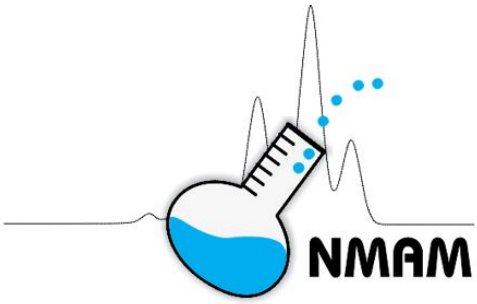


November 17, 2016

NIOSH Manual of Analytical Methods (NMAM), 5th Edition

Editors: Kevin Ashley, Ph.D. and Paula Fey O'Connor, NIOSH

[This document is current as of the publication date above and will be periodically updated. For the most current listing of methods and guidance chapters, please visit the NMAM website at www.cdc.gov/niosh/nmam.]

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

Foreword

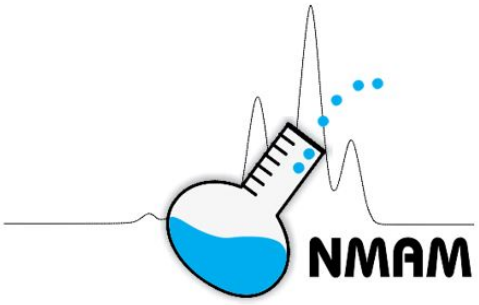
The National Institute for Occupational Safety and Health (NIOSH) is the U.S. federal agency responsible for conducting research and making recommendations for the prevention of work-related injury and illness. NIOSH is part of the Centers for Disease Control and Prevention (CDC) in the U.S. Department of Health and Human Services. The NIOSH Manual of Analytical Methods (NMAM) is a compilation of validated sampling and analytical methods that are used globally for occupational exposure assessment in the industrial (occupational) hygiene field and related professions. The methods that are published in NMAM are evaluated and validated in consideration of their fitness-for-purpose for exposure monitoring in work areas. NIOSH methods primarily address workplace air sampling and analysis, but NMAM also includes protocols for biological, surface, dermal, and bulk samples. Within NMAM, but separate from the methods themselves, are assorted chapters providing background and guidance covering a number of subjects. Explanatory chapters on quality assurance, sampling guidance, method development and evaluation, aerosol collection, etc., provide valuable information to users of NIOSH methods. NMAM chapters provide a convenient resource that augments technical information often (but not always) available elsewhere in texts and monographs. Now in its fifth edition, NMAM is continuously updated as new or revised methods are evaluated and their performance verified.

This document is a compilation of its guidance chapters and methods, current as of the date shown on the front page. NMAM is published online on the NIOSH web page (www.cdc.gov/niosh/nmam) and is available worldwide free of charge. Users are encouraged to visit the NMAM 5th edition website for the most current methods and guidance chapters.

CHAPTERS

METHODS

CHAPTERS



NIOSH Manual of Analytical Methods (NMAM), 5th Edition

Purpose, Scope and Use of the NIOSH Manual of Analytical Methods

by Kevin Ashley, Ph.D. and Paula Fey O'Connor, NIOSH

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
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1 Purpose and scope

The health of working people in myriad industries and occupations is potentially at risk through workplace exposure to airborne chemical and biological agents [Hathaway and Proctor 2004; Rose and Cohrssen 2011; Eduard et al. 2012; Jakubowski 2012]. 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 [DiNardi 2003; Vincent 2007, 2012; Kulkarni et al. 2011]. 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 [Semple and Cherrie 2003; Brisson and Ashley 2011; Behroozy 2013]. 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 [Angerer and Greim 2006].

The *NIOSH 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 1995]. NIOSH sampling and analytical methods are intended to promote accuracy, sensitivity, and specificity in industrial hygiene analyses and related applications. NMAM, which is published online (available at: www.cdc.gov/niosh/nmam), is constantly updated as new methods are developed and validated and as revised methods are evaluated and their performance verified. 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, measurement of fibers, aerosol sampler design, and other guidance on specific areas of interest.

Often there are situations during use where certain NIOSH methods may require modification, for instance, 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, recorded and reported. Examples where method modifications might be required include the following:

- The volume of air sampled on solid sorbents should be reduced in cases of high vapor concentration or high humidity and, in some cases, may be increased if such concentrations are relatively low.

- Automation of sample preparation and measurement procedures usually requires modification of the manual procedure on which the modified method is based.

- Chromatographic conditions, including choice of column and detector, can be modified to eliminate interferences or increase sensitivity during measurement.

- Acid mixtures used for sample dissolutions for elemental analysis may require modification for certain sample matrices that are difficult to dissolve.

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). Many NIOSH methods are developed in parallel with related voluntary consensus standards [Ashley 2015]. 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.

2 How to use NMAM

NIOSH methods are grouped alphabetically by method name, and some method names may refer to a group of related substances. It is also possible to locate methods through their arrangement by method number. Methods for particular analytes or groups of analytes can additionally be accessed by searching their Chemical Abstracts Service (CAS) number(s) through the online link.

a. Locating a NIOSH method

Often the easiest and fastest way to locate a method is to refer to the online method index, which contains an alphabetical listing of analytes and listing by method number. Each method's cover page contains information on alternate chemical names and information on: Compound(s), Method Number, Method Name, Sampling Rate, Minimum Volume, Maximum Volume, Reagents, Analytical Technique and Sampler (for a quick reference). It is also possible to search electronically by method number and/or CAS number (if known).

b. Method numbering system

The general NMAM method numbering system is outlined in the table below. Substances having the same sampling device, sample preparation procedure and measurement technique are often grouped together in one method (e.g., organic vapors; metals).

Method No.	Substances
0001-0799	General air samples
0800-0999	Bioaerosols
1000-1999	Organic vapors on charcoal sorbents
2000-3499	Organic vapors on other solid sorbents
3500-3999	Organic vapors on other samplers (e.g., liquids; direct-reading instruments)
4000-4999	Organic vapors on diffusive samplers
5000-5999	Organic aerosols
6000-6999	Inorganic gases and vapors
7000-7999	Inorganic aerosols
8000-8999	Biological samples
9000-9999	Bulk samples; wipe samples

c. Indexes and Appendixes

Within the NMAM website there is an online link to indexes that can be used to locate methods published in previous editions of the Manual:

1) Fourth Edition Methods

An index of fourth edition methods in order of method number. Note that the same method numbering system is used for third, fourth and fifth edition NIOSH methods. Also denoted is the current disposition of historical or discontinued methods.

2) First and Second Edition Method Numbers

An index of the first and second edition "P&CAM" and "S" methods, from which many of the subsequent methods were derived. This index shows the disposition of all of these earlier methods, whether they were later revised / updated or not.

3) Names and Synonyms

An alphabetical listing of chemical names and synonyms used in current (and many previous edition) methods, including CAS numbers.

An online "Appendixes" link is also available for obtaining unit equivalents or for carrying out air concentration calculations for comparisons to Occupational Safety and Health Administration (OSHA) standards.

d. Method format

NIOSH methods consist of three major parts:

1) Front page

The first page of each method concisely summarizes sampling and measurement parameters and gives estimates of limit of detection, working range, overall and measurement precision, and interferences. References to other relevant methods are given. Also provided are Method Classification, NIOSH Registry of Toxic Effects of Chemical Substances (RTECS) number, and an estimate of method accuracy (see Figure 1).

2) Instructions

The second page of each method begins with lists of required reagents and equipment. Please note that these reflect the conditions under which the methods were evaluated and that there may still be some latitude for variation. The user of the methods is responsible for assuring the accuracy of the results (e.g., to determine that breakthrough and recovery are acceptable for each lot of samplers used). For example, typical tolerances for sorbent tubes are illustrated:

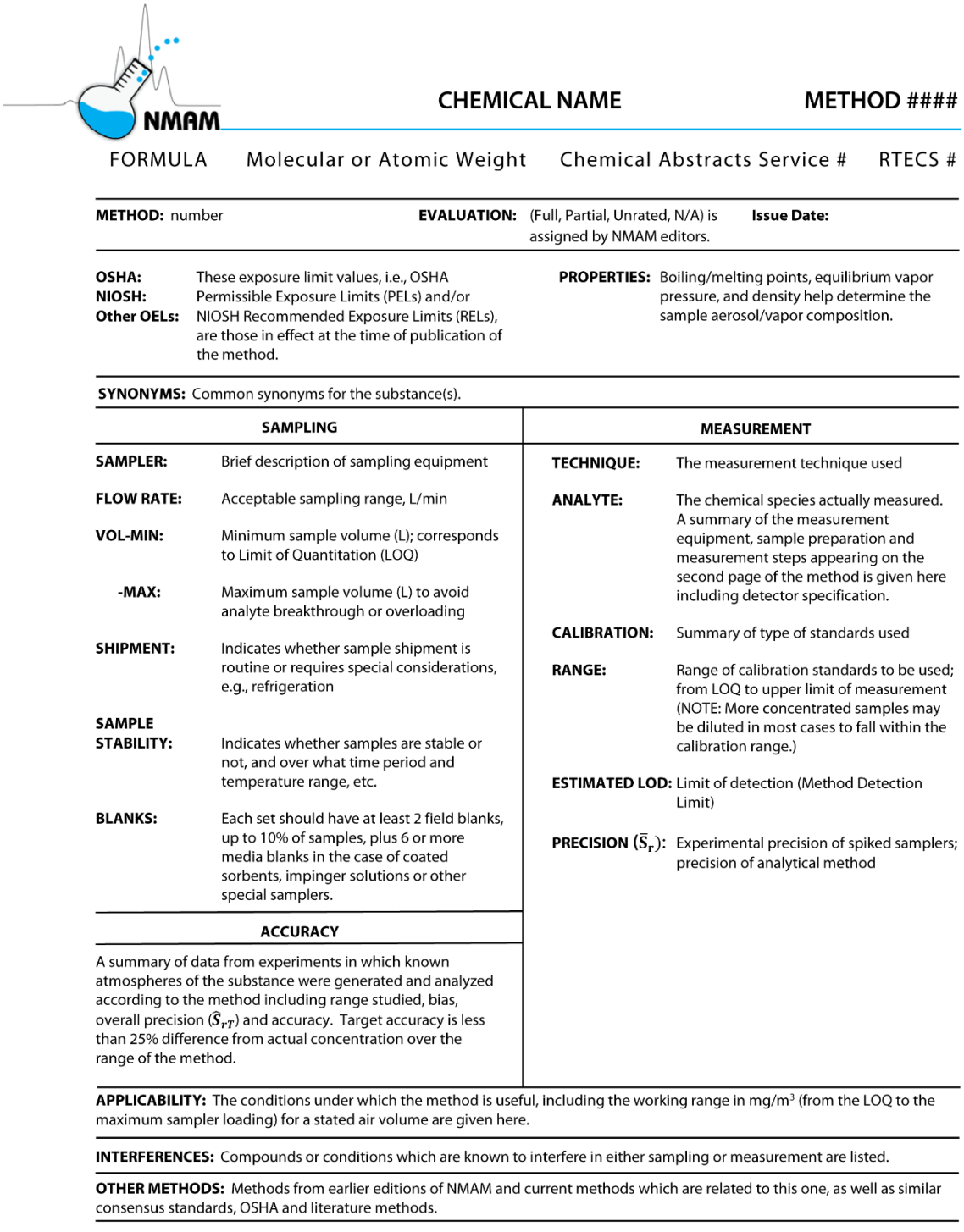
- Glass tubing used to contain solid sorbents: Inside diameter is usually not critical within the range of 4 to 6 mm; length should be sufficient to contain the specified mass of sorbent.

- Contents of sorbent tubes: Mass of sorbent within ±10% of specification; separators of either glass wool or cleaned polyurethane foam (unless otherwise indicated); sorbent mesh size of 20/40 unless sampling efficiency dictates otherwise. Filled sorbent tubes should be sealed to protect them from contamination.

The Special Precautions section gives guidance on safe practices to be observed during sampling, sampler preparation and measurement. Next are the step-by-step instructions for Sampling, Sample Preparation, Calibration and Quality Control, Measurement, and Calculations. Any lengthy instructions for sampler preparation and standardization of stock solutions appear in method appendixes. Nomenclature is consistent with the NMAM Glossary (chapter) of Abbreviations, Definitions and Symbols. (Note that additional general information relating to sampling and measurement is contained in other NMAM chapters.)

3) Supporting information

Laboratory and field data relating to the method are summarized in the Evaluation of Method section and on the summary page, along with pertinent references.



NMAM

CHEMICAL NAME METHOD ####

FORMULA Molecular or Atomic Weight Chemical Abstracts Service # RTECS #

METHOD: number **EVALUATION:** (Full, Partial, Unrated, N/A) is assigned by NMAM editors. **Issue Date:**

OSHA: These exposure limit values, i.e., OSHA
NIOSH: Permissible Exposure Limits (PELs) and/or
Other OELs: NIOSH Recommended Exposure Limits (RELs), are those in effect at the time of publication of the method.

PROPERTIES: Boiling/melting points, equilibrium vapor pressure, and density help determine the sample aerosol/vapor composition.

SYNONYMS: Common synonyms for the substance(s).

SAMPLING

SAMPLER: Brief description of sampling equipment

FLOW RATE: Acceptable sampling range, L/min

VOL-MIN: Minimum sample volume (L); corresponds to Limit of Quantitation (LOQ)

-MAX: Maximum sample volume (L) to avoid analyte breakthrough or overloading

SHIPMENT: Indicates whether sample shipment is routine or requires special considerations, e.g., refrigeration

SAMPLE STABILITY: Indicates whether samples are stable or not, and over what time period and temperature range, etc.

BLANKS: Each set should have at least 2 field blanks, up to 10% of samples, plus 6 or more media blanks in the case of coated sorbents, impinger solutions or other special samplers.

ACCURACY

A summary of data from experiments in which known atmospheres of the substance were generated and analyzed according to the method including range studied, bias, overall precision ($\hat{S}_{rT}$) and accuracy. Target accuracy is less than 25% difference from actual concentration over the range of the method.

MEASUREMENT

TECHNIQUE: The measurement technique used

ANALYTE: The chemical species actually measured. A summary of the measurement equipment, sample preparation and measurement steps appearing on the second page of the method is given here including detector specification.

