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Robert P. Streicher , Christopher M. Reh , Rosa Key-Schwartz , Paul C. Schlecht , Mary Ellen Cassinelli & Paula Fey O'Connor

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Analytical Instrument Performance Criteria

Selecting Isocyanate Sampling and Analytical Methods

Kevin E. Ashley, Ph.D., Column Editor

Reported by Robert P. Streicher, Christopher M. Reh, Rosa Key-Schwartz, Paul C. Schlecht, Mary Ellen Cassinelli, and Paula Fey O'Connor

Isocyanate-containing compounds are used in the production of a wide variety of surface coatings, polyurethane foams, adhesives, resins, elastomers, binders, and sealants. Examples of potential worker exposures to isocyanates in automobile painting and mining applications are shown in Figure 1. Selecting the most appropriate sampling and analytical methods for isocyanates in a specific workplace environment is difficult for the following reasons: Isocyanates may be in the form of vapors or aerosols of various particle sizes; the species of interest are reactive and, therefore, unstable; pure analytical standards exist only for monomeric isocyanates; and low limits of detection are needed. As a result, errors can be introduced during several stages of the sampling and analytical procedures. If an inappropriate method is selected, the result may be either a gross underestimation of the exposure or a failure to detect airborne isocyanates. Therefore, the ability to select the best analytical method is critical for an accurate assessment of the worker's isocyanate exposure.

A further complication is that most exposure standards address only a few isocyanate monomer species, even though many isocyanate formulations commonly used in today's industry have been reformulated so that monomers are only a small fraction (frequently less than 1%) of the isocyanate species present. Moreover, current exposure standards may be expressed in terms of the concentration of a specific isocyanate compound (e.g., National Institute for Occupational Safety and Health Recommended Exposure Limits [NIOSH RELs]), concentration of bulk polyisocyanate product (e.g., Bayer Manufacturer Guideline Level), or concentration of isocyanate functional group (e.g., United Kingdom Health and Safety Executive Total Reactive Isocyanate Group [TRIG] standard). As a result, many employers do not understand that most exposure standards are similar if molecular weights and the number of isocyanate groups per molecule are taken into account.

Because of analytical limitations, the difficulty of dealing with reactive, unstable mixtures, the failure of current exposure standards to keep pace with formulation changes, and a general lack of understanding that many exposure standards for various isocyanate species are similar have led to confusion. This confusion makes it difficult for laboratories and industrial hygienists to encourage clients (particularly small businesses) to use the best analytical method to assess health risks, especially when that method is not specified by regulation, may not be convenient to use, or is more costly.

Isocyanate Exposures

The feature common to all diisocyanates (monomers) is the presence of

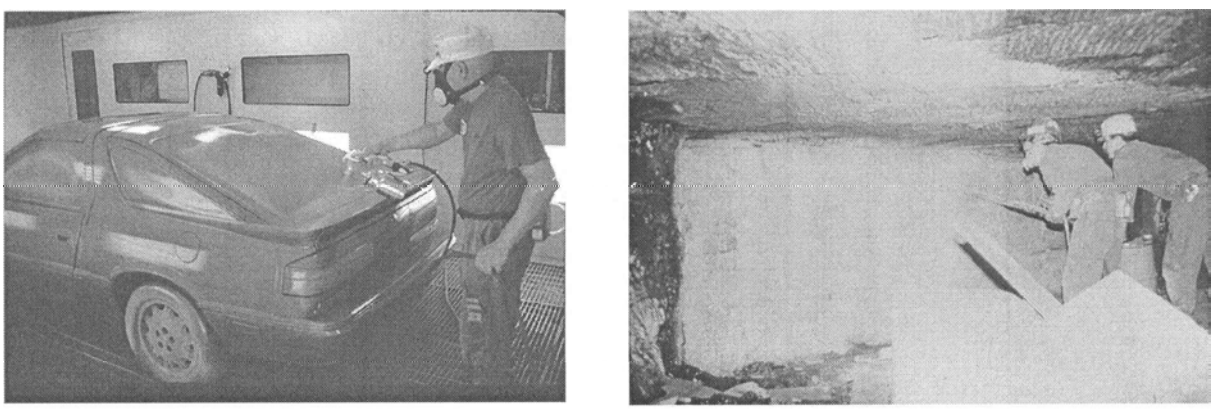
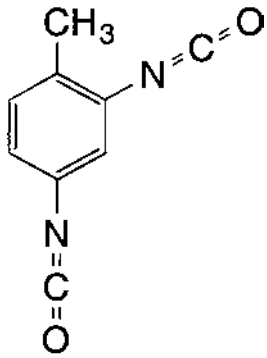
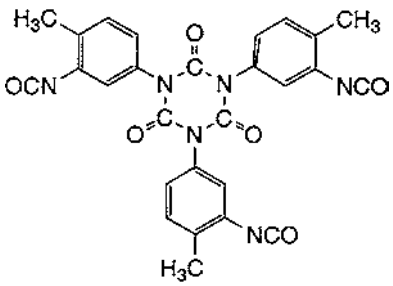


