NIOSH Manual of Analytical Methods 5th Edition and harmonization of occupational exposure monitoring

K. Ashley

Abstract The NIOSH Manual of Analytical Methods (NMAM) is a collection of methods for sampling and analysis of contaminants in workplace air (or surfaces) and in the blood and urine of workers who are occupationally exposed. NIOSH methods are used worldwide for occupational exposure assessment. They have been developed or adapted by NIOSH and/or its partners and have been evaluated according to established protocols and performance criteria. NMAM also includes chapters on quality assurance, sampling guidance, instrumentation, aerosol measurement, gas and vapor monitoring, portable monitoring devices, and so forth. Often NIOSH methods are developed in coordination with voluntary consensus standards organizations. Efforts to harmonize NIOSH methods with relevant consensus standards procedures are highlighted. NIOSH also has a formal Memorandum of Understanding (MOU) with the Institute for Occupational Safety and Health of the German Social Accident Insurance (IFA), whereby both are adopting selected methods. An overview of recent research and technology transfer activities relating to NMAM methods is provided. Included are newly approved methods and those under development, as well as needs for new methods and updates. Of particular interest are recent NIOSH recommendations on air samplers used for sampling and analysis of airborne particles.

Das NIOSH Manual of Analytical Methods (NMAM) und die Harmonisierung der Expositionsermittlung

Zusammenfassung Das NIOSH Manual of Analytical Methods (NMAM) ist eine Sammlung von Methoden für die Probenahme und Analyse von Schadstoffen in der Luft am Arbeitsplatz (und von Oberflächen) sowie im Blut und Urin von Beschäftigten, die beruflich gegenüber Gefahrstoffen exponiert sind. Die Verfahren werden weltweit zur Expositionsbeurteilung eingesetzt. Sie wurden von NIOSH oder Partnern entwickelt, angepasst und nach festgelegten Verfahren und Leistungskriterien evaluiert. Das Handbuch enthält zudem u. a. Kapitel zur Qualitätssicherung, zu Probenahmeverfahren und -geräten, zur Messung von Gasen, Dämpfen und Aerosolen sowie über tragbare Messgeräte. NIOSH-Methoden werden häufig in Abstimmung mit Organisationen aus dem Bereich der freiwilligen Normung entwickelt. Aktivitäten zur Harmonisierung der NIOSH-Methoden mit relevanten Verfahren aus der Normung werden hervorgehoben. Das NIOSH hat auch eine formelle Absichtserklärung mit dem Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA) abgeschlossen, nach dem die Partner ausgewählte Methoden gegenseitig übernehmen. Ein Überblick über aktuelle Aktivitäten des NIOSH zum Forschungs- und Technologietransfer wird gegeben. Schließlich umfasst der Beitrag neue und aktualisierte Verfahren und zeigt Bedarf für neu zu entwickelnde Verfahren und für Aktualisierungen auf. Von besonderem Interesse sind die jüngsten NIOSH-Empfehlungen zur Probenahme und Analytik luftgetragener Partikel.

Kevin Ashley, Ph. D.
US Department of Health and Human Services,
Centers for Disease Control and Prevention, National
Institute for Occupational Safety and Health,
Cincinnati, Ohio, USA

1 Introduction

The health of working people in myriad industries and occupations is potentially at risk through workplace exposure to airborne chemical and biological agents [1 to 4]. Commonly it is the responsibility of occupational hygienists and often other public health professionals to determine the effectiveness of measures taken to minimize and control worker exposures to airborne toxins and toxicants, and this is normally achieved by monitoring workplace air quality [5 to 8]. Air monitoring is vital because inhalation is ordinarily the most likely route of exposure in occupational settings. Frequently other routes of workplace exposure, notably dermal contact with chemical and biological agents, must also be considered [9 to 11]. Complementary biomonitoring methods are also often used to assess occupational exposures to toxic chemical compounds through measurement of specific analytes, e.g., metabolites and/or biomarkers, in body fluids (normally blood and urine) and tissues [12].

The NIOSH[1] Manual of Analytical Methods (NMAM®) is a compilation of analytical methods for air, biological, surface (including dermal) and bulk samples that have been evaluated and validated in consideration of their fitness for purpose for workplace exposure monitoring. NIOSH sampling and analytical methods are intended to promote accuracy, sensitivity, and specificity in industrial hygiene analyses and related applications. NMAM is published online and is available worldwide free of charge [13]. Now in its 5th edition, NMAM is constantly updated as new methods are developed and validated and as revised methods are evaluated and their performance verified. Often there are situations during use where certain NIOSH methods may require modification, for example, to accommodate interfering compounds from a particular workplace, to take advantage of unique laboratory capabilities, to make use of equivalent sample preparation or analysis techniques, or to make possible the analysis of a single sample for multiple contaminants. When method modifications are made, quality control data demonstrating the reliability of the modified method must be obtained,

This article was prepared by US government employees as part of their official duties and legally may not be copyrighted in the United States of America.
Disclaimers: Mention of company names or products does not constitute endorsement by the Centers for Disease Control and Prevention. The findings and conclusions in this article are those of the author and do not necessarily represent the views of the National Institute for Occupational Safety and Health.
Presented at AIRMON 2014, Marseille, France.

---

[1] NIOSH: National Institute for Occupational Safety and Health

Table 1. Method development and evaluation components for validating NIOSH air sampling and analytical methods [14].

Preliminary research
Identification of analyte(s) and environment of concern
Literature searches
Identification of suitable sampler
Choice of candidate analytical method
Method development
Preliminary experimentation
Recovery studies of analyte(s) from sampling medium
Stability studies of analyte(s) on sampling medium
Method evaluation and validation
Atmospheric generation of analyte(s)
Sampler capacity and sampling rate studies
Sampling and analysis evaluation – detection limit, dynamic range
Sample stability studies
Assessment of precision, bias, and accuracy
Independent laboratory tests
Field evaluation

recorded and reported. The methods published in NMAM are relied upon by authoritative bodies such as accrediting organizations and regulatory agencies. Besides sampling and analytical methods, NMAM also includes chapters on quality assurance, portable instrumentation, analysis of fibers, aerosol sampler design, and other guidance on specific areas of interest.