CALIBRATION: Summary of type of standards used

RANGE: Range of calibration standards to be used; from LOQ to upper limit of measurement (NOTE: More concentrated samples may be diluted in most cases to fall within the calibration range.)

ESTIMATED LOD: Limit of detection (Method Detection Limit)

PRECISION ($\bar{S}_r$): Experimental precision of spiked samplers; precision of analytical method

APPLICABILITY: The conditions under which the method is useful, including the working range in mg/m³ (from the LOQ to the maximum sampler loading) for a stated air volume are given here.

INTERFERENCES: Compounds or conditions which are known to interfere in either sampling or measurement are listed.

OTHER METHODS: Methods from earlier editions of NMAM and current methods which are related to this one, as well as similar consensus standards, OSHA and literature methods.

NIOSH Manual of Analytical Methods (NMAM), Fifth Edition

Figure 1. Layout of front page of NIOSH methods

e. Method classification

Methods in previous (fourth) edition of NMAM are classified into evaluation categories: Full, Partial, Unrated and Not Applicable. Classification is based on the results of laboratory testing and evaluation criteria as described in a NIOSH guidelines document [NIOSH 1995] and in Chapter ME (Development and Evaluation of Methods). Most methods in the fifth edition are classified as 'fully validated.'

The performance data from these evaluations are summarized in the Evaluation of Method section in each method. This section may also contain other corroborating data, e.g., results from collaborative testing, Proficiency Analytical Testing (PAT) data, or field data from NIOSH studies. For partially evaluated methods, this section will state which evaluation points were not tested, thus providing the user with information on which to make a reasonable judgment on the quality of the data obtained.

Evaluation – Full: Fully evaluated methods are those that have been tested and found to have met all of the factors of the NIOSH evaluation protocol [NIOSH, 1995].

Evaluation – Partial: Partially evaluated methods are those that have been subjected to some of the evaluation experiments but have not received a full evaluation (e.g., short-term method development). These may also include methods that were fully tested but did not meet one or two of the evaluation criteria specified in the NIOSH protocol [NIOSH, 1995]; for example, some of the earlier-developed methods that do not meet the current ±25% accuracy criterion.

Evaluation – Unrated: Unrated methods have not been tested by NIOSH, but may have been developed by a recognized independent source such as OSHA.

Evaluation – N/A: The designation, Not Applicable (N/A), is applied to methods where no quantitative data are collected, such as:

- Procedures for sample collection only. The collected samples are analyzed subsequently by an appropriate analytical method.

- Qualitative methods that indicate results as a positive or negative (or inconclusive).

f. User experience with NIOSH methods

NIOSH strives to make the methods published in NMAM useful and fit for purpose in industrial hygiene analyses. Therefore, feedback on the experiences of people using the methods is important to us. Suggestions for improvement and questions relating to

NMAM are welcome and should be directed to the editors of the Manual. Their contact information is provided on the NMAM webpage.

Disclaimer

Mention of any company or product does not constitute endorsement by NIOSH. In addition, citations to websites external to NIOSH do not constitute NIOSH endorsement of the sponsoring organizations or their programs or products. Furthermore, NIOSH is not responsible for the content of these websites. All web addresses referenced in this document were accessible as of the publication date.

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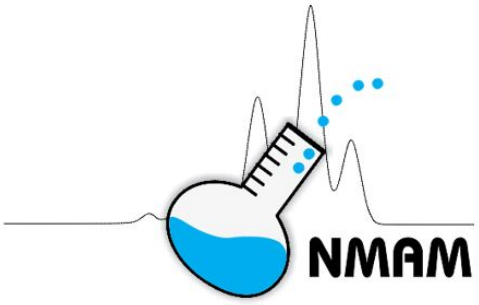

NIOSH Manual of Analytical Methods (NMAM), 5th Edition

Development and Evaluation of Methods

by Eugene R. Kennedy, Ph.D., Thomas J. Fischbach, Ruiguang Song, Ph.D., Peter M. Eller, Ph.D., Stanley A. Shulman, Ph.D., and R. DeLon Hull, Ph.D., NIOSH

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1 Method development

The development and evaluation of analytical methods that are useful, reliable and accurate for industrial hygiene monitoring problems require the application of some general guidelines and evaluation criteria. The guiding objective in this work requires that, over a specified concentration range, the method provide a result that differs no more than ±25% from the true value 95 times out of 100. The application of consistent evaluation criteria and guidelines is particularly important when methods are developed by different individuals and organizations (e.g., contractors or outside laboratories) and compiled into a single manual. Adherence to guidelines should minimize overlooking potential problems in the methodology during its development, as well as provide cohesiveness and uniformity to the method that is developed. This chapter provides an outline of a generalized set of evaluation criteria prepared by NIOSH researchers for the evaluation of sampling and analytical methodology [NIOSH 1995].

In the development of a sampling and analytical method, there is a logical progression of events that cover a search of the literature to gather pertinent information and the preliminary experimentation for selection of analysis technique and sampling medium. To initiate the development of a method, the identity of the analyte must be as fully defined as possible. Physical and chemical properties of the analyte should be defined so that procedures for proper handling and use of the analyte can be prepared. These also aid in establishment of analyte purity. Potential sources of this information include chemical reference books, health hazard evaluation reports, bulk sample analyses, material safety data sheets, chemical process information, etc.

Since innovation is a key element in the sampling and analytical method development process, detailed experiments for the initial development of the sampling approach and optimization of the analytical procedure are better left to the discretion of the researcher. During development, it should be recognized that appropriate, statistically designed experiments will optimize the amount of information obtained. Therefore, consultation with a statistician about appropriately designed experiments will be of value during this phase of the research.

a. Preliminary experimentation

Several key points, including calibration and selection of measurement technique and sampling media, should be studied during the initial method development experiments. The selection of sampling medium and procedure is a decision that usually is made early in the method development process. The physical state of the analyte (i.e., gas, aerosol, vapor, or combination thereof) plays an important factor in the selection of an appropriate sampler. Analytes which can exist in more than one physical state may require a

combination of sampling media in one sampler for efficient collection [NIOSH 1995]. Where possible, commonly available and easily used samplers should be investigated initially. As the preliminary testing of a sampling method progresses, further modification in the sampling medium or sampler design may be required and may affect the measurement procedure. Sampler design and media selection considerations should include U.S. Department of Transportation regulations and restrictions for shipment back to a laboratory for analysis.

Since industrial hygiene analytical methods are geared toward measuring personal exposure, the size, weight, and convenience of the sampler are important elements in sampler design. The personal sampler should allow freedom of movement and should be unobtrusive, unbreakable, and not prone to leakage. The pressure drop across the sampler should not be so great as to limit sample collection times to 10 h with personal sampling pumps. For situations where only a short term sample will be required (i.e., 15 min for ceiling determinations), this 10 h recommendations can be reduced to 1 h. The use of potentially toxic reagents should be avoided unless they can be used safely. Reagents used should not pose any exposure hazard to the worker wearing the sampler or to the industrial hygienist taking the samples.

b. Recovery of the analyte from the medium

During the course of method development experiments, the ability to recover the analyte from the sampling medium should be determined. A suggested experiment to accomplish this entails the fortification of sets of 6 samplers with amounts of analyte equivalent to sampling concentrations of 0.1, 0.5, 1.0, and 2.0 (or higher) times the exposure limit for a minimum of 4 h at the typical sampling rate used for that type of sampler. If the analyte has a ceiling or short-term exposure limit, the amount of analyte fortified should be adjusted for the shorter sampling time required for this type of exposure limit. If the sampler has a backup section, then a like number of separate backup sections should be fortified with amounts of analyte equivalent to 25% of the amount fortified on the front sections of the samplers, since this amount has been used to characterize the breakthrough limit of useful samples [Streicher et al. 1994]. Samples (and backup sections) should be prepared for analysis and analyzed according to previously determined procedures. Results of these analyses should be expressed in terms of estimated percent recovery according to the following formula:

$$\text{Percent Recovery}_{(\text{est.})} = \left[\frac{Amount\ of\ analyte\ found\ on\ sampler}{Amount\ of\ analyte\ fortified\ on\ sampler}\right] \times\ 100\ \%$$

After initial analyses of the samples, the samples should be resealed and analyzed on the following day, if possible. If the sample workup procedure results in a solution of the

sample, these solutions should be recapped after the initial analysis, if possible, and reanalyzed on the following day using fresh standards.

The recovery of the analyte should be calculated for the primary and backup media in the sampler. Although complete recovery of the analyte from the sampler is most desirable, at a minimum, the estimated recovery of the analyte from the primary collection medium should be greater than or equal to 75% for concentrations equivalent to sampling 0.1, 0.5, 1.0, and 2.0 times the exposure limit. If recovery varies with analyte loading, results should be graphed as recovery versus loading during calibration of the method, so that appropriate correction can be made to sample results, as long as recovery is greater than 75% [Melcher et al. 1978]. If estimated recovery does not exceed 75%, the method is not suitable for monitoring at this limit.

Estimated recovery from any backup media should be noted so that appropriate corrections can be applied if breakthrough of the sampler has occurred during sampling. The recovery of the analyte from the medium in the backup section of a sampler may be different from that of the front section, since the backup section of a sorbent-based sampler usually contains only half of the sorbent of the primary section. If the same volume of desorption solvent is used for both the primary and backup sections of the sampler, the desorption equilibrium can be shifted, since the backup section is being desorbed by twice the volume (i.e., on a mL solvent/mg sorbent basis) [Saalwaechter et al. 1977].

Reanalysis of the samples on the day after initial analysis indicates if immediate analysis after sample preparation is required. Often when processing a large number of samples, it may be necessary to prepare the samples for analysis as a batch. In these instances, the last samples may not be analyzed for up to 24 h or more after preparation because of the time required for analysis. If samples prepared for analysis exhibit time-dependent stability after desorption, analyses must be conducted within acceptable time constraints. Analysis and reanalysis results should agree within 5% of each other.

c. Stability of the analyte on the medium

An extension to the experiment described above may be performed to investigate potential stability problems early in the experimentation. An additional set of fortified samples at each of the 4 concentrations should be prepared and analyzed after 7-days' storage at room temperature. Recovery should be similar to the above results within experimental error. Discrepancies larger than those expected by experimental error indicate sample stability problems that will need correcting by additional developmental effort (e.g., refrigerated storage). Comparison of results can be performed with statistical tests, such as an analysis

of variance (ANOVA) [Posner and Okenfuss 1981] test of the "Day" difference or a paired t-test [Box et al. 1978] of the means of the Day 1 and Day 7 storage results.

2 Method evaluation

After the initial development experiments for the method have been completed and a method has been proposed, the sampling and analysis approach should be evaluated to ensure that the data collected provides reliable, precise, and accurate results. Specifically, the goal of this evaluation is to determine whether, on the average, over a concentration range of 0.1 to 2 times the exposure limit, the method can provide a result that is within ±25% of the true concentration 95% of the time. For simplification, the true concentration is assumed to be represented by an independent method. An experimental approach for collecting the data necessary for this determination is described below.

As part of the evaluation of a method, the sampling of a generated atmosphere is needed to more adequately assess the performance of a method [NIOSH 1984; Nelson 1971; Nelson 1992]. This allows the determination of 1) the capacity of the sampler; 2) the efficiency of analyte collection by the sampler; 3) the repeatability of the method; 4) the bias in the method; 5) interferences in the collection of the sample. Concentration ranges to be used in the evaluation of the method should be based on several factors. These ranges, at a minimum, should cover 0.1 to 2.0 times the exposure limit. In some instances, higher multiples of the exposure limit can be added if needed (e.g., 10 times the exposure limit). In situations where multiple exposure limits (i.e., from different authorities) exist for an analyte, the lowest exposure limit should be used to set the lower limit of the evaluation range (0.1 times lowest exposure limit) and the highest limit used to calculate the upper limit of evaluation range (2 times the highest exposure limit). Intermediate evaluation concentrations should be within these exposure limits. The toxicity of an analyte (e.g., suspected carcinogenicity) may indicate that a concentration lower than that calculated by the exposure limit should be included in the measurement and evaluation ranges. Previous monitoring information from other methods may indicate that typical concentrations of the analyte may be below or above a concentration range based on the exposure limit. In this case, this lower or upper level may be included in the method evaluation.

a. Feasibility of analyte generation

In order to provide a realistic test of the method under study, air concentrations covering the range from 0.1 to 2 times the exposure limit of the analyte should be generated. The generated atmospheres should be homogeneous in concentration and representative of the environment encountered when sampling for the analyte in the workplace.

When attempting to generate a concentration of an analyte, the impact of environmental conditions, such as temperature, pressure, humidity, and interferences, on sampler performance and/or generation should be considered. The effect of elevated temperature on the collection medium of a sampler may decrease the capacity of the sampler or may decompose the analyte during generation and sampling. Reduced pressure may also reduce the capacity of a sampler. High relative humidity in many instances has been observed to reduce sampler capacity [Melcher et al. 1978]. In other instances it has increased sampler capacity [Cassinelli 1991]. A typical interference(s) should be generated along with the analyte to approximate a typical workplace sampling environment.

Generation of particulate material can be extremely complex [Willeke 1980; Hinds 1982], especially if particles of a required size range must be generated for the evaluation of a specified sampler inlet design. The aerodynamic performance of the generator is a factor in the generation of this type of atmosphere and should be evaluated carefully. Appropriate, independent methods should be available to verify particle size, if this is a critical element in the generation.

The concentration of the generated atmosphere should be verified either by well characterized gravimetric/volumetric means or by analysis of replicate samples (if possible) by an independent method at each concentration used. Further details on this verification are included in the literature [NIOSH 1995; Ashley 2015]. A statistician should be consulted for advice on the design and sample sizes to accomplish this validation. Ideally, the independent method should not be biased and should provide an accurate estimate of the concentration generated, assuming error is randomly distributed around the mean. Also the precision and bias of the independent method should be homogeneous over the concentrations investigated. (See NIOSH [1995] for the definitions of these attributes.) In instances where the concentration of the generator can be based only on calculations using flow rates in the generator and the amount of analyte injected, the generation system should be well characterized so that analyte losses are minimized.