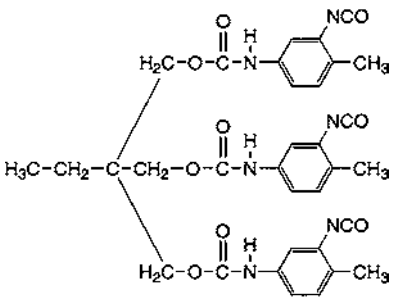
FIGURE 1
Auto body spray painting and mine shaft foam sealing.



(a) 2,4,-TDI monomer.



(b) Polyisocyanate of TDI.



(c) Prepolymer adduct of TDI and trimethylol propane.

FIGURE 2
(a) Toluene diisocyanate monomer, (b) oligomer, and (c) adduct.

two —N=C=O (isocyanate) functional groups attached to an aromatic or aliphatic parent compound. Examples of isocyanate compounds, i.e., toluene diisocyanate (TDI) monomer, oligomer, and prepolymer adduct therefrom, are illustrated in Figure 2. Industry has made an important contribution to reducing isocyanate exposures by replacing low-molecular-weight isocyanate monomers with higher-molecular-weight isocyanate species that have similar characteristics but are less volatile and, therefore, have a lower risk of inhalation exposure.

As a result, many prepolymer and polyisocyanate formulations commonly encountered in industry contain only a small fraction (usually less than 1%) of unreacted monomer. For example, the biuret of HDI consists of three molecules of HDI monomer joined together to form a higher-molecular-weight oligomer having similar characteristics to those found in the monomer. Also, many MDI product formulations consist of a combination of MDI monomer and oligomers (known as polymethylene polyphenyl isocyanate or polymeric MDI).

Not only are workers potentially exposed to a complex mixture of unreacted monomer, prepolymer, oligomer, and/or polyisocyanate species found in a given product formulation, they can also be exposed to partially reacted isocyanate-containing intermediates formed during polyurethane production. In addition, isocyanate-containing mixtures of vapors and aerosols can be generated during the thermal degradation of polyurethane materials. Examples of such situations include welding of polyurethane-coated surfaces and breakdown of polyurethane binders present in foundry molds.

Exposure Standards

Exposure to isocyanates is irritating to the skin, mucous membranes, eyes, and respiratory tract. The most common adverse health effect associated with isocyanate exposure is asthma due to sensitization; less prevalent are contact dermatitis (both irritant and allergic forms) and hypersensitivity pneumonitis (HP).

All isocyanate species formed during polyurethane production and thermal degradation, including monomers, prepolymers, oligomers, and polyisocyanates, are capable of producing irritation to the skin, eyes, mucous membranes, and respiratory tract. Prevalence estimates for isocyanate-induced asthma in exposed worker populations vary considerably—from 5 to 10 percent in di-isocyanate production facilities to 25 percent in polyurethane production plants, and 30 percent in polyurethane seat cover operations. Experience has shown that both monomeric and polyisocyanate species are capable of producing respiratory sensitization in exposed workers. After sensitization, any exposure, even to levels below existing occupational exposure limits or standards, can produce an asthma-like response, which may be life threatening.

Workplace inhalation exposure criteria have been established by a number of organizations, including the National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limits (RELs),[1] the American Conference of Governmental Industrial Hygienists (ACGIH®) Threshold Limit Values (TLV®s),[2] and the Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PELs).[3] These exposure criteria are for diisocyanate monomers.

Table I contains a comparison of the respective NIOSH RELs, ACGIH® TLV®s, OSHA PELs, and United Kingdom Health and Safety Executive (UK/HSE) exposure criteria for isocyanates. The UK/HSE has taken a unique approach, i.e., developing a nonspecific standard based on the total number of reactive isocyanate groups (TRIG) in a volume of air.[4] U.S. and U.K. isocyanate exposure standards are more similar than they may at first appear, if molecular weights and number of isocyanate groups per molecule are taken into account. In general, U.S. limits for six di-isocyanate monomers and UK/HSE TRIG limits listed in Table I are based on an 8-hour time-weighted average (TWA) exposure of approximately five parts per billion (ppb), or a short-term (ceiling) exposure of approximately 20 ppb.