In 2003, NIOSH management classified NMAM as an "influential document" which reflects the importance of validated sampling and analytical methods for exposure assessment purposes. Because of this official US Government classification, since 2004 the approval of new NIOSH methods has entailed a formal issuance process, requiring not only external peer review but also stakeholder review of draft methods. Potentially controversial methods or analytes may require a formal public comment period.

To address requirements for harmonized methods for use by occupational hygiene laboratories, international voluntary consensus standard test methods have been developed and promulgated by ASTM International, the European Committee for Standardization (Comité Européen de Normalisation, CEN) and the International Organization for Standardization (ISO). Like NIOSH methods, these consensus standard procedures describe aspects of sampling and sample preparation as well as analysis, although normally in exhaustive, specific detail. Other related consensus standards offer thorough guidance on sample collection, sample preparation and analytical protocols. Harmonization of NIOSH methods with related voluntary consensus standards is a key strategic goal for the 5th edition of NMAM.

Current efforts to update NMAM may also include validated methodologies developed by sister organizations both nationally and internationally, such as the US Occupational Safety and Health Administration (OSHA), the Health and Safety Laboratory (HSL) in the United Kingdom, the Institut National de Recherche et de Sécurité (National Institute of Research on Health and Safety at Work, INRS) in France and the Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (Institute for Occupational Safety and Health of the German Social Accident Insurance, IFA) in Germany. NIOSH must keep abreast of new industrial hygiene and biomonitoring methods and consensus standards developed globally. Thus, it is advisable to coordinate and collaborate externally and to consider suitable validated methods developed by other institutes and organizations, domestic as well as international.

2 Evaluation of sampling and analytical methods for workplace monitoring

Sampling and analytical method evaluation as carried out under the auspices of NIOSH guidelines has been well covered previously [14 to 16]; an overview of the various elements involved in the overall process of NIOSH method validation is presented in **Table 1**. The examples in this table are directed mainly to sampling and analysis of airborne agents in occupational settings, but can be extended to other matrices such as workplace or dermal surfaces and biological specimens like blood and urine. For the measurement of each analyte or group of analytes of concern in workplace environmental samples or in biological specimens obtained from workers, it is desired to produce sampling and analytical methods that will meet the needs of field investigators (e.g., industrial hygienists, control engineers or occupational physicians) as well as laboratory personnel (e.g., analytical chemists, biochemists, epidemiologists or toxicologists). The ultimate goal of the formalized NIOSH method development, evaluation and validation protocol is to make available sampling and analytical methods for applications in the occupational hygiene arena that are fit for purpose, analytically rigorous, and adequately ruggedized.

Table 2. Summary of NIOSH method evaluation criteria [14].

Criterion	Required value
Analytical recovery	> 75%
Method detection limit	<< Exposure limit value (ideally ≤ 0,1 × OEL*)
Sampler capacity	≥ 2 × OEL
Storage stability	Minimum seven days (tests carried out to at least 28 days)
Parameter study	Investigate conditions/potential interferences that may affect the method
Precision and bias	Should satisfy NIOSH accuracy criterion ($A_{95} \leq \pm 25\%$)

* Occupational exposure limit

Criteria for method evaluation that are used to validate candidate NIOSH sampling and analytical methods are summarized in Table 2 [14; 16]. The cited requirement for minimum recovery of > 75% stems largely from evaluations involving the collection of organic vapors onto solid sorbents [17]. It is required that recovery experiments be carried out at analyte concentrations ranging from a minimum of 0,1 times the occupational exposure limit (OEL) to at least twice the OEL. Ideally the method detection limit (MDL) should be no greater than one tenth of the OEL, which will ensure that the analyte of interest can be measured with high precision at levels at and above the limit of quantitation (LOQ). Another specification is that the sampler capacity at expected typical sampling rates should enable analyte loadings to at least twice the OEL. Moreover, samples should be stable on collection media for at least one week, with stability tests carried out to at least 28 days. Refrigeration or freezing may be necessary to maintain analyte stability after sample collection in the field. Derivatization of sampled analyte compounds may also be required for reactive species (such as aldehydes and isocyanates). Effects of various parameters such as temperature, relative humidity, analyte concentration and sampling rate must be studied. Additionally (and importantly), influences of potential interferences need to be investigated in order to fully characterize the performance and limitations of the candidate method.

Results from the above tests can be used to estimate the precision and bias of the method under evaluation in order to obtain a measure of method accuracy [14]. For NIOSH methods, the bias (uncorrected) cannot exceed ±10% and, to satisfy the NIOSH criterion for method accuracy (A_{95}), the method must provide results that are within ±25% of the expected ("true") values at least 95 times out of 100 [18]. In the course of method evaluation it is normally recommended to produce test atmospheres of analyte(s) so that sampler loadings spanning the range of (at least) 0,1 to 2 times the OEL are generated. To do this it may be necessary to produce atmospheres of gases/vapors or aerosols, with analyte(s) at known, desired concentrations under controlled temperature and humidity conditions. These experiments must take into account that the sampling rates and analyte concentrations should yield samples at loadings which are relevant to either short-term (typically 15 minute) exposure limits (STEL), ceiling (C) limits (theoretically instantaneously measured) or, more often, 8-hour time-weighted average (TWA) concentrations.