In some instances, generation of an analyte may be difficult and even hazardous. As an alternative to direct generation in these cases, samplers may be fortified with an amount of analyte expected to be sampled over a specified period of time at a specific flow rate. When this is necessary, fortification of the sampler by vaporization of a known amount of analyte onto the sampling medium is a more appropriate method, since this approach more closely approximates a generated atmosphere. The alternative of direct application of a solution of analyte onto the collection medium is less desirable but may be necessary in some instances. After fortification, air, conditioned at both high and low humidity, should be drawn through samplers at the flow rate and time period used in the calculations for the

amount of analyte expected to be collected. In the method report, the fact that samples were not collected from a generated atmosphere should be discussed.

b. Capacity of the sampler and sampling rate

To determine the applicability of the sampling method, the capacity of the sampler should be determined as a function of flow rate and sampling time. This is particularly important if the analyte has both a short-term exposure limit (STEL) and a time-weighted average. Flow rates typical for the media selected should be used. These may range from 0.01 to 4 L/min, depending on sampler type. At extremely low flow rates (ca. 5 mL/min), the effect of diffusion of the analyte into the sampler must be considered. Flow rates should be kept at a high enough rate to prevent diffusion from having a positive bias in the sampler. Sampling should be performed at three different flow rates covering the range appropriate for the particular sampler type, unless the sampler is designed to operate at only one flow rate.

Sampling times should range from 22.5 min for STELs to 900 min (15 h) for time-weighted averages. Shorter sampling times (e.g., 7.5 to 22.5 min) may be used for ceiling (C) measurements. Flow rates should be based on accurately calibrated sampling pumps or critical orifices. The amount of analyte collected at the lowest flow rate and shortest sampling time should be greater than the limit of quantitation of the method. The generated concentration used for capacity determination should be at least 2 times the highest published exposure limit and verified by an independent method.

Sampling should be conducted at ambient, elevated (>35 °C), and low (<20 °C) temperatures to assess the effect of temperature on sampling. To assess the effect of humidity on capacity, sampling should be performed at both low and high humidity (20% and 80%), since both have been observed to affect capacity [Cassinelli 1991; Melcher et al. 1978]. Triplicate samplers at three different flow rates should be included to verify capacity at each of the six different humidity and temperature levels. For samplers which contain backup sampling media, only the front section of the sampler should be used. A means is required to quantitate analyte in the effluent from the sampler. This may involve the use of a backup sampler, continuous monitor or other appropriate means which can provide a measure of analyte concentration in the sampler effluent (ca. 1 to 5% of the influent concentration). If the mass of analyte found on a backup sampler totals 5% of the mass found on the front sampler or if the effluent concentration of the sampler contains 5% of the influent concentration, breakthrough has occurred and the capacity of the sampler has been exceeded.

If the analyte is a particulate material and collected with a filter, the capacity of the filter is defined by the pressure drop across the sampler or by the loading of the filter. For 37-mm filter-based samplers, pressure drop should be less than 1000 mm of water for total loading less than 2 mg. Larger filters and especially filter capsules [Harper and Ashley 2013; O'Connor et al. 2014] will tolerate higher loadings (e.g, up to 5 mg).

If the collection process is based primarily on adsorption, breakthrough time should be proportional to the inverse of the flow rate [Jonas and Rehrmann 1973]. This relationship can be checked by plotting the 5% breakthrough time versus the inverse of the flow rate. If the resulting plot is a straight line, then this relationship should hold for all flow rates in the flow rate range studied. Some nonlinearity in the plot may be noted due to experimental variability and assumptions made to simplify the relationship of breakthrough time and flow rate. Results from these experimental trials should provide a prediction of the capacity of the sampler at various flow rates and sampling times. If the flow rates and sampling times used in the experiment do not provide for sufficient capacity, a lower flow rate range may have to be studied and the experiment repeated.

With samplers which use reagents for collection of the analyte, the amount of the reagent in the sampler will also be a limiting factor in the capacity of the sampler, based on the stoichiometry of the reaction. Other factors, such as residence time in the sampler and kinetics of reaction between analyte and reagent, may affect the capacity of this type of sampler.

The combined temperature and humidity conditions that reduce sampler capacity to the greatest extent should be used in all further experiments. The Maximum Recommended Sampling Time (MRST) for a specific flow rate is defined as the time at which sampler capacity was reached, multiplied by 0.667. This adds a measure of safety to this determination. The relationship of breakthrough time with flow rate can be used to adjust flow rates to optimize specific sampling times.

c. Sampling and analysis evaluation

To assess the performance of a method, certain additional experimental parameters should be evaluated through a series of defined experiments. The effect of environmental conditions (e.g., pressure, interferences) on sampling efficiency of the sampling medium can be evaluated by a factorial design [Box et al. 1978]. The temperature, relative humidity, flow rate, and sampling times, determined in the experiment described above to have most severely limited sampler capacity, should be used in these experimental runs [Ashley 2015]. At a minimum, the effect of concentration on method performance should be investigated. Three sets of 12 samples should be collected from an atmosphere containing

concentrations of 0.1, 1.0, and 2.0 times the exposure limit at the humidity determined above to have reduced sampler capacity for the MRST determined in the preceding experiment.

If the analyte has a short-term or ceiling exposure limit in addition to an 8-hour time-weighted average, an additional 12 samplers should be collected at the STEL or C limit for the recommended sampling period at the appropriate flow rate. Potential interferences in the work environment should be included in the generation experiments to assess their impact on method performance. Concentrations up to 2 times the exposure limit value for the interference should be included. Other environmental factors may be studied, but will require a more comprehensive experimental design.

The effects of environmental conditions on analyte recovery should be assessed. A factorial design can be used to evaluate these factors to determine which exert a significant effect on analyte recovery. Those factors which are found to influence analyte recovery should be investigated further to determine if their impact is predictable. If these effects are not predictable, the utility of the method will be limited, based on the conditions defined by this experiment. If only concentration is evaluated, the analyte recovery should be the same at all concentrations after correctable biases have been included, such as desorption efficiency.

d. Sample stability

To assess sample stability, samples should be collected from a generated atmosphere, stored under defined conditions (i.e., ambient or refrigerated, light or dark), and analyzed at specified time periods. A concentration of 0.5 times the lowest exposure limit should be sampled with 30 samplers for a minimum of ½ the MRST. The humidity and temperature of the generator should be at the same level as defined in the sample capacity experiment to reduce sample capacity. The samplers should be divided randomly into one group of 12, one group of 6, and four groups of 3, with the group of 12 analyzed as soon after collection as possible (Day 0). The group of 6 samplers should be analyzed after 7 days. The four remaining sets of 3 samplers should be analyzed after 10, 14, 21, and 30 days. The conditions of storage are determined by the nature of the analyte. If there is an indication of analyte instability on the sampling medium, refrigeration of the samplers may be required. However, storage for the first 7 days should be at room temperature.

Samples should normally be stable for a minimum of 7 days under ambient conditions to simulate shipping to a laboratory for analysis. If the average analysis results of the samplers analyzed on day 7 differs from the set analyzed on day 0 by more than 10%, the method does not meet the sample stability criterion. Either additional precautions, such as

shipment on ice and refrigerator storage, may be required or the method may have to be modified to address this problem. (Note: In practice, reactive or unstable samples should be shipped by overnight mail and analyzed as quickly as possible.) If a plot of recovery versus time indicates that recovery decreased by more than 10% after the initial 7-day storage period, sample instability is a problem. If samples need to be stored for longer periods, more restrictive storage conditions are required. Remedial action, such as cold storage may solve this longer term storage problem. After remedial precautions have been instituted in the method, the sample stability of the method must be determined anew.

e. Precision, bias, and accuracy

Results from four sets of samplers used in the analyte recovery experiment, the sampling and analysis experiments (e.g., the environmental parameters experiments), and the sample stability experiment can be used for the estimation of precision, bias, and accuracy of the method. A more exacting treatment of this is described elsewhere [NIOSH 1995]. Sampler results from the multi-level factorial design at the 0.1, 1.0, and 2.0 times the exposure limit value; the sampler stability experiment (at 0.5 times the exposure limit); and the environmental factors experiment are used in the calculations of method precision. The calculations for the estimated method precision, $\hat{S}_{rT}$, have been described previously [NIOSH 1995; Anderson et al. 1981; Busch and Taylor 1981; NIOSH 1980]. Before obtaining a pooled estimate of method precision from the four sets of samplers listed above, the homogeneity of the precision over the range of concentrations studied should be checked using a test, such as Bartlett's test [NIOSH 1995; Anderson et al. 1981; Busch and Taylor 1981]. If the precision is not found to be constant over concentrations, the sample set collected at 0.1 times exposure limit should be removed and Bartlett's test recalculated. Homogeneity of the method precision at all concentration levels is an assumption required to obtain pooled estimate of method precision.

Bias is assumed to be homogeneous over the evaluation range. This assumption should be tested by estimating the bias at each concentration and testing these for homogeneity using the procedures described in the literature [NIOSH 1995]. Method bias should be less than 10%. A test for this is also described [NIOSH 1980].

The bias and precision estimates can be used with the graph presented in Figure 1 or in Table I to estimate accuracy [NIOSH 1995]. The bias and precision estimates are plotted on the x- and y-axes of the graph. The intersection of these points on the parabolic grid in the graph can be used to estimate the accuracy of the method. This procedure gives an estimate of method accuracy but does not yield the statistic required to test compliance of the method with the ±25% accuracy criterion. Techniques for the latter determination are discussed in the Appendix and elsewhere [NIOSH 1995].

If the results for 4 concentrations fail the 25% accuracy criterion, then the set of samples collected at the lowest concentration level should be excluded from the data set. The pooled $\hat{S}_{rT}$ and the bias should be recalculated on this reduced data set before performing the accuracy analysis described in the previous paragraph.

For the 12 samplers collected at the ceiling limit, the accuracy analysis described above should be repeated using only the data collected at the ceiling limit.

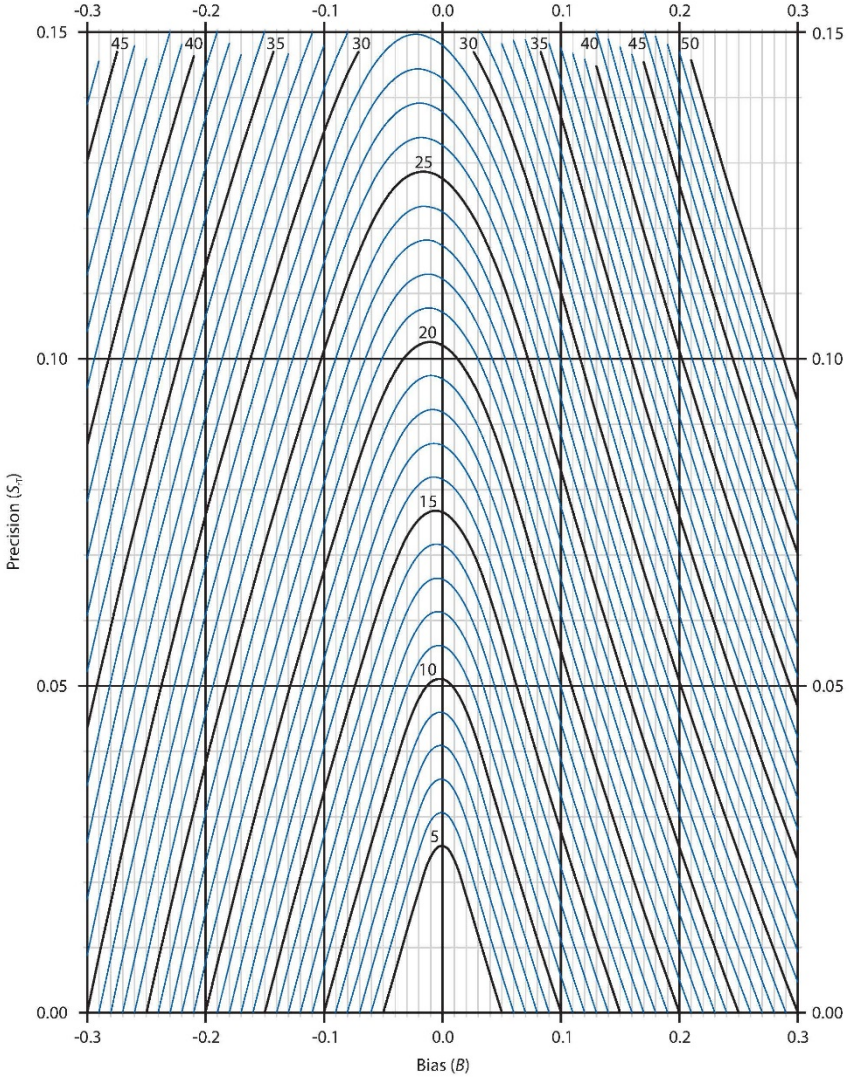

Figure 1. Nomogram relating accuracy to precision and bias. Accuracy (A), in percentage units, is a function of the bias (B) and the precision (S_{rT}). Each curve is the locus of all points (B, S_{rT}) that yield the value of A indicated on the curve.

Table I. Values of the bias (B) and the precision (S_{rT}) required to obtain designated values of accuracy (A) in percentage units[#]

A (%)	B (%)	S_{rt} (%)
5	-3.5	0.945*
5	-2.5	1.559*
5	0.0	2.551*
5	2.5	1.483*
5	3.5	0.881*
10	-7.5	1.643*
10	-5.0	3.200
10	0.0	5.102
10	5.0	2.895*
10	7.5	1.414*
15	-10.0	3.378*
15	-5.0	6.381
15	0.0	7.653
15	5.0	5.774
15	10.0	2.764*
20	-10.0	6.755
20	-5.0	9.448
20	0.0	10.20
20	5.0	8.548
20	10.0	5.527
25	-10.0	10.13
25	-5.0	12.39
25	0.0	12.75
25	5.0	11.21
25	10.0	8.287
30[$]	-15.0[&]	10.73
30[$]	-7.5	14.55
30[$]	0.0	15.31
30[$]	7.5	12.52
30[$]	15.0[&]	7.930
35[$]	-15.0[&]	14.31
35[$]	-7.5	17.59
35[$]	0.0	17.86
35[$]	7.5	15.14
35[$]	15.0[&]	10.57

[#] Note: the values shown in this table are population or theoretical values.

* Below the minimum attainable precision with a 5% pump correction.

