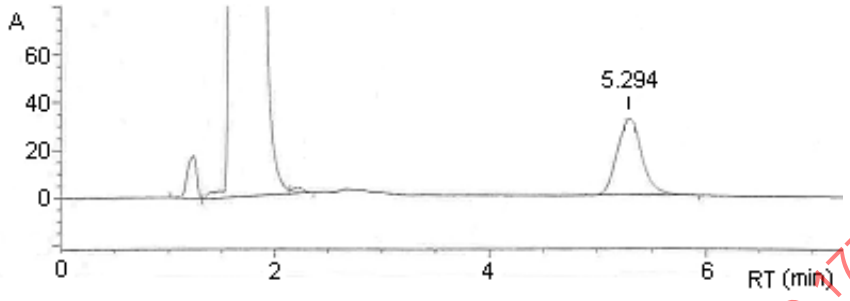
[b] Desmodur N-3200 and Mondur MR-200 are trade names of products supplied by Bayer. This information is given for the information of users of this document and does not constitute an endorsement of these products by ISO.

A.2 Expanded uncertainty

By using a coverage factor of 2, the expanded uncertainty is 50 % for isocyanate vapour and 90 % for isocyanates present as an aerosol (monomer and oligomers combined).

Annex B
(informative)

Sample chromatograms

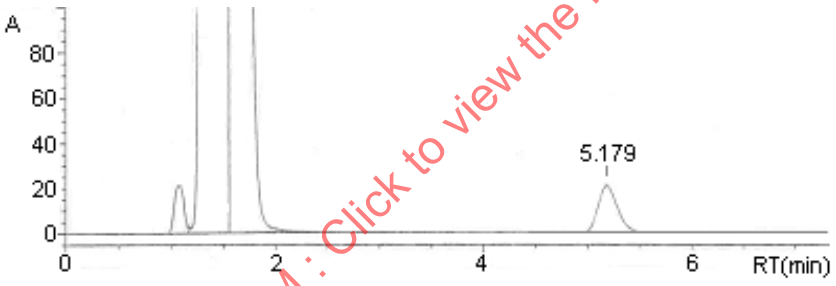


Key

A absorbance

RT retention time

Figure B.1 — UV-chromatogram of 2,4-TDI MAMA derivative at wavelength $\lambda = 254$ nm

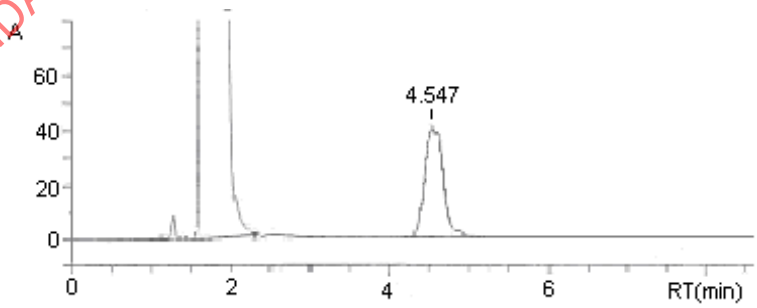


Key

A absorbance

RT retention time

Figure B.2 — UV-chromatogram of HDI MAMA derivative at wavelength $\lambda = 254$ nm

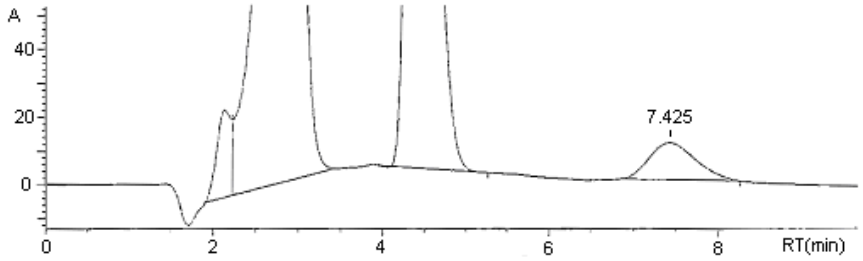


Key

A absorbance

RT retention time

Figure B.3 — UV-chromatogram of MDI MAMA derivative at wavelength $\lambda = 254$ nm

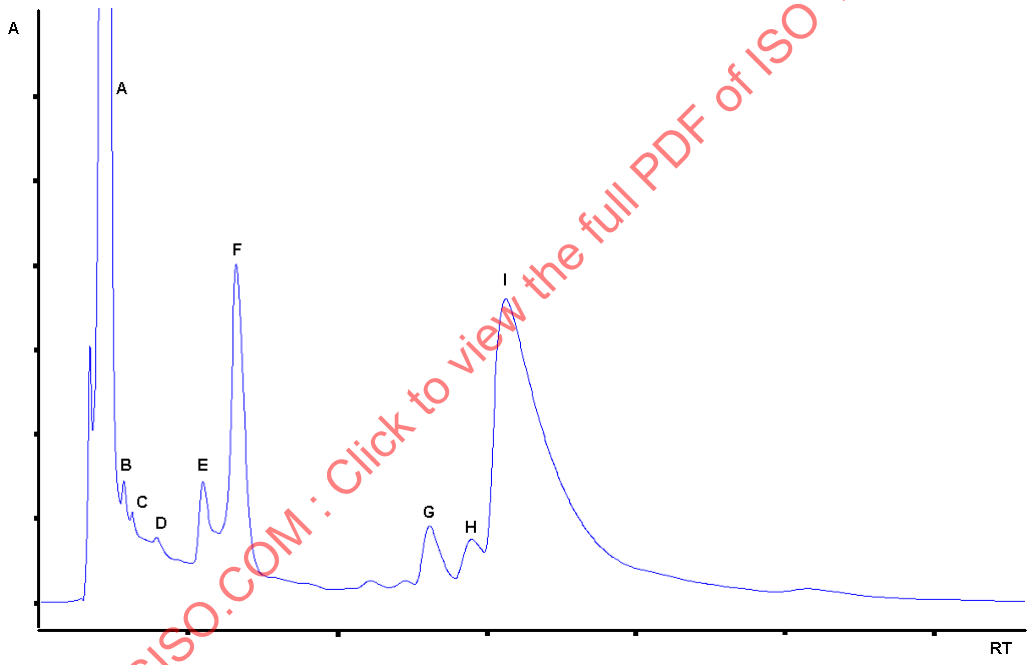


Key

A absorbance

RT retention time

Figure B.4 — UV-chromatogram of 2,4-TDI MP derivative at wavelength λ = 242 nm



Key

A absorbance

RT retention time

A, B, C, D, E, F, G, H, I peaks

Figure B.5 — UV (DAD) chromatograms for Desmodur N-3200[3)] (poly HDI) derivatized with MP derivatization solution (4.10.2)

3) Desmodur N-3200 is a trade name of a product supplied by Bayer. This information is given for the information of users of this document and does not constitute an endorsement of this product by ISO.