Both the U.S. and U.K. exposure standard approaches have limitations. The traditional substance-specific approach in the United States only covers a small number of monomeric di-isocyanate

TABLE I
NIOSH, ACGIH®, OSHA, and UK/HSE exposure criteria for isocyanates

	Exposure criteria—full-shift TWAs micrograms per cubic meter of air (μg NCO group per cubic meter of air)			Exposure criteria—short-term or ceiling limits micrograms per cubic meter of air (μg NCO group per cubic meter of air)			
Isocyanate species	NIOSH REL	ACGIH® TLV®	UK-HSE	NIOSH REL ceiling 10 min.	ACGIH® TLV®-STEL 15 min.	UK-HSE ceiling	OSHA PEL ceiling
TDI	CA-LFC[1]	36 (17)	None	None	140 (68)	None	140 (68)
MDI	50 (17)	51 (17)	None	200 (67)	None	None	200 (67)
HDI	35 (18)	34 (17)	None	140 (70)	None	None	None
HMDI	None	54 (17)	None	110 (35)	None	None	None
IPDI	45 (17)	45 (17)	None	180 (68)	None	None	None
NDI	40 (16)	None	None	170 (68)	None	None	None
TRIG[2]	None	None	20	None	None	70	None

[1]NIOSH considers TDI to be an occupational carcinogen (CA), and recommends that exposures be reduced to the lowest feasible concentration (LFC).
[2]Total reactive isocyanate group.

species (currently TDI, MDI, HDI, HMDI, IPDI, and NDI), and does not address the wide variety of isocyanate species and mixed isocyanate exposures where nonmonomeric species are the major isocyanate component. Conversely, the UK/HSE total reactive isocyanate group (TRIG) standard does not take into account that polyisocyanate species may be less toxic than monomeric species.

Sampling and Analytical Method Selection

The capability to measure all isocyanate-containing substances in air, whether they are in monomer, prepolymer, oligomer, or polyisocyanate forms found in the original formulation, or intermediate forms produced during the industrial process, is important when assessing a worker's total airborne isocyanate exposure. All published sampling and analytical methods have significant limitations. Table II summarizes OSHA and NIOSH isocyanate methods, and gives the criteria for choosing a method. Selection depends on (1) the chemical nature of the isocyanate species, (2) the physical state of the isocyanate species, (3) the cure rate of the product, (4) the required sampling time, (5) whether personal or area sampling is required, and (6) the sensitivity of detection needed, as shown in Table II. Measurement accuracy, selectivity, and sensitivity are considered for the entire sampling and analytical measurement process including collection, derivatization, sample preparation, separation, identification, and quantification.

Unfortunately, the need to measure highly reactive isocyanate species at low levels is frequently in conflict with the desire of industrial hygienists and chemists to choose methods that are convenient to use in the field and easy to run in the laboratory. It is also in conflict with the desire of employers to select the least expensive method for monitoring, or to conduct monitoring limited to demonstrating compliance with existing U.S. regulatory exposure standards.

The information in Table II is used to select methods for NIOSH research studies and health hazard evaluations. It is provided when employers, industrial hygienists, or laboratories request NIOSH technical assistance concerning isocyanate methods. A thorough discussion of the sampling and analytical issues, as well as the advantages and disadvantages of isocyanate sampling and analytical methods used in the United States and abroad, is contained in both the NIOSH Manual of Analytical Methods (NMAM),[5] and in an updated article on the subject.[6]

All isocyanate sampling and analytical methods have significant limitations that affect the ability to ensure that exposures are minimized and controlled. These limitations also affect the ability of regulatory and voluntary standard-setting organizations to set exposure standards. More research is needed to resolve the limitations of current sampling and analytical methods. Such research is ongoing at NIOSH and elsewhere in government, in academia, and in the private sector. Therefore, this guidance is subject to revision as isocyanate exposure standards change, and as new or improved isocyanate measurement methods are developed and published.