[$] Does not fulfill the Accuracy Criterion (±25% of the true value).

[&] Does not fulfill the bias criterion (±10%).

3 Field evaluation

While field evaluation is not required in method evaluation, it does provide a further test of the method, since conditions which exist in the field are difficult to reproduce in the laboratory. Also unknown variables may affect sampling results when field samples are taken. This type of evaluation is recommended to further study the performance of the method in terms of field precision, bias, interferences and the general utility of the method. Both the collection of area samples and personal samples should be included in the field evaluation of the method.

Area samples should provide an estimate of field precision and bias. Personal samples may confirm these values and also provide a means to assess the utility of the method. A statistical study design should be prepared, based on the variability of the method and the statistical precision required for estimates of the differences in analyte concentrations yielded by the independent method and the method under evaluation [CEN 2015].

If this type of statistically designed study is not feasible, a minimum of 20 pairs of samples of the method under study and an independent method should be used for personal sampling. Placement of the samplers on the workers should be random to prevent the biasing of results due to the "handedness" of the worker. Workers sampled should be in areas where both low and high concentrations of the analyte may be present.

As a minimum, sets of 6 area samplers paired with independent methods should be placed in areas of low, intermediate, and high analyte concentration. If the atmosphere sampled is not homogeneous, precautions may have to be taken to ensure that all samplers are exposed to the same concentrations. This can be done by using field exposure chambers, such as those described in the literature [Cassinelli et al. 1985; Kennedy et al. 1985].

Field precision and bias of the area sampler results of the method under study should compare with laboratory evaluation results, provided that precautions have been taken to ensure that all samplers have been exposed to the same homogeneous atmosphere. Differences in precision and bias should be investigated. Sources of variation should be studied and corrections implemented where necessary. Evaluation of personal sampler results should be done cautiously, because observable differences may be due to work practices or other situations which are beyond the control of the method.

A field evaluation of a method also allows the developer of the method to determine its ruggedness. Although this may be a subjective judgement, first-hand experience with the method in the field may suggest changes in the sampler or method that may make the method more easily used in the field and less subject to variability.

4 Documentation

Development and evaluation research on a sampling and analytical method should be documented in a final report. The report should describe what was determined about the method. If the results of the statistical analysis of the data indicate there is not 95% confidence that the accuracy of the method is less than or equal to ±25%, the report should state this fact. In some instances, the method may actually have an accuracy of less than 25%, but a larger sample size must be used to prove this statistically (See Appendix 1 of NIOSH 1995).

The final report can be either a technical report or a failure report. The technical report (acceptable method developed) documents the successful development of the method. This report may be prepared in a format appropriate for submission to a peer-reviewed journal for publication. The failure report (no acceptable method developed) documents the research performed on an attempted method development for an analyte or analytes. The report should describe the failure of the method, as well as other areas of the method research that were successful. Recommendations to solve the failure of the method may be included.

If an acceptable method is developed, a sampling and analytical method should be prepared in appropriate format. The format of the resulting method should provide clear instructions for the use of the method. Sampling, sample workup, and analysis procedures should be clearly described. The necessary equipment and supplies for the method should be listed clearly in the method. A summary of the evaluation of the method should be included, as well as a discussion of method applicability and lists of interferences and related references. As a check on the clarity and performance, new methods should be reviewed and submitted to a user check (i.e., the method is used to analyze spiked or generated samples of known concentration by someone other than the researcher who developed it) and to a collaborative test, if feasible.

5 Appendix - Accuracy and its evaluation

In the development of a sampling and analytical method, one of the goals is to minimize the measurement error to the lowest feasible and practical levels. It is assumed that all feasible corrections to reduce error have been made in the laboratory experimentation process. Method evaluation requires adequate characterization of the magnitude and distribution of the uncorrectable error that cannot be prevented. One might consider a hypothetical experiment in which a method is used repeatedly to measure the same concentration, T, under the same conditions. These measurements would tend to exhibit a pattern or statistical distribution, here assumed to be normal, with a mean, μ, and standard deviation, Š. The distribution can be characterized in terms of two components: its location relative to T, which is the systematic error termed bias (B), is given by (μ-T)/T; and its spread, which is the random error termed imprecision ($\hat{S}_{rT}$), is given by Š/μ. The bias and imprecision are used to determine the inaccuracy of the method but they are also important characteristics of the error in and of themselves, as will be discussed below.

Accuracy refers to the closeness of the measurements to T but it is defined in terms of the discrepancy of the measurements from T. Inaccuracy (I) is defined as the maximum error, regardless of sign, expressed as a percentage of T that occurs with a probability of 0.95. Thus, an inaccuracy (or accuracy) of 20% means that on the average 95 of every 100 measurements will differ from T by no more than 0.2T. The accuracy criterion for single measurements mentioned at the beginning of this chapter, often termed the "NIOSH Accuracy Criterion," requires inaccuracy to be less than or equal to 25%.

Accuracy, bias, and imprecision have the following relationship:

$$0.95 = \varphi((1-B)/((1+B)S_{rT})) - \varphi((-1-B)/((1+B)S_{rT}))$$

where (φ) denotes the probability that a standard normal random variable is less than or equal to φ. A practically exact numerical solution to Equation (1) can be readily programmed using statistical software packages [Press et al. 1986]. A DOS program, ABCV.EXE, is also available which solves for I (denoted by A in the program), $\hat{S}_{rT}$ (denoted by CV in the program), or B when the values for the other two quantities are input. An estimate of I can be obtained in either case by entering estimates of B and $\hat{S}_{rT}$. An approximate solution, which is accurate to about 1.1 percent, is given as follows [NIOSH 1995]:

$$I = 1.57\,(B+1)S_{rT} + \sqrt{((0.39\,(B+1)\cdot S_{rT})^2 + B^2)} \quad \text{for theoretical or true I}$$

$$\hat{I} = 1.57\,(\hat{B}+1)\hat{S}_{rT} + \text{"}\sqrt{((0.39\,(\hat{B}+1)\cdot \hat{S}_{rT})^2 + \hat{B}^2)} \quad \text{for estimates of I}$$

Also, the nomogram in Figure 1 can be used to solve for I or an estimate of I by entering B and S_{rT} or their estimates. Procedures for obtaining "best" single point and 95% confidence interval estimates of B, and S_{rT} and a 90% confidence interval estimate for I are given in NIOSH [1995].

The 90% confidence interval for I can be used to infer whether the method passes or fails the 25% accuracy criterion (AC) for single measurements with 95% confidence as follows:

1) The method passes with 95% confidence if the interval is completely less than 25%.
2) The method fails with 95% confidence if the interval is completely greater than 25%.
3) The evidence is inconclusive if the interval includes 25% (there is not 95% confidence that the AC is true or that it is false).

When researchers interpret the results from analyses of the type described above, it is important to consider that most methods have many uses in addition to individual measurement interpretation. Because accuracy is very important whenever any quantity is to be estimated, the ideal ("other things being equal") is to use the most accurate estimator regardless of its bias or imprecision. However, it is crucial to distinguish between the accuracy of the source or "raw" measurements and that of the final estimator, which might involve many intermediate analyses or operations. Unfortunately, the most accurate input or raw measurements do not always produce the most accurate final result unless the latter is a single measurement. The bias and imprecision of the source measurements can be differentially affected by intermediate operations in producing the final estimate. For example, if the final estimate is a function of a single average of many source measurements, its bias is not affected by the averaging while imprecision is reduced as a function of the square root of the number of measurements. Thus, a lower biased method might be preferable to another even if the inaccuracy of the latter is less. On the other hand, in comparative studies, the desired estimate is either a difference or ratio of means of measurements in which there can be partial or complete cancellation of the bias in the source measurements. Thus, the bias of the method used for the source measurements may be of little importance. If there are several methods applicable for a given user's project (regardless of whether all fulfill the accuracy criterion for single measurements), the analyst would be well-advised to consult with the user (preferably in advance of measurement) to determine which of those methods would produce the optimal accuracy for the final results or estimates needed by that particular user. Accuracy, bias, and imprecision jointly form a complete or sufficient set for the efficient description of the measurement error characteristic of any method.

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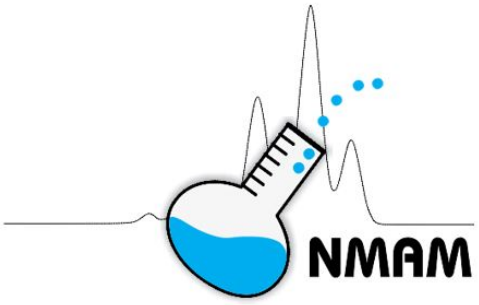

NIOSH Manual of Analytical Methods (NMAM), 5th Edition

Measurement Uncertainty and NIOSH Method Accuracy Range

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1 Introduction

Recently, the ISO Guide to the Expression of Uncertainty in Measurement (GUM) has come close to being universally adopted as the standardized way to characterize and document measurement uncertainty [ISO 2002, 2005, 2009, 2010; Ellison and Williams 2012]. Since the mid-1970s, accuracy criteria have been an integral part of the evaluations of the sampling and analytical methods used by the National Institute for Occupational Safety and Health (NIOSH), the Occupational Safety and Health Administration (OSHA), the Mine Safety and Health Administration (MSHA), and others. NIOSH has previously published extensive discussions addressing the issue of accuracy as a factor in the development, evaluation, and characterization of analytical methodology. Both traditional method accuracy and new measurement uncertainty concepts are intended to communicate measurement limitations to laboratory clients. Naturally, laboratories are interested in how NIOSH accuracy requirements [Busch 1977; NIOSH 1995] relate to measurement uncertainty.

This chapter provides guidance for achieving consistency in determining measurement uncertainty by those laboratories using NIOSH methods. Minor modifications to NIOSH accuracy measures, and an expansion of ISO GUM to cover situations unique to workplace atmospheric measurement can improve consistency and utility. See Bartley [2004] for additional information.

ISO GUM proposes pooling estimated variance components from diverse error sources. The square root of the pooled variance estimate is termed the *combined uncertainty* u_c. Multiplication of u_c by a *coverage factor k* (generally in the range of 2 to 3) results in an *expanded uncertainty U*. The purpose of the expanded uncertainty is for each measurement to provide an interval bracketing the *measurand* (the true value of what is to be measured) to account for errors in both the measurement and the determination of the uncertainty components themselves.

ISO GUM is somewhat unclear about the *coverage factor k*. Furthermore, the coverage factor can be interpreted in several ways. Most straightforward is the limited case where the uncertainty components can be re-evaluated each time the method is used (resulting in *k* proportional to a Student-t quantile). In this case, the covering intervals bracket the *measurand* for (for example) 95% of the measurements.

Alternatively, the coverage factors based on the Student-t quantile specify intervals containing measurand values at levels of evaluation confidence in the *mean* (i.e., averaging over many method evaluations). In other words, for roughly 50% of method evaluations, intervals used at each measurement contain the measurand value greater than (for example) 95% of the time. The concept is consistent with the statistical theory of tolerance or prediction intervals.

This approach is important to industrial hygiene since workplace air concentrations vary spatially and over time to such a degree that a method cannot be evaluated by simply taking replicate measurements [Vaughan et al. 1990]. However, industrial hygiene measurement methods have traditionally required confidence levels greater than 50% in the method evaluation. Generally, 95% confidence in a method validation is required. The different types of confidence levels are reflected simply in the numerical value and interpretation of the coverage factor.

Of equal importance in the industrial hygiene field are details needed to handle systematic error (*bias*) relative to reference concentration measurements found during method evaluation. For example, the sampling rate of a given diffusive sampler for gases or vapors is generally measured once by the diffusive sampler manufacturer prior to use by multiple clients. As the samplers are not re-calibrated for each use, residual *bias* exists in the measurements due to uncertainty in sampling rates used [ASTM 2013a]. (NIOSH methods typically do not cite performance for passive samplers because agreement among diffusive monitor manufacturers on test protocols has not yet been achieved, and a system of third party evaluation of diffusive monitor manufacturers sampling rates is not available.) Similarly, the calculation of desorption efficiencies may be performed only once or infrequently and can, therefore, introduce residual *bias* in measurements that use sorbent-captured samples, e.g., charcoal tubes.

In aerosol sampling, detailed knowledge of the particle size-dependent *bias* of a sampler relative to a sampling convention, such as adopted by ISO/CEN/ACGIH/ASTM [ISO 1995; CEN 1993; ACGIH 2015; ASTM 2013b] for defining respirable dust, is often necessary to judge the usefulness of a given sampler. Each type of aerosol sampler is characterized by specific particle collection characteristics, and some analytical methods (e.g. silica) may also exhibit particle size effects. Typically the issue of aerosol sampler *bias* is avoided or minimized in the industrial hygiene field by narrowing use to a specific aerosol sampler. For example, common industrial hygiene practice establishes a single sampler type, such as the 1.7 L/min 10-mm nylon Dorr-Oliver cyclone, for respirable dust sampling in a particular application.

Sensitivity to other environmental factors, referred to in ISO GUM as *influence variables*, must be acknowledged. Suppose a sampler is sensitive to temperature changes that are impractical to measure in the field; i.e., sampler estimates are not temperature corrected. Then, suppose during method evaluation in the laboratory, measurement of this sensitivity is combined with knowledge of the expected temperature variation for a given field application. Putting together both would determine the uncertainty associated with the effect. Examples of the important effects of influence variables - such as wind velocity, temperature, pressure, and fluctuating workplace concentrations - on diffusive monitor uptake rates are common.

2 ISO GUM

ISO GUM presents several concepts. One of these calls for the identification of sources (labeled j = 1, 2,...) of uncertainty u_j (standard deviation estimate components) in a measurement method and for their classification into Type A or Type B uncertainties. Type A uncertainty is one that has been characterized by a statistically sound approach. In this case, u_j^2 is given by s_j^2, an unbiased estimate (with v_j degrees of freedom) of variance σ_j^2. On the contrary, Type B uncertainty generally requires professional judgment. See Table 1 for examples of possible uncertainty components.

A common example of Type B uncertainty is the conservative assignment of a 5% relative standard deviation component (without error, i.e., with infinite degrees of freedom) as the random sampling pump uncertainty. As described in ISO GUM, such an assignment would be a result of sampling pump random errors that had a uniform distribution and fell within $\pm\sqrt{3} \times 5\%$ of zero with a probability "for all practical purposes equal to one". Therefore, if it is judged that sampling pump variations are *within* these bounds, then the assignment of 5% as the relative standard deviation component is conservative. Other similar ways of handling Type B uncertainties are found in ISO GUM.