Field evaluations, whereby the candidate sampling procedure is tested on-site in actual representative workplace conditions, should be carried out to further evaluate and ruggedize the sample collection aspects of method. If a method performs well under laboratory conditions but cannot be reliably applied under realistic situations, it is of little practical use. Also the candidate method's sample preparation and analytical protocols must be tested separately in at least one independent laboratory; however, interlaboratory evaluations by at least six participating laboratories are preferred [19] and are undertaken when possible. Ideally the method performance of independent laboratory tests should satisfy the NIOSH accuracy criterion and ought to agree closely (within ±10%) with the analytical figures of merit for the test method evaluated in-house. Once a candidate sampling and analytical method is challenged under all test conditions (Table 1) and is found to satisfy all of the established performance criteria (Table 2), only then it is eligible for approval and publication as a validated NIOSH method.

Apart from the NIOSH guidelines [14], analogous validation protocols for industrial hygiene chemistry measurement methods have been promulgated by other global occupational health organizations, for example OSHA in the United States [20], the Deutsche Forschungsgemeinschaft (German Research Foundation, DFG) in Germany [21] and the Instituto Nacional de Seguridad e Higiene en el Trabajo (National Institute of Workplace Security and Hygiene, INSHT) in Spain [22]. Similarly, three international voluntary consensus standards organizations have produced indispensable standards covering sampling and analytical method validation for a great many workplace monitoring applications: ASTM International [23], ISO [24] and CEN [25]. Through international coordination and collaboration, efforts are underway to harmonize sampling and analytical procedures for purposes of occupational hygiene monitoring.

3 Harmonization of workplace air quality assessment methods

In accordance with and observance of the National Technology Transfer and Advancement Act (NTTAA) [26], a main goal of ongoing NIOSH methods development activities is to ensure that NIOSH methods are harmonized with relevant international voluntary consensus standards. The NTTAA directs US federal government agencies to

- rely on applicable voluntary consensus standards in lieu of procedures and documents developed in-house; and
- participate in the development of pertinent consensus standards that are related to the agencies' activities.

In the course of sampling and analytical methods development, NIOSH may consider adapting applicable existing standards promulgated by ISO, CEN and/or ASTM International.

As regards method evaluation and validation, an important standard published by CEN, i.e., EN 482, outlines the general requirements for measurement of chemical agents in workplace air [27]. This European standard specifies an upper limit for expanded uncertainty of ±30% for an acceptable sampling and analytical method when applied to measurements spanning the OEL (i.e., between 0,5 to 2 times the OEL). EN 482 also cites an upper limit for expanded uncertainty of ±50% for measurement of analyte levels between the method quantitation limit and one half of the applicable OEL. It is pointed out that for most applications expanded uncertainty (for coverage factor k of 2 to 3) is equivalent to accuracy as defined by NIOSH [28; 29]. Both NIOSH [14] and CEN [27] method evaluation protocols account for all potential sources of experimental error (both random and systematic), in accordance with the ISO guidelines on measurement uncertainty [30]. For a given measurement method, the final estimate of accuracy or expanded uncertainty is a result of combined contributions from propagated errors occurring throughout the sampling and analytical process.

Of the more than 300 published NIOSH sampling and analytical methods [13], a large number, at least a third of the total, have related or parallel international voluntary consensus standards that have been produced by ASTM International [23], ISO [24] and/or CEN [25] (**Table 3**). In many instances the consensus standard procedures listed were developed with a basis on NIOSH methods, while in some cases NIOSH

Table 3. NIOSH sampling and analytical methods and related/parallel international voluntary consensus standards.

NIOSH Method(s) [13]	ASTM Standard(s) [23]	ISO Standard(s) [24]	CEN (EN) Standard(s) [25]
0500 and 0501, Particles not otherwise regulated, total (gravimetric) 5000 and 5100, Carbon black (gravimetric)	D6552, Controlling and characterizing errors in weighing collected aerosols	15767, Controlling and characterizing uncertainty in weighing collected aerosols	–
0600, Particles not otherwise regulated, respirable (gravimetric)	D4532, Respirable dust in workplace atmospheres D6552, Controlling errors in weighing collected aerosols	15767, Controlling and characterizing uncertainty in weighing collected aerosols	–
0800, Bioaerosols (by pumped sampling) 0900, Mycobacterium tuberculosis (filter sampling)	–	13137, Pumps for sampling chemical and biological agents	13098, Guidelines for measuring microorganisms and endotoxin 13137, Pumps for sampling chemical and biological agents 14583, Bioaerosol sampling – requirements and methods
1003, Halogenated hydrocarbons, by sorbent tube and gas chromatography (GC) 1022, Trichloroethylene by sorbent tube and GC	D3686, Sampling organic vapors by charcoal tube D3687, Analysis of organic vapors collected by charcoal tube	9486, Vaporous chlorinated hydrocarbons by charcoal tube/solvent desorption/GC	1076, Gases and vapor measurement by pumped sampling – requirements and test methods
1007, Vinyl chloride by charcoal tube and GC	D4766, Vinyl chloride by charcoal tube	–	–
1008-1460, Organic vapors (various) by charcoal tube and GC	D3686, Sampling organic vapors by charcoal tube D3687, Analysis of organic vapors collected by charcoal tube	16017-1, Organic vapors by charcoal tube and GC	1076, Gases and vapor measurement by pumped sampling – requirements and test methods
1500, Hydrocarbons, BP 36-126 °C, by charcoal tube and GC 1501, Aromatic hydrocarbons by charcoal tube and GC	D3686, Sampling organic vapors by charcoal tube D3687, Analysis of organic vapors collected by charcoal tube	16017-1, Organic vapors by charcoal tube and GC 9487, Vaporous aromatic hydrocarbons by charcoal tube/solvent desorption/GC	1076, Gases and vapor measurement by pumped sampling – requirements and test methods
1614, Ethylene oxide by charcoal tube and GC	D4413, Ethylene oxide, charcoal tube sampling D5578, Ethylene oxide, derivatization technique	–	–
2001, Aromatic amines by sorbent tube and GC 2010, Aliphatic amines by sorbent tube and GC	D3686, Sampling organic vapors by charcoal tube D3687, Analysis of organic vapors collected by charcoal tube	–	–
2018, Aliphatic aldehydes by derivatized silica cartridge and liquid chromatography (LC) 2539, Aldehydes, screening, by GC/GC GC-mass spectrometry (MS)	D5197, Formaldehyde and other carbonyls by derivatized silica cartridge and LC	–	–
2549, Volatile organic compounds (VOCs) by sorbent tube/thermal desorption/GC-MS	–	16200-1, VOCs by solvent desorption/GC	–
3600 and 3601, Maneb by dermal patch and hand wash (respectively)	–	TR 14294, Measurement of dermal exposure	TS 15278, Evaluation strategy for dermal exposure TR 15279, Measurement of dermal exposure
3700, Benzene by portable GC	–	–	4554-1, -2, -3 and -4, Direct measurement of toxic gases and vapours
3800, Inorganic and organic gases by extractive Fourier transform infrared (FTIR) spectrometry	E1982, Gases and vapors by open-path FTIR spectrometry	–	4554-1, -2, -3 and -4, Direct measurement of toxic gases and vapours