This article is an update of one previously published.[7] A more complete discussion of isocyanate sampling and analysis considerations, isocyanate health effects, and isocyanate exposure standards is presented in a chapter of the NMAM,[5] and in a similar American Industrial Hygiene Association Journal article.[6]

TABLE II
Comparison of NIOSH and OSHA isocyanate methods

	NIOSH 5521	NIOSH 5522	NIOSH 2535	OSHA 42/47	DRAFT NIOSH 5525
Isocyanate					
a) Monomers	TDI, MDI, HDI, NDI, HMDI[2]	TDI, MDI, HDI, NDI, HMDI,[2] IPDI [2]	TDI, HDI	42 TDI, HDI 47 MDI	TDI, HDI, MDI, NDI,[2] HMDI, IPDI
b) Oligomers	HDI	TDI, MDI, HDI	None	None	HDI, MDI, TDI[2]
Sampler	Impinger	Impinger	Coated glass wool/opaque tube	Coated GFF	Impinger; GFF; impinger + GFF
Reagent	MOPP in toluene	Tryptamine in DMSO	Nitro reagent	1–2 PP 42 0.1 mg; 47 1 mg	MAP in butyl benzoate or on GFF
shelf life	7d 0°C	6 mo 25°C in dark	7d 25°C in dark	6 mo 0°C sealed	Solid: 2 yr@−13°C; MAP on GFF: 3 mo@−13°C
Sampling rate	1 L/min	1–2 L/min	0.2–1 L/min	1 L/min	1–2 L/min
volume	5–500 L	15–360 L	2–170 L	15 L	1–500 L
Personal	No	No	Yes	Yes	Yes
Vapor	Yes	Yes	Yes	Yes	Yes
Particles $\leq 2\,\mu$m	No	No	No	Yes	Impinger: no Filter: yes
Particles $\geq 2\,\mu$m					
a) Half-life of product > 3× sampling time (typically aliphatic isocyanate products)	Yes	Yes	No	No[3]	Impinger: yes Filter: yes (with immediate field extraction)
b) Half-life of product < 3× sampling time (typically aromatic isocyanate products)	Yes	Yes	No	No	Impinger: yes Filter: no

Sample stability	7d 25°C: 78% 7d 4°C: 88%	28d 25°C in dark: 95–104%	14d 25°C: 91%	15d 22°C: 42 80–86%; 47 94.8%	1 yr@−13°C: no appreciable loss
Laboratory sample preparation	Impinger: evap/ redissolve in methanol	None	Ultrasonic extraction in methanol	Extraction in ACN/ DMSO, 9/1	Impinger: SPE Filter: extract or SPE
Technique	HPLC/RP, isocratic	HPLC/RP, gradient	HPLC/RP, isocratic	HPLC/RP, isocratic	HPLC/RP, pH gradient
Detector 1 LOD[4]:	UV@242 nm/ PDA	FL ex 275 nm em 320 nm	UV@254 nm	FL ex 240 nm em 370 nm	UV@253 nm
a) amount injected	14 pmol	0.7 pmol	14 pmol	47 0.2 pmol	0.5 pmol
b) 15 L air conc.	1.2 ppb	0.9 ppb	0.9 ppb	47 0.06 ppb	0.08 ppb
Detector 2 LOD[4]:	EC (+0.8V)	EC (+0.8V)	None	UV@254 nm	FL ex 368 nm em 409 nm
a) amount injected	0.5 pmol	4.4 pmol		42 1.0–1.1 pmol	0.2 pmol
b) 15 L air conc.	0.04 ppb	5.7 ppb		42 0.13–0.14 ppb	0.03 ppb
Identification	Monomer: retention time Aliphatic oligomers: PDA	Monomer: FL retention time Other isocyanate: EC confirmation	Retention time	Retention time	Monomer: retention time Other isocyanate: UV/FL ratio and comparison to bulk product

[1]This method is under development; procedures may change somewhat, pending validation.
[2]Determination possible; lacks validation data.
[3]Usually underestimates concentration; immediate field extraction may improve accuracy.
[4]Instrumental limit of detection.

Abbreviations: ACN = acetonitrile; conc = concentration; d = days; DMSO = dimethyl sulfoxide; EC = electrochemical detector; em = emission; evap = evaporate; ex = excitation; FL = fluorescence detector; GFF = glass fiber filter; HPLC = high performance liquid chromatography; LOD = limit of detection; MAP = 1-(9-anthracenylmethyl)piperazine; mo = months; MOPP = 1-(2-methoxyphenyl)piperazine; nitro reagent = *N*-[(4-nitrophenyl)methyl]propylamine; PDA = photodiode array detector; 1-2PP = 1-(2-pyridyl)piperazine; RP = reversed phase; SPE = solid phase extraction; UV = ultraviolet detector; yr = years.

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EDITORIAL NOTE: Dr. Streicher, Dr. Key-Schwartz, Mr. Schlecht, Ms. Cassinelli, and Ms. O'Connor are with the U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Cincinnati, OH 45226-1998. Dr. Reh is with Gillette Medical Evaluation Laboratories, 37 A Street, Needham, MA 02492-9210.