Table 1. Examples of potential uncertainty component sources.

Sampling
personal sampling pump flow rate: setting the pump and subsequent drift sampling rate of diffusive sampler
sampler dimension (aerosol and diffusive sampling)
Sample handling
sample preparation (e.g., handling silica quasi-suspensions) sample loss during transport or storage
Analytical
aerosol weighing
recovery (e.g, GC-based methods)
Poisson counting (e.g., in XRD methods)
Sensor variation
operator effects giving inter-lab differences (if data from several labs are to be used)

Evaluation
- calibration material uncertainty
- evaluation chamber concentration uncertainty
- other bias-correction uncertainty

Environmental influence parameters
- temperature (inadequacy of correction, if correction is made as with diffusive samplers)
- atmospheric pressure
- humidity
- aerosol size distribution (if not measured by a given aerosol sampling method)
- ambient wind velocity
- sampled concentration magnitude itself (e.g., sorbent loading)

Within the field of industrial hygiene, the quantities u_j are often standard deviation component estimates obtained from a *single* measurement-method evaluation, rather than from replicates. When the estimates are independent, a *combined uncertainty* u_c may be computed (through the propagation of uncertainty approximation) as:

$$u_c = \sqrt{u_1^2 + u_2^2 + \cdots} \qquad (1)$$

Through a *coverage factor k*, generally approximated conservatively (e.g., see *Technical Note 2* at end of chapter), as equal to 3 for a single method evaluation, an *expanded uncertainty U* may be computed as:

$$U = k \times u_c \qquad (2)$$

The purpose of the expanded uncertainty *U* is to provide intervals, which generally contain measurand values (often referred to as the *true* values). In particular, given a concentration estimate $\hat{c}$ (hats, as here, indicate estimates), the measurand value *C* is bracketed at better than 95% confidence by intervals of the type:

$$\hat{c} - U < C < \hat{c} + U \qquad (3)$$

at 95% confidence in the method evaluation. The coverage factor *k* is intended to account for both (1) the fluctuation of the measurement about the measurand value and (2) the uncertainty in the assessment of this fluctuation.

Note: Requiring only mean confidence in the evaluation leads to *k* given in terms of a *Student-t* quantile. Here, however, in fixing the method evaluation confidence (e.g., at 95%), the *chi-*

square distribution takes the place of the Student-t distribution. Double confidence levels (in the measurement and evaluation) directly relate to a well-developed [Bartley 2001; Bartley and Irwin 2002; Hald 1952; Wald 1942, 1943; Wald and Wolfowitz 1946; Wilks 1941, 1942; Aitchison and Dunsmore 1975] statistical theory of *tolerance* or *prediction intervals*. Another point of ISO GUM is semantic. *Uncertainty*, as in common usage, covers only what is *unknown* about a measurement. The *known* but uncorrected systematic deviation or *bias* relative to reference concentrations does not enter into measurement uncertainty.

A related concept, *accuracy*, is defined qualitatively within ISO GUM as the "closeness of agreement between the result of a measurement and a true value of the measurand". Accuracy can have both random and systematic components. It is not surprising then that if a *bias* correction is made and if accuracy is quantified reasonably, the expanded uncertainty and an accuracy confidence limit can be equivalent.

As mentioned above, another aspect of ISO GUM deals with *influence factors*. If measurement results are expected to be sensitive to an environmental factor (e.g., ambient temperature), then the effect of such a factor on the measurement method must be measured in the laboratory. Given estimates of the environmental variations expected during method application, influence components of the combined uncertainty can be estimated for inclusion in the uncertainty budget of Eq. 1. Table 1 lists several *influence factors*, which may or may not be significant.

3 The symmetric accuracy range A as used by NIOSH

a. Definition and its approximation

The *symmetric accuracy range A* is defined as the fractional range, symmetric about the true concentration *C*, within which 95% of sampler measurements $\hat{c}$ are to be found. Another way of saying this is:

$$C\ x\ (1 - A) < \hat{c} < C\ x\ (1 + A) \quad \text{for 95\% of measurements } \hat{c} \quad (4)$$

It is clear from this simple definition that the accuracy range function *A* must increase with both random effects and *bias* magnitude and therefore, is one means of quantifying accuracy as defined above according to ISO GUM.

More specifically, suppose that estimates $\hat{c}$ are normally distributed about population mean *c* with standard deviation σ. Then we may characterize random measurement effects

in terms of the (true) relative standard deviation *TRSD* and *bias* of the mean concentration estimate *c* relative to the true concentration *C* as:

$$bias = \frac{c - C}{C}$$
$$TRSD = \frac{\sigma}{c}. \qquad (5)$$

The descriptive definition of Eq. 4 implies that the symmetric accuracy range *A* increases with both *TRSD* and *bias* magnitude |*bias*|. This feature can be seen directly in the following close approximation to the accuracy range function *A*, which follows [See Bartley 2001; Bartley and Irwin 2002 for derivation] from the definition in Eq. 4:

$$A = 1.960\ x\ \sqrt{bias^2 + TRSD^2}, if\ |bias| < \frac{TRSD}{1.645};$$
$$A = |bias| + 1.645\ \times TRSD, otherwise. \qquad (6)$$

This expression is simple enough for calculation by most hand-held calculators, and it is also a useful starting point for estimating the 95% confidence limit $A_{95\%}$ on the accuracy range as measured during a method evaluation, accounting for evaluation errors.

b. Uses of the symmetric accuracy range

1) Method validation

One application of the symmetric accuracy range is for evaluating measurement methods. As mentioned in NMAM guidance chapters, a method evaluation consists of a number of measurements taken from replicate samplers at each of several controlled and known concentrations covering the range of expected method application. This type of experiment gives information about the samplers' random errors and also the *bias* relative to reference concentrations. A confidence limit on the accuracy range can then be computed. One objective in a method suitable for NIOSH application is that the 95% confidence limit $A_{95\%}$ not exceed 25%. A includes both the uncertainty (as the term is used by ISO GUM) and the systematic deviation or *bias*, so that correction of the *bias* by the sampler vendor or developer is encouraged by the very statement of this objective. See Eqs. 9-11 below for computing $A_{95\%}$ when *bias* is negligible.

2) Measurement uncertainty

Suppose then that *bias* correction has been made. For example, suppose that following evaluation, the sampler is used for future measurement with *bias* corrected on the basis of its measurement during the evaluation itself. Then computation of the confidence

limit $A_{95\%}$ is possible accounting for the residual *bias* which is uncorrectable due to evaluation limitations, but nevertheless will be present in all future measurements. The quantity $\hat{c}$ x $A_{95\%}$ forms the counterpart to the expanded uncertainty U of ISO GUM for specifying evaluation confidence at 95%.

The relationship between $\hat{c}$ x $A_{95\%}$ (with corrected *bias*) and *expanded uncertainty U* can be seen most clearly in the case that $A_{95\%}$ is significantly smaller than 100%. In this case, Eq. 4 can be rewritten as the approximation:

$$\hat{c} - \hat{c} \times A_{95\%} < C < \hat{c} + \hat{c} \times A_{95\%}, \qquad (7)$$

which means that at 95% confidence in the method evaluation, the inequality bracketing the measurand value C holds at probability > 95%. A study using 10,000-point simulations indicates that $A_{95\%}$ can be as large as 25%, with method evaluation confidence close to 95% using the approximation of Eq. 7. As can be seen directly, Eq. 7 is the analogue to Eq. 3 when $\hat{c}$ x $A_{95\%}$ is adopted as the *expanded uncertainty U*:

$$U = \hat{c} \times A_{95\%}. \qquad (8)$$

In the case that *bias* is known to equal zero (*Technical Note 1* at the end of this chapter), $A_{95\%}$ (at 15 degrees of freedom in the evaluation experiment) is simply:

$$A_{95\%} = 2.8 \times T\hat{R}SD. \qquad (9)$$

Eq. 8 then gives:

$$U = 2.8 \times T\hat{R}SD \times \hat{c}$$
$$U = 2.8 \times u_c\,. \qquad (10)$$

Therefore, the coverage factor k is

$$k = 2.8, \qquad (11)$$

consistent with the use of $k = 3$ as a conservative but not excessive value.

The user of a method then may report the expanded uncertainty U in a concentration Estimate $\hat{c}$ using Eq. 8, knowing the accuracy range confidence limit $A_{95\%}$ as reported in the method. Of course, this approach relies on the sense of double confidence—in the evaluation and also in the subsequent application.

Note: The European Assessment of Workplace Exposures Technical Committee, CEN TC 137, has adopted a similar viewpoint regarding method performance [CEN 2015]. In this case, an *overall uncertainty*, defined as $|bias| + 2 \times RSD$, is used to quantify accuracy. When compared to Eq. 6, the overall uncertainty can be regarded as an approximation to the symmetric accuracy range.

4 Uncertainty and analytical lab procedures

Interest in measurement uncertainty and ISO GUM is currently finding its way into the criteria for the accreditation of analytical labs [ISO 2005]. The result will no doubt be high confidence in understanding one component of the combined or expanded uncertainty—namely the analytical component. Several general approaches to controlling and characterizing analytical uncertainty in routine lab practices seem reasonable.

a. Validated method adoption

One possibility is for a lab to adopt a published, evaluated method. Such an adoption would require an initial establishment of the method within the lab's capabilities. Equivalence to the published method would be established during this initial phase. Thereafter, the method's uncertainty as documented in the original publication would be claimed for the lab results. Ongoing analysis of a limited number of quality control samples would provide evidence that the method as implemented in the lab remains stable.

An example of this approach is the current practice in some labs that handle sorbent tubes to analyze about 4 lab blanks per set of field samples analyzed. The variability in the blank results are then continually compared to past lab performance so as to detect problems which may occur in analysis. Though the small number of degrees of freedom (= 3) does not give a tight figure on the uncertainty, it nevertheless gives assurance that the method is stable.

As a specific example of method evaluation data and documentation of an uncertainty budget, data from $n = 16$ exposures of diffusive samplers in a controlled environment are shown in Table 2. The evaluation is somewhat simplified for this example; a more comprehensive evaluation would also measure effects of wind velocity, humidity, temperature, and concentration time-dependence (potentially significant to diffusive monitoring). Analysis of these data can be handled by an ordinary calculator capable of computing means and standard deviations.

Note that the uncertainty ($T\hat{R}SD/\sqrt{n}$, where n = 16 is the number of measurements) in the *bias* is the value that accounts for residual *bias* due to imperfect correction. Very similarly, the uncertainty in the reference concentration is pooled to arrive at a combined uncertainty. Interestingly, neither of these two contributions corresponds to quantities that vary during sampler application subsequent to its initial evaluation. The background for documenting residual (uncorrectable) *bias* can be seen in *Technical Note 2* at the end of this chapter.

Table 2. Example of method evaluation and uncertainty budget

Evaluation of experimental results

The following are results from a simplified evaluation of a specific diffusive sampler for o-xylene. There were four experimental runs with four samplers each. The reference concentration set within the exposure chamber is denoted as $\hat{C}$ having an assigned (Type B) relative uncertainty = 1%.

Run	$\hat{C}$ **(ppm)**	**replicates (ppm)**	$\Rightarrow T\hat{R}SD_{inter}[s/\hat{C}]$	***biâs***
1	123	139.2	2.6%	14.0%
		138.2		
		138.6		
		145		
2	101.1	108.3	1.8%	9.2%
		110		
		110.7		
		112.8		
3	12.7	14.2	7.9%	12.2%
		15.3		
		12.9		
		14.6		
4	91.3	109	2.1%	17.8%
		109.2		
		107.1		
		105		

Averaging the above *bias* estimates and pooling the inter-sampler estimates $T\hat{R}SD^2_{inter}$ results in: Mean *bias* estimate: *biâs* = 13.3% from average of 4 × 4 = 16 data points. The *TRSD* estimate is $T\hat{R}SD_{inter} = 4.4\%$ having 4 × 3 = 12 degrees of freedom.

Table 2. Continued

Uncertainty budget

The following includes *bias* correction by dividing future concentration estimates by (1 + biâs) as in *Technical Note 2*.

Source	*Component*	*Category*
Inter-sampler	3.9% [= 4.4% / (1+.133)]	Type A
Bias Correction Uncertainty	0.97% [= 3.9%/√16]	Type A
Ref Concentration Uncertainty	0.5% [1%/√4, but not /(1 + *biâs*)]	Type B
Combined (Relative) Uncertainty	$u_c = \sqrt{3.9\%^2 + 0.97\%^2 + 0.5\%^2} =$	4.0%
Expanded (Relative) Uncertainty	$U = k \times u_c = 12.1\%\ (k = 3).$	

Notes: Here k = 3.0. A more accurate determination based on the chi-square quantile at 12 degrees of freedom and prob = 0.05, gives k = 2.97, which is consistent with conventional use of 3 as a conservative value.

Again, an expanded (relative) uncertainty U means that with greater than 95% of future *bias*- corrected estimates $\hat{c}$, true concentrations C are bracketed by:

$$\hat{c}\ x\ (1 - U) < C < \hat{c}\ x\ (1 + U),$$

at 95% confidence in the above evaluation experiment. Generally, a quality control program is required to ensure that the method remains stable following evaluation.

Note that many methods (e.g., those based on sorbent tubes) employ personal sampling pumps, in which case normally a 5% (Type B) component representing sampling pump uncertainty would be included in the uncertainty budget.

Note also that the inter-sampler component includes both analytical and sampling sub-components. Further refinement of the inter-sampler component may perhaps be useful for improving a method, but is not needed for establishing confidence intervals around (true) measurand values.

Note further that storage effects require estimating and inclusion in the budget if considered significant.

b. Pooled quality control results

Another approach utilizes a large number (e.g., 50) of the most recent quality control sample results. By pooling uncertainty values, a running method evaluation can be

effected. The result is (1) a direct measure of the analytical uncertainty of the method as implemented in the lab, and (2) a means of detecting any problems that may creep into a method during routine use. Note that a running uncertainty average is similar to a partial method evaluation and not to a method re-evaluation at each measurement because consecutive running averages are strongly correlated.