NIOSH Method(s) [13]	ASTM Standard(s) [23]	ISO Standard(s) [24]	CEN (EN) Standard(s) [25]
5040, Elemental carbon (diesel particles) by thermo-optical analysis	D6877, Diesel particulate exhaust by thermo-optical analysis	–	14530, Diesel particulate matter – general requirements
5042, Benzene-soluble particulate matter	D4600, Benzene-soluble particulate matter D6494, Asphalt fume in benzene-soluble fraction	–	–
5503, Polychlorobiphenyls by filter + sorbent and GC	D4861, Pesticides and polychlorinated biphenyls – guidance on sampling and analytical methods	–	–
5521, Monomeric isocyanates by impinger sampling and LC 5522, Isocyanates by impinger sampling and LC 5525, Isocyanates, total, by filter or impinger sampling and LC	D5836 and 5932, Toluene diisocyanates (TDI) by LC D6561, Hexamethylene diisocyanate (HDI) aerosol by LC D6562, Gaseous HDI by LC	11734-1, Isocyanates by LC-MS; 11734-2, Amines and aminoisocyanates by LC-MS 11735, Total isocyanates by LC 11736, Isocyanate by double-filter sampling and LC 16702, Total organic isocyanates by LC 17737, Guidelines for selecting isocyanate methods	–
5524, Metalworking fluids – filter sampling and gravimetric analysis	D7049, Metal removal fluid aerosol	–	–
5506, Polynuclear aromatic hydrocarbons by filter + sorbent and LC 5515, Polynuclear aromatic hydrocarbons by filter + sorbent and GC 5800 Polycyclic aromatic compounds by filter + sorbent and flow-injection analysis	D6209, Polycyclic aromatic compounds by sorbent-backed filter and GC-MS	–	–
5600, Organophosphorus pesticides by filter + sorbent and GC 5601, Organonitrogen pesticides by filter + sorbent and LC	D4861, Pesticides and polychlorinated biphenyls	–	–
6004, SO_2 by treated filter and ion chromatography (IC)	D2914, SO_2 by bubbler and colorimetry	–	–
6009, Hg by sorbent tube and cold vapor atomic absorption (CVAA)	–	17733, Hg by CVAA or cold vapor atomic fluorescence	–
6013, H_2S by charcoal tube and IC	4913, H_2S by length of stain reading	–	–
6014, NO and NO_2 by sorbent tube and visible absorption spectrophotometry 6700, NO_2 by diffusive sampler and visible absorption spectrophotometry	–	8761, NO_2 by detector tube and direct indication	–
6604, CO by electrochemical sensor	–	8760, CO by detector tube	4554-1, -2, -3 and -4, Direct measurement of toxic gases and vapours
7013, Al; 7020, Ca; 7024, Cr; 7027, Co; 7029, Cu; 7030, Zn; 7048, Cd; 7074, W (insoluble); 7082, Pb, by flame atomic absorption spectrometry (FAAS)	D4185, Metals by FAAS D6785, Pb by FAAS or graphite furnace atomic absorption spectrometry (GFAAS)	8518, Pb by FAAS or electrothermal atomic absorption (ETAAS) 11174, Cd by FAAS or ETAAS	13890, Metals and metalloids – requirements and test methods
7056, Ba, soluble compounds; 7074, W (solubles), by FAAS	–	15202-2, Annex 8: Soluble metals and metalloids in workplace air	13890, Metals and metalloids – requirements and test methods

NIOSH Method(s) [13]	ASTM Standard(s) [23]	ISO Standard(s) [24]	CEN (EN) Standard(s) [25]
7105, Pb by GFAAS	D6785, Pb by FAAS or GFAAS	8518, Pb by FAAS or ETAAS	13890, Metals and metalloids – requirements and test methods
7300, 7301, 7302, 7303, 7304 Elements by ICP-AES	D7035, Metals and metalloids by ICP-AES	15202-1, -2 & -3, Metals and metalloids by ICP-AES (sampling, preparation and analysis)	13890, Metals and metalloids – requirements and test methods
7400, Asbestos fibers by phase-contrast microscopy (PCM) 7402, Asbestos fibers by transmission electron microscopy (TEM)	D7200, Airborne fibers in mines and quarries, including asbestos, by PCM and TEM D7201, Asbestos fibers by PCM with TEM option	8672, Airborne inorganic fibres by PCM	–
7401, Alkaline dusts, by acid-base titration	–	17091, LiOH, NaOH, KOH and $Ca(OH)_2$ by suppressed IC	–
7500, Respirable crystalline silica (RCS) by X-ray diffraction (XRD) 7602, RCS by infrared (IR) 7603, RCS in coal mine dust	D7948, RCS by IR	24095, Guidance for measuring respirable crystalline silica	–
7600 and 7703, Cr(VI) by Ultraviolet-Visible (UV-Vis) spectrophotometry 7605, Cr(VI) by IC and UV-Vis detection	D6832, Cr(VI) by IC and UV-Vis detection	16740, Cr(VI) by IC and UV-Vis detection	–
7704, Be in air by fluorescence 9110, Be in wipes by fluorescence	D7202, Be in air or wipes by fluorescence D7296, Be in dry wipes D7707, Be wipe specification	–	–
7910, Arsenic trioxide by GFAAS	–	11041, Arsenic and arsenic trioxide by atomic absorption	–
7902, Fluorides, aerosol and gas, by ion-selective electrode (ISE)	D4765, Fluorides by ISE	–	–
7906, Fluorides, aerosol and gas, by IC	–	21438-3, Fluorides, aerosol and gas, by IC	–
7907, HCl, HBr and HNO_3 by IC	D7773, HCl, HBr and HNO_3 by suppressed IC	21438-2, HCl, HBr and HNO_3, by IC	–
7908, H_2SO_4 and H_3PO_4 by IC	D4856, H_2SO_4 by IC	21438-1, H_2SO_4 and H_3PO_4 by IC	–
9100 and 9105, Pb on wipes 9102, Elements on wipes	D6966, Wipe sampling for metals D7659, Guide for elemental surface sampling D7822, Dermal wipe sampling for elemental analysis E1792, Pb wipe specification	TR 14294, Measurement of dermal exposure	TS 15278, Evaluation strategy for dermal exposure TR 15279, Measurement of dermal exposure
9200 and 9201, Chlorinated and organonitrogen herbicides, hand wash and dermal patch (respectively) 9202 and 9205, Captan and thiophanate-methyl in hand rinse and dermal patch (respectively)	–	TR 14294, Measurement of dermal exposure	TS 15278, Evaluation strategy for dermal exposure TR 15279, Measurement of dermal exposure

methods are themselves based on more recently developed ASTM and/or ISO standards. Ideally sampling and analytical methods for toxic agents in workplaces are performance-based, and harmonizing NIOSH methods with consensus standards is not necessarily as important as ensuring that the methods are adequately validated, sufficiently accurate and fit for purpose. NIOSH scientists have participated in the development of related consensus standards for many years, in keeping with the goals of the NTTAA. This helps to ensure that NIOSH methods are harmonized with applicable consensus standards and also fosters cooperation and collaboration between NIOSH experts and fellow scientists from domestic organizations and sister institutes in countries around the world.

Table 4. List of NIOSH Manual of Analytical Methods chapters [13].

Chapter	Content
A	Purpose and Scope
B	How to use NMAM
C	Quality Assurance
D	General Considerations for Sampling Airborne Contaminants
E	Development and Evaluation of Methods
F	Application of Biological Monitoring Methods
G	Aerosol Photometers for Respirable Dust Measurements
H	Portable Electrochemical Sensor Methods
I	Portable Gas Chromatography
J	Sampling and Characterization of Bioaerosols
K	Determination of Airborne Isocyanate Exposure
L	Measurement of Fibers
M	Sampling and Analysis of Soluble Metal Compounds
N	Aerosol Sampling: Minimizing Particle Loss from Cassette Bypass Leakage
O	Factors Affecting Aerosol Sampling
P	Measurement Uncertainty and NIOSH Method Accuracy Range
Q	Monitoring of Diesel Particulate Exhaust in the Workplace
R	Determination of Airborne Crystalline Silica

As a related resource, the IFA in Germany, in cooperation with experts from other member European nations participating in deliberations of CEN Technical Committee (TC) 137 [25], has made available a database of over 225 validated sampling and analytical methods for more than 125 substances [31]. Ratings of methods for these analytes are provided based on factors established by a European expert committee [32]. Presently, within CEN TC 137 [25], there is an ongoing project to update and expand this very useful methods database. Many NIOSH methods and international consensus standards can be found cited in this database.

Various older NIOSH methods for organics listed in Table 3, such as those for organic gases and vapors, are based on the use of packed gas chromatography (GC) columns. In practice, packed GC columns are rarely used now and have been largely replaced by capillary GC columns. The use of capillary GC columns has been described in many of the more recently published consensus standards (ASTM International and ISO) listed in Table 3. In order to modernize many of these older NIOSH methods (which were developed mostly in the 1970s and 1980s), currently there is a concerted effort to update a number of the NIOSH GC analytical methodologies for organic vapors and gases. Thus, a project is now underway to validate a multi-analyte procedure (or procedures) that can be used to measure multiple gaseous organic compounds in occupational atmospheres by means of sorbent sampling and capillary GC separation/isolation, followed by appropriate detection schemes like flame ionization detection (FID), photoionization detection (PID) or mass spectrometry (MS). This will result in the promulgation of new NIOSH methods for toxic organic gases and vapors that are up to date and are better harmonized with applicable international consensus standards.

4 Chapters, protocols and guidance

Within NMAM, separate from the methods themselves, eighteen chapters are covering a variety of subjects (**Table 4**) [13]. Explanatory chapters on quality assurance, sampling guidance, portable instrumentation, method development and evaluation, aerosol collection, measurement of specific analytes or groups of analytes, etc., provide valuable guidance to the users of NIOSH methods. These chapters provide a convenient resource that augments related consensus standards and technical information often available elsewhere in monographs and texts. Presently, efforts are underway to update several chapters that have not been revised in a number of years. Also, new chapters on key subjects including guidelines for the performance of biomonitoring methods and direct-reading instruments are planned. Similarly for sampling and analytical methods, harmonization of the guidelines put down in these chapters with relevant consensus standards guidance is essential and will be ensured.