This approach is adopted within a current MSHA procedure for the analysis of silica. A sampling filter is dissolved and re-deposited onto an analysis filter where the silica is quantified by infrared absorption. From each batch of samples to be analyzed, an analysis filter is retained for re-dissolution, re-deposition, and re-analysis within a subsequent batch. The result is a large number of pairs of nearly identical samples, which can give a running estimate of the method's analytical uncertainty.

c. Continual method re-evaluation

A third possibility, the closest to the original measurement approach of GUM uses a large number (e.g., 30) of *independent control* samples for each application measurement. This is the most expensive approach, but also may give the best estimate of the analytical uncertainty, especially in cases where uncertainties may be measurement-dependent. Because many more evaluative measurements per application measurement are needed, this approach is not easily implemented for most industrial hygiene applications.

As an example of this approach [ISO 2002], suppose that a lab estimates only a 30-day average concentration of a given gas or vapor. Further, every day a measurement is taken of a known calibration gas concentration. Then, if the method is expected to behave similarly for measurements of gas and field samples calibrations, the 30 control samples give analytical uncertainty estimates that differ month-to-month and from field measurement to field measurement.

d. Limit of detection and detection limit

When the concentration is low, approaching the method uncertainty u_c, concepts of the limit of detection (*LOD*) and a related detection limit L_D may be useful. *LOD* is used for controlling false positives when asserting the presence of a substance. On the other hand, the detection limit specifies what measurand value (e.g., concentration) is required so that the false negative rate is negligible when the substance is actually present. The limits can refer to the analytical measurement only or, as in this section, to the entire sampling and analytical measurement method.

In the following examples, several often realistic assumptions are made. The standard deviation in concentration estimates is assumed constant (i.e., independent of the sampled

concentration), unlike the commonly occurring constant *relative* standard deviation at larger concentrations. Also, *bias* (or uncertainty in its correction) is assumed to be negligible. More complicated cases generally have specific difficulties that are best be approached by a statistician.

With these assumptions, in terms of the combined uncertainty u_c the limit of detection is traditionally [Keith et al. 1983; Currie 1997] taken to be:

$$LOD = 3 \times u_c\,, \qquad (12)$$

and the detection limit may be defined as

$$L_D = 2\,x\,LOD. \qquad (13)$$

Note that u_c includes the uncertainty associated with correction, if any, with blank subtractions. See ISO [2009] for a detailed example.

After *LOD* and L_D have been determined for a method they may be used as follows. A substance may be asserted as present if an estimate $\hat{x}$ exceeds *LOD*. Moreover, if unknown (true) concentration *X* exceeds L_D, an estimate $\hat{x}$ is likely to exceed *LOD*. Given the above definitions and assumptions, the false positive rate *r* on asserting presence is closely equal to the non-detection rate.

Note: If the combined uncertainty u_c is determined from a method evaluation providing an effective number υ (as in *Technical Note 2*) degrees of freedom, then at 95% confidence in the method evaluation, the false positive rate *r* is limited by:

$$r < 1 - \phi\left[3 \times \sqrt{\frac{\chi^2_{0.05,\upsilon}}{\upsilon}}\right], \qquad (14)$$

where ϕ is the cumulative normal function. For example, if υ=15, then *r* < 3.5%.

5 Discussion

The approach presented here to document method accuracy range and uncertainty relates to the statistical theory [Bartley 2001; Wald and Wolfowitz 1946; Wilks 1941, 1942; Aitchison and Dunsmore 1975; CEN 2015; Smith 1936; Saterthwaite 1946] of *tolerance* or *prediction intervals*. This theory was originally developed in simplified form to predict the range of future measurements of a normally distributed random variable on the basis of *n* initial

measurements. The *initial measurements* are analogous to the method evaluation, whereas the *future measurements* represent method application subsequent to evaluation.

Because of measurement cost, workplace assessments cannot at present be conducted in such a way that continual re-evaluation is done at each measurement. The prediction interval approach given here shows a less costly way to document measurement uncertainty in those cases where a method has been initially evaluated and then used many times without re-evaluation. The approach closely follows ISO GUM. Of course, for such an approach to actually make sense, an adequate quality control program must be instituted so that the measurement method remains stable during the time of its application following evaluation.

Several generalizations and variations of the material presented in this chapter are possible. The relative standard deviation and relative *bias* sometimes depend on the concentration sampled in a complicated way, requiring special attention. See, for example Currie [1997]. Also, asymmetric confidence intervals are sometimes required. Single-sided intervals are useful in some instances, e.g., alarm systems, as well as in quantifying limits of detection or quantitation, described briefly above. Ways to handle environmental influence parameters may also be complicated. See, for example ASTM [2013a]. In any case, despite the complexities possible, the examples given in this chapter may help to characterize method uncertainty in a reasonable manner. For additional examples and explanations, see Appendices A and D of Components for Evaluation of Direct-Reading Monitors for Gases and Vapors [NIOSH 2012] and ASTM standards on accuracy and uncertainty [ASTM 2014, 2015].

6 Technical notes

a. Note 1: Example of accuracy range confidence limit:

Suppose it is known that the *bias* is zero. For example, an exposure standard may be set that specifies a given sampling and analytical method. In this case, the hazardous concentration may be said to be *operationally defined*. Operationally defined methods include NIOSH Methods 7400 and NIOSH 5040.

If the *bias* is zero, Eq. 6 simplifies to:

$$A = 1.960\ x\ TRSD.$$

Furthermore, if the relative standard deviation is estimated as $\hat{TRSD}$ with υ degrees of freedom (computed using the Smith-Satterthwaite approximation [ISO 2010; Hald 1952;

Wald 1942] if *TRSD* has more than one component), then the 95% confidence limit on *TRSD* is:

$$TRSD_{95\%} = \hat{TRSD} \times \sqrt{\frac{\upsilon}{\chi^2_{\upsilon,0.05}}},$$

where $\chi^2_{\upsilon,0.05}$ is a 5% quantile value for the chi-square distribution, which can be read from a table in most elementary statistics texts. This determines the 95% confidence limit on the accuracy range itself as:

$$A_{95\%} = \hat{A} \times \sqrt{\frac{\upsilon}{\chi^2_{\upsilon,0.05}}}.$$

If $\upsilon = 15$, $\sqrt{\frac{\upsilon}{\chi^2_{\upsilon,0.05}}}$ giving coverage factor k = 2.8 (Eq. 11).

Note that $TRSD_{95\%}$ can be interpreted as a conservative estimate of *TRSD* and therefore can be treated as a Type B uncertainty with infinite number of degrees of freedom as described following Table 1.

b. Note 2: Single-evaluation correction of *bias*:

Details are given here illustrating the tolerance interval approach, *bias* correction, imprecise reference concentrations, and the use of the symmetric accuracy range function. The derivation is not entirely general, but is given here for guidance in handling the myriad possibilities in measurement uncertainty. Though the derivation is slightly complicated, the result obtained is simple.

Suppose that estimates $\hat{c}$ having an as-yet-unknown constant *bias* relative to true concentrations *C* (not necessarily constant) may be modeled as:

$$\hat{c} = C \cdot [1 + bias + \hat{\varepsilon}],$$

where the random variable $\hat{\varepsilon}$ is approximately normally distributed about zero with variance $TRSD^2$. For evaluating the method, assume that reference concentration measurements $\hat{C}$ can be made simultaneously and modeled by:

$$\hat{C} = C \cdot [1 + \hat{\varepsilon}_{ref}],$$

where $\hat{\varepsilon}_{ref}$ has variance $TRSD_{ref}^2$ assumed known accurately. Measure n values of the ratio $\widehat{\theta}$:

$$\hat{\theta} \equiv \frac{\hat{c}}{\hat{c}} = 1 + bias + \hat{\varepsilon}_c$$

and compute estimates $bi\hat{a}s$ and $T\hat{R}SD_c^2$ at $\upsilon = n-1$ degrees of freedom, where the approximately normally distributed random variable $\hat{\varepsilon}_c$ has variance $T\hat{R}SD_c^2$ given by:

$$TRSD_c^2 = TRSD^2 + (1 + bi\hat{a}s)^2 x\, TRSD_{ref}^2$$

(to the order of *TRSD*, neglecting Cauchy effects of reciprocals of random variables).

Future *bias*-corrected measurements $\hat{x}'$ of unknown concentration X can be defined in terms of raw measured values $\hat{x}$ as:

$$\widehat{x'} \equiv \frac{\hat{x}}{1+bi\hat{a}s}.$$

The residual corrected *bias′* is then given by:

$$bias' = \frac{bias - bi\hat{a}s}{1+bi\hat{a}s}$$

If n is large enough, $|bias'|$ will be small enough that the corrected symmetric accuracy range A' can be accurately approximated (Eq. 6) as:

$$A'^2 = \frac{a^2 1.960^2}{(1+bi\hat{a}s)^2},$$

where the unknown a^2 is:

$$a^2 = (bias - bi\hat{a}s)^2 + TRSD^2,$$

whose confidence limit is now required.

First note that the expected value of the first term is:

$$E[(bias - bi\hat{a}s)^2] = \frac{TRSD_c^2}{n}.$$

Therefore, an estimate $\hat{a}^2$ for a^2 can be constructed as:

$$\hat{a}^2 \equiv \frac{T\hat{R}SD_c^2}{n} + T\hat{R}SD^2$$

$$T\hat{R}SD^2 \equiv T\hat{R}SD_c^2 - (1 + bi\hat{a}s)^2 \; x \; TRSD_{ref}^2 .$$

Expressed in terms of $T\hat{R}SD^2, \hat{a}^2$ is:

$$\hat{a}^2 = T\hat{R}SD^2$$

$$+\frac{1}{n}T\hat{R}SD^2$$

$$+\frac{1}{n} \cdot (1 + bi\hat{a}s)^2 \; x \; TRSD_{ref}^2 .$$

Each term can now be identified, forming the basis for an uncertainty budget: the first is the (uncorrected) method uncertainty (squared); the second and third reflect the *bias*-correction uncertainty owing to finiteness of the validation experiment and the uncertainty in the reference concentration (as here measured n times).

A confidence limit a_β^2 at confidence level β (e.g., 95%) on a^2 is now constructed using $\hat{a}^2$:

$$a_\beta^2 = K^2 \cdot \hat{a}^2,$$

where the constant K is to be determined so that

$$prob\{a_\beta^2 < a^2\} = 1 - \beta.$$

First of all, the distribution of $\hat{a}^2$ is approximated as chi-square:

$$\upsilon_{eff} \frac{\hat{a}^2}{E[\hat{a}^2]} \approx \chi^2 ,$$

where υ_{eff} is determined as with the Smith-Satterthwaite [Keith et al. 1983; Currie 1997] approximation, forcing variances to agree; often $\upsilon_{eff} \approx n - 1$.
Now,

$$a_\beta^2 < a^2 \Leftrightarrow \hat{a}^2 < K^{-2}a^2,$$

or, in other words:

$$\chi^2 < \frac{\upsilon_{eff}(K^{-2}a^2)}{E[a^2]}.$$

[Note that, $E[\hat{a}^2] = E[a^2], but \neq a^2$unlike *Technical Note 3*.]

Remembering that a^2 depends on the estimate $bi\hat{a}s$, K is given as a solution of the following integral equation:

$$1-\beta = \int_{-\infty}^{+\infty} dbi\hat{a}s\, P[bi\hat{a}s] \int_0^{\upsilon_{eff}\cdot K^{-2}\cdot a^{-2}/E[a^2]} d\chi^2 P_{\upsilon_{eff}}[\chi^2]$$

$$= \int_0^{\upsilon_{eff}\cdot K^{-2}} d\chi^2 P_{\upsilon_{eff}}[\chi^2] \times (1 + O[1/n^2]),$$

where the correction $O[1/n^2]$ is easily proved by expanding the integrand about $TRSD_c^2$ in$(bi\hat{a}s - bias)^2$. Therefore, the following simple asymptotic expression for K^2 results:

$$K^2 \approx \frac{\upsilon_{eff}}{\chi^2_{1-\beta,\upsilon_{eff}}}.$$

Thus, the coverage factor k is approximated as:

$$k \approx 1.960 \cdot \sqrt{\frac{\upsilon_{eff}}{\chi^2_{1-\beta,\upsilon_{eff}}}},$$

which is less than and close to 3.0, if the effective number of degrees of freedom υ_{eff}≥12, and β=0.95.

In summary, the *bias* uncertainty is pooled together with the uncertainty components in $T\hat{R}SD^2$. It should be remembered, however, that only $T\hat{R}SD$ refers to quantities, which vary at each of the future measurements following the initial evaluation.

c. Note 3: Characterizing effects of uncorrected *bias*:

If the systematic error (*bias*) is non-zero, confidence limits on the accuracy range A may be approximated as follows. The Smith-Satterthwaite approximation is generalized in approximating estimates $\hat{A}$ in terms of a chi-square random variable χ^2_υ for the two cases in Eq 6 by:

$$\frac{\hat{A}}{A} = \sqrt{\frac{\chi^2_\upsilon}{\upsilon}}, if |bias| < \frac{RSD}{1.645};$$

$$\frac{\hat{A}}{A} = \frac{\chi^2_\upsilon}{\upsilon}, otherwise$$

The effective number of degrees of freedom υ is determined by forcing the variance of χ_υ^2 to reproduce the estimated variance of $\hat{A}^2$ or $\hat{A}$ in their respective cases:

$$\upsilon = \frac{2A^4}{var[\hat{A}^2]}, if\ |bias| < \frac{RSD}{1.645};$$

$$\upsilon = \frac{2A^2}{var[\hat{A}]}, otherwise$$

Calculation of $var\left[\hat{A}^2\right]\ or\ var\left[\hat{A}\right]$ is generally straightforward and depends on specifics of the evaluation experiment and on significant influence parameters. The confidence limit $A_{95\%}$ is then determined as in Eq 9:

$$A_{95\%} = \hat{A} \times \sqrt{\frac{\upsilon}{\chi^2_{0.05,\upsilon}}}, if\ |bias| < \frac{RSD}{1.645};$$

$$A_{95\%} = \hat{A} \times \frac{\upsilon}{\chi^2_{0.05,\upsilon}}, otherwise$$

This expression has been found [Bartley and Irwin 2002] quite accurate, exhibiting negligible effects from the discontinuity: The chi-square approximation is expected to be worst when $|bias|$is large relative to *TRSD*. As an example, suppose the uncertainty has the following components: 5% from pump error and also a 5% analytical relative standard deviation. Suppose *bias* = 20%. Suppose *bias* and the analytical uncertainty are measured with υ = 15 degrees of freedom. Then 10,000-point simulations indicate that the calculated $A_{95\%}$ is slightly conservative, giving 96% confidence.