Many of the methods published in NMAM specify the collection of workplace aerosol samples using filter samplers such as 37-mm closed-face filter cassettes (CFCs). NIOSH considers that all particles entering the sampler (e.g., CFC) should be included as part of the sample whether they deposit on the filter or on the inside surfaces of the sampler [33]. This subject has been discussed in detail by *Baron* in NMAM [13] Chapter O (Table 4). All aerosol particles entering occupational air samplers should comprise the sample for gravimetric analysis as well as for analytes such as metals and metalloids. Hence, during sample preparation and analysis, procedures should be used to account for material adhering to the internal walls of sampling cassettes. In the spirit of harmonization, consideration of internal sampler wall deposits is included in related international voluntary consensus standards that describe the sampling and analysis of airborne metals and metalloids [34; 35].

Also linked to guidance on NMAM sampling and analytical procedures for gases and vapors are relevant ASTM International and ISO standards describing the evaluation of diffusive samplers [36; 37]. Guidance on diffusive sampling [38] will be beneficial for evaluating newer passive monitoring techniques such as canister sampling, helium-diffusive sampling and solid-phase microextraction.

Table 5. Analytical figures of merit for inorganic acids sampling and analytical methods.

Method No.	Acid species	Sampling filter(s)	Analytical range in mg/m^3	Air sample volume in l	U$^{1)}$ in %
7906	Particulate fluoride	Cellulose nitrate filter, untreated$^{2)}$	0,04 to 5,9	120	< 20
	Hydrofluoric acid vapor	Sodium carbonate-treated cellulose nitrate filter$^{2)}$	0,25 to 5,0	120	< 22
7907	Hydrochloric acid vapor	Sodium carbonate-treated quartz fiber filter$^{3)}$	0,01 to 2,0	240	< 12
	Nitric acid vapor	Sodium carbonate-treated quartz fiber filter$^{3)}$	0,01 to 2,0	240	< 14
	Hydrobromic acid vapor	Sodium carbonate-treated quartz fiber filter$^{3)}$	0,01 to 2,0	240	< 12
7908	Sulfuric acid mist	Quartz fiber or PTFE filter$^{4)}$	0,002 to 1,0	420	< 23
	Phosphoric acid mist	Quartz fiber or PTFE filter$^{4)}$	0,01 to 2,0	420	< 23

$^{1)}$ Expanded uncertainty (calculated in accordance with EN 482 [27]; $k = 2$)

$^{2)}$ Filters in series

$^{3)}$ Preceded by untreated filter

$^{4)}$ No prefilter

Table 6. Gravimetric analysis with PVC internal capsules housed within CFC samplers – Analytical figures of merit [39].

Parameter	Value
Method detection limit (MDL)	≈ 0,075 mg/sample
Method quantitation limit (MQL)	≈ 0,25 mg/sample
Analytical range	MQL to > 5 mg/sample
Weight stability	> 28 days
Accuracy (A_{95}*)	< ±16 %

*NIOSH accuracy estimate [14]

5 Newly validated methods

Newly-drafted NIOSH methods for inorganic acids, Methods 7906, 7907 and 7908, are technically harmonized with a relevant parallel 3-part ISO standard, ISO 21438 (Table 3). Analytical figures of merit for these three methods are presented in Table 5. These protocols – which were first developed and evaluated by IFA [21] – have been extensively validated through interlaboratory trials and field studies. Compared to the use of sorbent tubes, they represent significant improvements in sampling and analytical methodologies for inorganic mists and vapors in workplace atmospheres, owing to superior detection limits and increased analyte capacity.

Evaluations were carried out to investigate the suitability of polyvinyl chloride (PVC) internal capsules, housed within air sampling devices, for gravimetric analysis of airborne particles collected in workplaces. The use of internal capsules addresses the shortcomings of filter-only sampling which can result in wall losses and low sampler capacity. As a result of this work, a newly evaluated gravimetric sampling method for collected aerosol particles using PVC internal capsules has been validated using Arizona Road Dust of ≈ 10 µm median aerodynamic diameter [39]. Analytical figures of merit for this sampling and measurement protocol are given in **Table 6**. The gravimetric measurement procedure entails the use of a weight-stable PVC internal capsule, attached to a PVC filter, for collection of particulate matter from workplace atmospheres. By using an internal capsule within the CFC in lieu of a filter (only), all of the collected aerosol is captured within the capsule and can subsequently be weighed in its entirety (minus of course the tare weight of the pre-weighed PVC capsule). Thus potential wall losses from CFC filter-only measurement (discussed earlier) are avoided.

Similarly, a new methodology for the sampling and analysis of metals and metalloids in workplace samples has been evaluated using acid-soluble cellulosic internal capsules attached to mixed-cellulose ester (MCE) filters [40]. An interlaboratory study (ILS) was carried out to evaluate the use of cellulosic CFC capsule inserts for their suitability in the determination of trace elements in airborne samples. Aerosol samples of uniform loadings at desired particulate levels were generated that contained multiple target analyte elements (Cd, Co, Cr, Cu, Fe, Pb, Mn, Ni) [40]; the samples were then prepared and analyzed by eight volunteer laboratories in accordance with ASTM D7035 [34]. Representative results from this ILS are summarized in **Table 7**. All interlaboratory RSD values (Table 7) are ≤ 12% and compare

Table 7. Representative multielement interlaboratory precision statistics for aerosol-dosed cellulosic filter capsules (n = 3) from eight laboratories [40].

Element	Loading level in µg	Number of reporting laboratories	Mean ± std. dev. in µg/m^3	RSD in %
Cd	7,5	8	5,5 ± 0,53	9,6
Cr	75	6	340 ± 18	5,2
Co	3,0	7	13 ± 0,42	3,2
Cu	150	8	110 ± 6,0	5,3
Fe	150	7	630 ± 44	7,0
Pb	60	8	260 ± 15	5,8
Mn	3,0	8	16 ± 1,4	9,0
Ni	75	8	59 ± 7,0	12

std. dev.: standard deviation, RSD: relative standard deviation

Table 8. Summary multielement ILS results (nine laboratories) from spiked cellulosic internal capsules after acid dissolution and analysis by ICP-AES.

Elements with U* < 30%:**	Al, As, Ba, Be, Ca, Cd, Co, Cr, Cu, Fe, La, Li, Mg, Mn, Mo, Ni, P, Pb, Sb, Se, Sr, Te, Ti, Tl, V, Y, Zn, Zr
Elements with U > 30%:	Ag, In, K, Sn, W

* Expanded uncertainty (*k* = 2) computed in accordance with EN 482 [27]

** EN 482 uncertainty criterion for measurements about the occupational exposure limit

Table 9. Newly validated NIOSH biomonitoring methods.

Method		Biological indicator of
No.	Title	
8007	Toluene in blood	Exposure to toluene
8319	Acetone and methyl ethyl ketone in urine	Exposure to acetone and methyl ethyl ketone
8322	Trichloroacetic acid in urine	Exposure to trichloroacetic acid, trichloroethylene, tetrachloroethylene, methyl chloroform, and other chlorinated compounds
8324	3-Bromopropionic acid in urine	Exposure to 1-bromopropane
8326	*S*-Benzylmercapturic acid and *S*-phenylmercapturic acid in urine	Exposure to toluene and benzene

favorably with the upper limit of variability which is typically observed (< 20%) in interlaboratory multi-element analysis of occupational hygiene air samples [41 to 43]. A subsequent nine-laboratory ILS of 33 elements spiked onto cellulosic filter capsules (three levels and blank media) was carried out in order to obtain performance data for many more metals and metalloids of concern or interest in occupational hygiene. Results from this investigation, summarized in Table 8, demonstrate the utility of cellulosic internal capsules for multielement workplace sampling and analysis of over two dozen elemental analytes.

Several NIOSH biomonitoring methods for various biomarkers of exposure in blood or urine have been validated recently and are briefly summarized in Table 9. Numerous other biomonitoring methods are presently undergoing evaluation and validation and will be published in the NMAM if their performance is found to meet desired acceptance criteria. It is expected that future NIOSH biomonitoring methods will not only include blood and urine samples but will also apply to metabolites and/or biomarkers of occupational exposures in sample matrices such as hair, fingernails and other tissues and also in samples of workers' sweat and exhaled breath.

6 Concluding remarks

Further efforts are underway that will fulfill requirements for fully validated NIOSH and consensus standard procedures for workplace exposure measurements. For example, new procedures describing the analysis of all aerosol particles entering a given air sampling device are being developed and evaluated. Through effective use of national and international collaborations and resources, further advances in the field of industrial hygiene chemistry are underway and improvements in sampling and analytical protocols are continually being explored. The NIOSH Manual of Analytical Methods remains an invaluable global resource for the occupational hygiene profession. Harmonization with voluntary consensus standards organizations such as ASTM International, CEN and ISO is crucial in leveraging current and future applied research, as well as technology transfer endeavors, within the discipline of occupational hygiene chemical and biochemical sampling and analysis.

References

[1] *Rose, V. E., Cohrssen, B.* (Eds.): Patty's Industrial Hygiene and Toxicology (6th ed.). New York: Wiley 2011.

[2] *Hathaway, G. J., Proctor, N. H.* (Eds.): Chemical hazards of the workplace (5th ed.). New York: Wiley 2004.

[3] *Eduard, W.; Heederik, D.; Duchaine, C.; Green, B. J.*: Bioaerosol exposure assessment in the workplace – The past, present and recent advances. J. Environ. Monit. 14 (2012), p. 334-339.

[4] *Jakubowski, M.*: Biological monitoring versus air monitoring strategies in assessing environmental-occupational exposure. J. Environ. Monit. 14 (2012), p. 348-352.

[5] *Kulkarni, P., Baron, P. A., Willeke, K.* (Eds.): Aerosol measurement – principles, techniques, and applications (3rd ed.). New York: Wiley 2011.

[6] *DiNardi, S. R.* (Ed.): The occupational environment – its evaluation, control, and management (2nd ed.). Published by: American Industrial Hygiene Association (AIHA), Fairfax, Virginia, USA 2003.

[7] *Vincent, J. H.*: Aerosol sampling – science, standards, instrumentation, and applications. New York: Wiley 2007.

[8] *Vincent, J. H.*: Occupational and environmental aerosol exposure assessment – A scientific journey from the past, through the present and into the future. J. Environ. Monit. 14 (2012), p. 340-347.

[9] *Behroozy, A.*: On dermal exposure assessment. Int. J. Occup. Environ. Med. 4 (2013), p. 113-127.

[10] *Semple, S., Cherrie, J. W.*: Dermal exposure assessment. In: *Nieuwenhuijsen, M. J.* (Ed.). Exposure assessment in occupational and environmental epidemiology. Oxford: Oxford University Press 2003.

[11] *Brisson, M., Ashley, K.* (Eds.): Surface and Dermal Sampling (ASTM Special Technical Publication No. 1533). ASTM International: West Conshohocken, Pennsylvania, USA 2011.

[12] *Angerer, J.; Greim, H.* (Eds.): Essential Biomonitoring Methods. Weinheim: Wiley-VCH 2006

[13] NIOSH Manual of Analytical Methods. Published by: US National Institute for Occupational Safety and Health (NIOSH), Cincinnati, Ohio, USA. www.cdc.gov/niosh/nmam (accessed 9 September 2014)

[14] *Kennedy, E. R., Fischbach, T. J., Song, R.; Eller, P. M.; Shulman, S. A.:* Guidelines for air sampling and analytical method development and evaluation (NIOSH Publication No. 95-117). Published by: US National Institute for Occupational Safety and Health (NIOSH), Cincinnati, Ohio, USA 1995

[15] *Kennedy, E. R.; Fischbach, T. J.; Song, R.; Eller, P. M.; Shulman, S. A.:* Summary of the NIOSH guidelines for air sampling and analytical method development and evaluation. Analyst 121 (1996), p. 1163-1169.