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8 Terminology

A — *symmetric accuracy range*, relative (%) range of 95% of a method's measurements about the (true) measurand

$A_{95\%}$ — 95% confidence limit on the symmetric accuracy range

bias — mean concentration estimate *bias* relative to the (true) measurand

biâs — bias estimate

$\hat{c}$ — concentration estimate

C— true concentration

$\hat{C}$ — reference concentration (estimate)

k — *coverage factor*, a constant containing confidence information for obtaining the expanded uncertainty U as a factor of the combined uncertainty u_c

L_D— *detection limit* (for controlling false negatives)

LOD — *limit of detection* (for controlling false positives)

n — number of measurements in a method evaluation

s_j^2 — unbiased estimate of variance σ_j^2

σ_j^2 — jth population variance component

TRSD— (true) relative standard deviation

u_j — jth *uncertainty* component, an estimated standard deviation

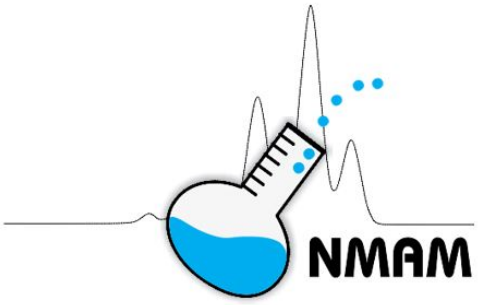
u_c— *combined uncertainty*, pooled uncertainty components

U— *expanded uncertainty*, a value giving intervals bracketing the (true) measurand at given confidence in the measurement and method evaluation

U_j— degrees of freedom in an estimate

$\chi^2_{\upsilon,0.05}$ — chi-square quantile. This quantity by definition exceeds the chi-square variable at probability = 5%. Note that many tables use the notation $\chi^2_{\upsilon,0.05}$ for this quantity.

In general, hats represent estimates. Primes indicate bias-corrected quantities.



NIOSH Manual of Analytical Methods (NMAM), 5th Edition

General Considerations for Sampling Airborne Contaminants

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1 Choosing measurement methods and sampling media

In choosing methods for sampling of chemical and biological agents related to occupational exposures, thorough advance planning is required. Proper planning minimizes sampling and measurement costs while enabling the collection of high-quality data. Many criteria must be considered before collecting field samples from workplaces [ASTM International 2014]. The first step is to define the sampling objectives. These may include: a) documenting exposures in particular work settings; b) assessing compliance/non-compliance with existing regulatory or recommended occupational exposure limits (OELs); and/or c) determining sources of airborne contaminants. Sampling parameters that should be considered might include: a) type of sample (area vs. personal); b) contaminant(s) to be sampled; c) physical nature of airborne sample (vapor and/or aerosol); d) duration of sample collection; e) potential interferences; and f) estimated contaminant concentrations. Once these parameters are established, the suitable analytical method(s) and sampling media can be selected. For instance, when sampling for aerosols, the relevant particle size fraction to be sampled must be taken into account. Other general information needed to properly plan a sampling campaign include: a) the number of employees; b) the sampling strategy plan (discussed later); c) process flow diagram; d) safety data sheets on all process materials; and e) potential hazards involved in collecting and shipping field samples.

An accredited analytical laboratory should be used to conduct analysis of collected samples, and it is essential to consult with the analytical laboratory before sampling to ensure that the measurement methods available can meet the defined measurement needs. Consultation with the laboratory should be an early part of survey planning. The laboratory can also assist in choosing sampling media that are compatible with the sampling needs and the measurement methods available. The APPLICABILITY sections of the individual methods in NMAM can be helpful in choosing which of the available methods is best for a particular situation. Apart from NIOSH methods, methods from other organizations such as OSHA, ASTM International and ISO may be appropriate [Ashley 2015].

Whether through consultation with the laboratory or as cited in the relevant measurement method, the sampling media will be specifically identified. Methods will specify parameters such as: a) pore size and type of filter (for aerosol collection); b) concentration and amount of liquid media required (e.g., for impinger sampling or impregnation of filters); and c) type and amount of solid sorbent (for collection of gases / vapors); see below for common types and characteristics of various sampling media.

The physical state(s) of the contaminant(s) being sampled may also be a factor in determining the media required. In the case of polyaromatic hydrocarbons (PAHs), for example, the correct sampler consists of a membrane filter to collect particulate matter and a solid sorbent tube to trap the vapors of certain PAHs so that total collection is assured. Also, for sampling of gases and vapors, it is generally necessary to mount a prefilter in front of the gas/vapor collection media in order to trap aerosols that might otherwise interfere with subsequent analysis of target analytes.

The sampling pump used to collect the sample must also be compatible with the sampling needs and the media used. Specifically, the pump must be capable of maintaining the desired flow rate over the time period needed using the sampling media specified. Some pumps may not be able to handle the large pressure drop of the media. This may be the case for fine mesh solid sorbent tubes, small pore size filters or when attempting to take a short-term sample on a sorbent tube of a higher than normal pressure drop at higher flow rates. As a rule of thumb, higher-flow pumps (>1 L/min) can handle at least 3 kPa pressure drop at 1 L/min for 8 h. Some pumps can handle up to 7.5 kPa pressure drop at flows up to 5 L/min. Most low flow pumps (0.01 to 0.2 L/min) can handle the pressure drops of available sorbent tubes without problems, except that the nominal flow rate may decrease for certain models. All pumps should be calibrated with representative sampling media prior to use. It is good practice to check the pump calibration before and after use each day. As a minimum, calibration should be done before and after each use.

2 Types and uses of solid sorbents* [Melcher 1987]

a. Activated charcoal

By far the most commonly used solid sorbent is activated charcoal. This sampling medium is characterized by a very large surface area to weight ratio. It has a reactive surface and high adsorptive capacity. This surface reactivity means that activated charcoal is not useful for sampling reactive compounds (e.g., mercaptans, aldehydes) because of poor desorption efficiency. The high capacity, however, makes it the sorbent of choice for those compounds that are stable enough to be collected and recovered in high yield. Breakthrough capacity is a function of type (source) of the charcoal, its particle size and packing configuration in the sorbent bed. Humidity may affect the adsorption characteristics as well.

*NOTE: Solid sorbents are used for the collection of vapors only. Aerosols are notcollected effectively by most sorbent beds, but may be collected by other components of the sampler (e.g., a prefilter).

b. Silica gel

Silica gel is less reactive than charcoal. In part because of its polar nature, coated silica gel has been shown to be effective for sampling airborne ketones and aldehydes [Tejada 1986; García-Alonzo and Pérez-Pastor 1998].

c. Porous polymers

Porous polymers feature lower surface area and much less reactive surface than charcoal. Adsorptive capacity is, therefore, generally lower, but reactivity is much lower as well.

d. Synthetic sorbents

Synthetic carbonaceous sorbents demonstrate properties midway between charcoal and porous polymers.

e. Coated sorbents

Coated sorbents are those upon which a layer of a reagent has been deposited. The adsorptive capacity of such systems usually approaches the capacity of the reagent to react with the particular analyte of interest [Kennedy 1988].

f. Molecular sieves

Zeolites and carbon molecular sieves retain adsorbed species according to molecular size. A limiting factor is that the water molecule is of similar size to many small organic compounds and is usually many orders of magnitude higher in concentration than the species of interest. This unfavorable situation may result in the displacement of the analyte by water molecules. Drying tubes may be used during sampling to eliminate the effects of humidity [Langhorst 1983].

g. Thermal desorption

Thermal desorption tubes may contain several different sorbents in order to collect a wide range of different chemical agents [Hodgson et al. 1988]. These tubes are generally used in situations where unknown chemicals or a wide variety of organics are present, e.g., in indoor environmental air quality investigations. Subsequent analysis is often by gas chromatography/mass spectrometry (GC/MS).

3 Types and uses of aerosol samplers

[Baron 1998]

a. Membrane filters

By far the most frequently used as sampling media for aerosols are membrane filters. This class of filters includes those made from polyvinyl chloride, polytetrafluoroethylene (PTFE), copolymers, and mixed cellulose esters (MCE). Filters from this class are used for sampling airborne particles such as asbestos, crystalline silica, particulate PAH's, particles not otherwise regulated, and elements for atomic spectrometric analysis.

b. Glass and quartz fiber filters

Quartz filters have replaced glass fiber in many applications. They are used in applications such as sampling for mercaptans and diesel exhaust. Impregnated quartz filters are often used to sample reactive aerosols.

c. Polycarbonate straight pore filters

Because of their characteristics, polycarbonate filters are good for the collection of particles to be analyzed by electron microscopy and x-ray fluorescence.

d. Respirable dust samplers

Cyclone samplers are used to collect airborne respirable dust. For instance, a high-flow cyclone attached to a sampler containing a polyvinyl chloride filter is used to collect respirable crystalline silica.

e. Inhalable dust samplers

Various samplers have been designed and/or evaluated for collecting samples of inhalable airborne particles. For example, the Institute of Occupational Medicine's (IOM) sampler is used, in conjunction with a polyvinyl chloride filter, for sampling formaldehyde on dust [NIOSH 1994a].

4 Factors affecting the collection of gases, vapors, and aerosols [Hebisch et al. 2009; Jones 1994; Baron 1994; Kulkarni et al. 2011]

a. Temperature

Since adsorption is typically exothermic, adsorption is generally reduced at higher temperatures. Additionally, if there is a reaction between an adsorbed species and the surface, or between two or more adsorbed species (e.g., hydrolysis or polymerization), the

rate of such reactions increases at higher temperatures. The temperature stability of a filter must be considered when sampling in hot environments.

b. Humidity**

Water vapor is adsorbed by polar sorbents; their breakthrough capacity for the analyte is thereby reduced for most organic compounds. However, for water-soluble compounds, the breakthrough capacity is increased, e.g., for chlorine and bromine [Cassinelli 1991] and formaldehyde [NIOSH 1994b]. This effect varies from substantial for more polar sorbents, such as charcoal and silica gel, to a smaller effect for synthetic carbonaceous and porous polymers.

Filter media may also be affected by humidity; moisture may affect a filter's collection efficiency. Very low humidities (≤10% RH) may make some filters (e.g., MCE) develop high charge levels, causing non-uniform deposits and repulsion of particles [Chen and Baron 1996]. Water absorption by some filters (e.g., MCE) can cause difficulty in obtaining tare weights for gravimetric analysis; thus weight-stable filter materials must be used for this application.

c. Sampling flow rate**/face velocity

Breakthrough volume of a solid sorbent bed tends to be smaller at higher sampling flow rates, particularly for coated solid sorbents. For sorbents such as charcoal, whose breakthrough capacity for most organic compounds can be significantly reduced by high humidity, lower sampling flow rates may actually result in smaller breakthrough volumes [Foerst 1979]. The collection efficiency of membrane filters will change with face velocity.

d. Concentration**

As the concentration of contaminant in air increases, breakthrough capacity (mg adsorbed) of a solid sorbent bed increases, but breakthrough volume (L of air sampled) decreases [Foerst 1979]. The effect of concentration is similar for filters.

****NOTE:** It is important to distinguish between equilibrium (saturation) adsorptive capacity and kinetic (breakthrough) adsorptive capacity of the solid sorbent. Breakthrough capacity is the important characteristic in actual sampling situations; it may be affected significantly by sampling flow rate and relative humidity of the air being sampled and may be significantly less than saturation capacity, which is not dependent on sampling flow rate or relative humidity.

e. Particle characteristics

Filter collection efficiency is a function of effective pore size [Lee and Ramamurthi 1993]. Particles smaller than about 0.2 µm are collected primarily by diffusion, while particles larger than about 0.2 µm are collected primarily by impaction and interception. Most sampling filters are highly efficient (>95%) for all particle sizes, with the minimum efficiency in the 0.2 µm size range. Polycarbonate straight pore filters exhibit poor collection by diffusion, so particles smaller than the pores are not collected efficiently.

f. Filter considerations

The pressure drop of a filter can limit the sampling time because of the load on the personal sampling pump [Breuer 2012]. In addition, pressure drop increases with dust loading on the filter [Lippman 1995]. Fine particles (<0.5 µm) will increase the pressure drop much faster than coarse particles (>10 µm). Heavy loading (> about 2 mg) may result in poor adhesion of collected particles to the filter surface.

5 Establishing sampling parameters

Once the sampling media and measurement method are chosen, the specific sampling parameters need to be determined [Eller 1986; ASTM International 2013]. For most methods, this will not pose a problem as the flow rate recommended in the method can be used for the desired sampling period, e.g., 1 to 5 L/min for 8 h for most aerosols or 10 to 200 mL/min for 8 h for most sorbent tube samples. It is necessary to consider the applicable OEL for short-term (e.g., 15 min) or long-term (e.g., 8 h) time-weighted average (TWA) sampling. Generally, the parameters which must be considered are flow rate, total sample volume, sampling time (tied into the two previous parameters), and limit of quantitation (LOQ). Some of these variables will be fixed by sampling needs, e.g., sampling time or by the measurement method of choice (LOQ or maximum sampling volumes). The choice of these variables can best be explained through the use of the following examples.

a. Sampling for gases and vapors using solid sorbents

NIOSH Method: 1453 for Vinyl Acetate [NIOSH 2013]
Recommended Sample Volume: 1.5 – 24 L
Applicable Range: 0.07 to 46 mg/m^3 (0.02 to 13.1 ppm)
NIOSH REL: 14 mg/m^3 (4 ppm) - Ceiling
17.5 mg/m^3 (5 ppm) – (European OEL) TWA
Recommended Flow Rate: 0.05 to 0.2 L/min
Breakthrough Time: 30 min @ 0.2 L/min and 150 mg/m^3
Breakthrough Capacity: 9 mg

Suppose it is desired to determine both ceiling and TWA exposures of workers exposed to vinyl acetate and the concentrations are unknown.