[16] *Kennedy, E. R., Fischbach, T. J., Song, R., Eller, P. M.; Shulman, S. A., Hull, R. D.:* Development and evaluation of methods (Chapter E). In: NIOSH Manual of Analytical Methods (4th ed). Published by: US National Institute for Occupational Safety and Health (NIOSH), Cincinnati, Ohio, USA 1998

[17] *Melcher, R.; Langner, R., Kagel, R.:* Criteria for the evaluation of methods for the collection of organic pollutants in air using solid sorbents. Am. Ind. Hyg. Assoc. J. 39 (1978), p. 349-361

[18] *Roper, C. P.:* The NIOSH detector tube certification program. Am. Ind. Hyg. Assoc. J. 35 (1974), p. 438-442.

[19] ASTM E691: Standard practice for conducting an interlaboratory study to determine the precision of a test method. ASTM International: West Conshohocken, Pennsylvania, USA 2011

[20] OSHA Sampling and Analytical Methods. Published by: US Occupational Safety and Health Administration (OSHA): Sandy, Utah, USA. www.osha.gov/dts/sltc/methods

[21] Deutsche Forschungsgemeinschaft (DFG): The MAK Collection for Occupational Health and Safety. Weinheim: Wiley-VCH. http://onlinelibrary.wiley.com/book/10.1002/3527600418

[22] Índice General de Protocolos y Métodos. Madrid: Instituto Nacional se Seguridad e Higiene en el Trabajo (INSHT) www.insht.es

[23] ASTM International: Committee D22 on Air Quality, Subcommittee D22.04 on Workplace Air Quality. ASTM International: West Conshohocken, Pennsylvania, USA. www.astm.org

[24] International Organization for Standardization (ISO): ISO Technical Committee 146 on Air Quality, Subcommittee 2 on Workplace Air Quality. Geneva: International Organization for Standardization (ISO). www.iso.org

[25] European Committee for Standardization (CEN): Technical Committee 137 on Assessment of Workplace Exposure to Chemical and Biological Agents. Brussels: Comité Européen de Normalisation (CEN). http://standards.cen.eu

[26] National Technology Transfer and Advancement Act (NTTAA), Public Law 104-113. Washington: United States Government, 1996

[27] EN 482: General Requirements for the Performance of Procedures for the Measurement of Chemical Agents. Brussels: Comité Européen de Normalisation (CEN) 2012

[28] *Bartley, D. L.:* Reconciling traditional accuracy assessment with the ISO Guide to the Expression of Uncertainty in Measurement (ISO/GUM). J. Occup. Environ. Hyg. 1 (2004), p. D37-D41.

[29] ASTM D7440: Standard practice for characterizing uncertainty in air quality measurements. ASTM International: West Conshohocken, Pennsylvania, USA, 2008.

[30] Guide to the Expression of Uncertainty in Measurement (ISO GUM). Geneva: International Standardization for Standardization (ISO) 2011.

[31] GESTIS Analytical Methods Database. Published by: Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA), Sankt Augustin, Germany. www.dguv.de/ifa, Webcode d6247.

[32] *Breuer, D.; Quintana, M. J.; Howe, A. M.:* Results of the EU project entitled 'Analytical Methods for Chemical Agents' for the evaluation of methods for analysis of hazardous substances in workplace air. J. Occup. Environ. Hyg. 3 (2006), p. D126-D136.

[33] *Ashley, K., Harper, M.:* Closed-face filter cassette (CFC) sampling – Guidance on procedures for inclusion of material adhering to internal sampler surfaces. J. Occup. Environ. Hyg. 10 (2013), p. D29-D33.

[34] ASTM D7035: Standard test method for the determination of metals and metalloids in airborne particulate matter by Inductively Coupled Plasma Atomic Emission Spectrometry (ICP-AES). ASTM International: West Conshohocken, Pennsylvania, USA, 2010.

[35] ISO 30011: Workplace air – determination of metals and metalloids by Inductively Coupled Plasma Mass Spectrometry (ICP-MS). Geneva: International Organization for Standardization (ISO) 2011

[36] ASTM D6246: Standard practice for evaluating the performance of diffusive samplers. ASTM International: West Conshohocken, Pennsylvania, USA, 2013

[37] ISO 16107: Workplace atmospheres – protocol for evaluating the performance of diffusive samplers. Geneva: International Organization for Standardization (ISO) 2007

[38] *Cassinelli, M. E., Hull, R. D., Crable, J., Teass, A.:* Protocol for the evaluation of passive monitors. In: Diffusive Sampling. London: Royal Society of Chemistry, 1987, p. 190-212

[39] *O'Connor, S., O'Connor, P. F.; Feng, H. A., Ashley, K.:* Gravimetric analysis of particulate matter using air samplers housing internal filtration capsules. Gefahrstoffe – Reinhalt. Luft 74 (2014) No. 10, p. 403-410

[40] *Harper, M., Ashley, K.:* Acid-soluble internal capsules for closed-face cassette elemental sampling and analysis of workplace air. J. Occup. Environ. Hyg. 10 (2013), p. 297-306.

[41] *Ashley, K.; Shulman, S. A., Brisson, M. J., Howe, A. M.:* Interlaboratory evaluation of trace element determination in workplace air filter samples by inductively coupled plasma mass spectrometry. J. Environ. Monit. 14 (2012), p. 360-367

[42] *Butler, O. T., Howe, A. M.:* Development of an international standard for the determination of metals and metalloids in workplace air using ICP-AES: evaluation of sample dissolution procedures through an interlaboratory trial. J. Environ. Monit. 1 (1999), p. 22-32.

[43] *Stacey, P.; Butler, O. T.:* Performance of laboratories analysing welding fume on filter samples: results from the WASP proficiency testing scheme. Ann. Occup. Hyg. 52 (2008), p. 287-295.