1.) Ceiling Determination:

If sampling were done at 0.2 L/min for 30 min and a total sample volume of 6 L collected, would this present a breakthrough problem? Probably not, since breakthrough tests were carried out in concentrations ca. 10x above the NIOSH Ceiling value [NIOSH 2013]. In the breakthrough test, a concentration of 10 times the NIOSH Ceiling value (150 mg/m^3) was sampled at 0.2 L/min for 30 min (6 L) before breakthrough occurred, collecting a total weight of 9 mg of vinyl acetate. This test was conducted in a humid environment with only vinyl acetate present. A safety factor of 50% should normally be allowed to account for humidity effects. Thus, if sampling is done for about 15 min at 0.2 L/min, levels of vinyl acetate up to 40 ppm could still be collected without sample breakthrough.

Also to be considered are the other organics present. If a concentration of 200 ppm acetone exists in this environment, then an additional safety factor should be added. An arbitrary 50% reduction in sampling rate at 0.1 L/min might be done. With the safety factors built in, collecting a 6-L sample should be acceptable.

2.) TWA Determination:

In a similar situation, the goal is to collect 8-h samples for comparison to the 5 ppm TWA [NIOSH 2013]. If sampling were done at 0.1 L/min, then the total sample volume would be 48 L, substantially above the 24-L recommended sample volume. If the flow was dropped to 0.05 L/min, then the sample volume would be halved (to 24 L, the maximum recommended in the method). This sample volume might be acceptable if the vinyl acetate concentrations are around 10 ppm and no other competing organics are present, e.g., acetone. However, the safer approach would be to collect two consecutive samples at 0.05 L/min for 4 h (total sample volume of 12 L each).

b. Pushing a method to the limit – limit of quantitation

NIOSH Method 1009 for Vinyl Bromide (VB) [NIOSH 1994c]
Recommended Sample Volume: <10 L @ 0.20 L/min or less
Working Range: 0.3 to 33 ppm (1.3 to 145 mg/m^3) for a 6-L air sample;
this equals 8 to 355 µg VB per tube
Limit of Detection: 3 µg VB per tube

In this particular example, let us say that the object is to estimate exposure down to 0.1 ppm (0.44 mg/m^3), which is below the working range. In order to collect 8 µg of vinyl

bromide (the limit of quantitation) at this concentration, 20 L of air will have to be collected. This volume is substantially above the maximum recommended sample volume of 10 L. Since the recommended sample volume is generally a conservative value used to protect against breakthrough under worst case conditions (i.e., high humidity and high concentrations), considerable leeway exists for the size of the air sample. In this example, the 20-L air samples should be taken at 0.2 L/min or lower, and the possibility of breakthrough should be monitored by observing the relative amounts of analyte on the backup sections of the samples.

The best approach is to consult with the analytical laboratory and then to take a sufficient number of samples to determine the useful limits of the sampler in the particular application. The presence of high relative humidity and other organic solvents will severely reduce the number of active sites available on the sorbent for collection of the contaminant of interest (with concomitant breakthrough a concern). In pushing a method to the limit, it is often necessary to sample beyond the breakthrough volume, normally while observing recommended maximum sampling flow rate, in order to obtain the sensitivity to determine the concentration of interest. If this is done, then the risk must be accepted that the method may not apply outside the limits tested.

c. Sampling for aerosols using a filter

NIOSH Method 7908: Non-volatile Acids (Sulfuric and Phosphoric Acids)
[NIOSH 2014]
Recommended Sample Volume: 15 – 2000 L
Applicable Range of the Method: 0.010 to > 10 mg/m^3
NIOSH REL: 1 mg/m^3 (H_3PO_4) (TWA); 3 mg/m^3 (STEL)
Recommended Flow Rate: 1 to 5 L/min

Suppose it is desired to determine both an exposure taking place during a specific 15-minute operation as well as a TWA exposure of workers exposed to phosphoric acid, and the concentrations are unknown.

1.) **15-Minute Process Sample:**
This sample would meet the method conditions by sampling for the 15 minutes at 5 L/min, since this would collect 75 L. Sampling at 1 L/min for 15 minutes would probably not allow for the collection of sufficient sample required for analysis.

2.) TWA Determination:

In this situation, it is necessary to collect an 8-h sample to compare with the 1 mg/m^3 NIOSH REL. Since an 8-h TWA sample covers 480 minutes, sampling can no longer be done at 5 L/min since this would collect >2000 L, in excess of the upper recommended sample volume. Sampling at 1 L/min would collect a 480 L sample, and sampling at 2 L/min would collect a 960 L sample: both acceptable per the conditions of the method.

6 Bulk samples

The collection of bulk samples can often assist with air sampling efforts. This is especially true where there is mixed solvent exposure or unknown dust exposure, and for determining silica content of dusts. The primary purpose of obtaining bulk samples is to provide the analytical laboratory with a large enough sample for qualitative and sometimes quantitative analysis. The two main types of bulk samples are bulk air and mass bulk (liquid or solid) samples.

a. Bulk air samples

Generally, a bulk air sample is defined as a large volume area sample collected for the purpose of qualitative analysis. A good example is a multiple solvent exposure where the exact identity of the airborne solvents is unknown, e.g., painting operations. For most organic solvents, a bulk air sample consists of a sorbent tube collected at 1 L/min for an hour or more. Although the sample is likely to exhibit breakthrough, this does not matter since one is primarily interested in identifying which substances are present rather than their exact concentrations (the latter aim is accomplished through the separate collection of air samples in accordance with defined method parameters). Any questions concerning how or whether or not a bulk air sample is needed should be addressed to the analytical laboratory prior to sampling. In the case of silica sampling, either a bulk air or solid bulk sample (e.g., a deposited sample) or both are suggested so that enough material will be available to determine free silica content.

b. Bulk liquids and solids

Collection of bulk materials may be needed to identify the substances present in the workplace and, in some cases, to estimate the relative levels of certain substances present in the raw material. A good example of the latter is the case of mixed solvent exposure when determining whether a certain contaminant of interest is present, e.g., benzene. In some cases, up to 30 solvents may be present, but their identities and proportions are not certain. This example is also true for dusts, as was discussed previously for silica, and for metals, which may exist in trace quantities.

In choosing bulk samples for collection, the end goal must be considered: qualitative and/or quantitative analysis. Any information that can be given to the laboratory on what may or may not be present will help with the analysis. Advance consultation with the laboratory is desirable. In choosing bulk dust samples, the sample should be representative of the airborne dust to which the workers are being exposed. Usually this is a settled dust sample collected from locations near the workers' job site. In other cases, a process dust sample may be chosen to determine the composition of the material before it becomes airborne.

When shipping bulk samples, care must be taken to preserve the integrity of the samples and to follow established shipping regulations. If applicable, hazardous shipping procedures must be followed. Consult with an experienced hazardous goods shipper to determine appropriate protocol. Only 5 to 10 mL of the liquid or 10 to 100 mg solid is typically needed, so generally bulk sample sizes are kept small. It is important to consult with the laboratory before collecting bulk samples to ensure proper sample size and containers. In general, leak-proof glass containers are best since they will not react with most chemicals; however, polyethylene containers can be used in the majority of cases. A convenient container is a 20-mL scintillation vial with PTFE-lined cap. Specific chemicals for which polyethylene containers should not be used include aromatic compounds, chlorinated hydrocarbons and strong acids. The lids of the containers should be sealed with shrink bands or tape for further assurance against leakage. Specific restrictions and labeling requirements should be checked prior to shipping any samples.

In the case of volatile bulk samples (and some air samples), consideration should be given to shipping the samples on dry ice or with bagged refrigerant (e.g., "blue ice"). Do not ship volatile compounds together with air samples. Specific labeling is usually required when dry ice is used in shipping.

7 Blanks

Certain numbers of blanks are required by the analytical laboratory for each set of samples to be analyzed. The specific method being used should be consulted concerning the number and type of blanks required. There are two types of sampler blanks: field and media blanks. Field blanks are clean samplers taken to the sampling site, handled in the same way as the air samples, except that no air is drawn through them. Media blanks are simply unopened, new samplers which are sent to the laboratory with the field samples (these blanks are not usually taken to the field). It is also recommended that additional blind field blanks be sent along with the field samples, and labeled as field samples, as a further check on the analysis. Blanks are good insurance to deal with contamination, but the best approach is to avoid sample contamination by using careful sampling protocols. The general recommendation for the

number of field blanks is three field blanks for each batch of samples. Media blanks should also be included. These unexposed, unopened samplers are used to give an estimate of media background. The laboratory should analyze at least three (3) media blanks from the same lot as the field samples. This number should be increased for media which are coated or impregnated with reagent. Again, it is crucial to consult the specific method for the number and type of blanks as these numbers will vary. Another recommended practice is to include blind spiked samples as quality control checks of the analytical laboratory.

8 Direct-reading methods [Pearce and Coffey 2011]

The variety of types of direct-reading methods available is large and expanding, including detector tubes (both short- and long-term), aerosol monitors, passive monitors for certain gases and portable instrumentation for gas chromatography or infrared spectrometry [Todd 1997]. Many direct-reading instruments now used for personal or area measurements have evolved from laboratory or process control instruments [Woebkenberg and McCammon 1995; Todd 1997]. Some direct-reading instruments are screening devices while others give quantitative result and can be used for compliance purposes [Song et al. 2001; Ashley et al. 2002].

Some of the considerations (e.g., specificity and sensitivity) for the use of direct-reading methods for quantitative determinations are similar to those already given for filter or sorbent sampling and analytical methods. In many cases, direct-reading instruments, which are physically small and portable, qualify as personal sampling devices.*** These offer the additional advantages over classical methods by reducing labor and analytical costs and may be the methods of choice when instantaneous results are important, even at the expense of some degree of sensitivity or specificity. In general, manufacturers' instructions should be followed in the calibration and use of these devices. Because of the severe conditions to which direct-reading instruments may be subjected, performance checks and preventive maintenance on a periodic basis or before each use are very important. Many direct-reading instruments are powered by batteries which can fail to provide a full charge over the full sampling period unless frequently or fully discharged and recharged several times just prior to use. An additional responsibility, i.e., that of field calibration of the direct-reading instrument, falls on the field sampling personnel.

***__NOTE:__ Portable instrument are generally described as weighing less than 5 kg and powered by self-contained batteries [Ashley 2003]. For personal monitoring, the instrument configuration should be such that the breathing zone can be monitored.

9 Sampling Strategy

To obtain the maximum amount of information during the course of a sampling campaign with a minimum number of samples, a statistical sampling strategy should be developed before conducting any study [Leidel et al. 1977; ASTM International 2013]. Several pieces of information must be known in advance to plan a sampling strategy, including the size of the workforce to be sampled, the accuracy of the sampling and measurement method to be used and the confidence one wishes to have in predicting the occupational exposures.

For example, to determine with 90% confidence that at least one worker from a workplace subgroup will be in the top 10% of the exposures occurring in the group, the number of employees to sample would be chosen from the scheme below. (Other figures are applicable for confidence limits of 95% and for the top 20% of exposures.) Again, judicious use of sampling statistics will optimize the number of samples needed.

Table 1. Minimum sample size (n) for including (@ 90% confidence level) at least one high risk employee[A] [Leidel et al. 1977]

Size of employee group (N)																		
1	2	3	4	5	6	7	8	9	10	11-12	13-14	15-17	18-20	21-24	25-29	30-37	39-29	40-49	50+
Minimum number of measured employees (n)																			
1	2	3	4	5	6	7	7	8	9	10	11	12	13	14	15	16	17	18	22

[A] Exposure in highest 10% of N.

10 Sampling and calibration techniques

The following are suggested general techniques for active sampling using some of the more common samplers. These instructions elaborate on those given in NIOSH methods. Consult individual methods for details regarding sample size.

a. Calibration of personal sampling pumps

The accuracy of determining the concentration of a toxic substance in air is no greater than the accuracy with which the air volume is measured. Therefore, accurate calibration of the airflow rate through the sampling train is necessary. Ordinarily, pumps should be calibrated in the laboratory and the field, both before field use and after each field sampling campaign.

The choice of a reference instrument will depend on where the calibration is to be performed. For laboratory use, primary standards, such as a spirometer or soap-bubble meter, are recommended [Okladek 1988]. Several electronic soap-bubble calibrators and dry-cell calibrators are commercially available as primary calibrators. Other instruments, such as a wet-test, mass-flow or a dry-gas meter, may be used. The following instructions are for the soap-bubble meter. If another calibration device is used, equivalent procedures should be followed.

1.) Set up the apparatus as shown in Figure 1.

2.) Ensure that the rechargeable batteries will power the pump for the entire sampling interval by one of the following methods: 1) run the pump for that length of time, checking for satisfactory operation; or 2) test the battery independently of the pump using a current capacity tester [Kovein and Hentz 1988]. Fully recharge the batteries.

3.) Turn the pump on and moisten the inner surface of the soap-bubble meter with the soap solution. Draw bubbles upward until they travel the entire length of the buret without breaking.

4.) Adjust the pump to the desired nominal flow rate. Check the water manometer. The pressure drop across the sampler should not exceed 2.5 cm Hg of water.

5.) Start a soap bubble in the buret and, with a stopwatch, measure the time that it takes to traverse two calibration marks. For a 1000-mL buret, a convenient calibration volume is 500 mL. Repeat the determination at least twice more. Average the results and calculate the flow rate by dividing the calibration volume by the average time.

6.) Record the following data:
   a. volume measured
   b. elapsed time
   c. pressure drop
   d. air temperature
   e. atmospheric pressure
   f. serial number of the pump
   g. pump model
   h. date and name of operator.

7.) If the sampling pump used for sample collection uses a variable area flow meter (rotameter) for flow rate indication, the calibrated flow rate must be adjusted for the actual air pressure and temperature during sampling [Okladek 1988]. The expression for this correction is as follows.

NOTE: This correction is not used for non-rotameter sampling pumps.

V (Corrected volume, L) = Q t (P_cT_s /P_sT_c) 0.5 where:
Q = indicated flow rate (L/min)
t = sampling time (min)
P_c = pressure during calibration of sampling pump (kPa)
P_s = pressure of air sampled (same units as P_c)
T_c = temperature during calibration of sampling pump (K)
T_s = temperature of air sampled (K).

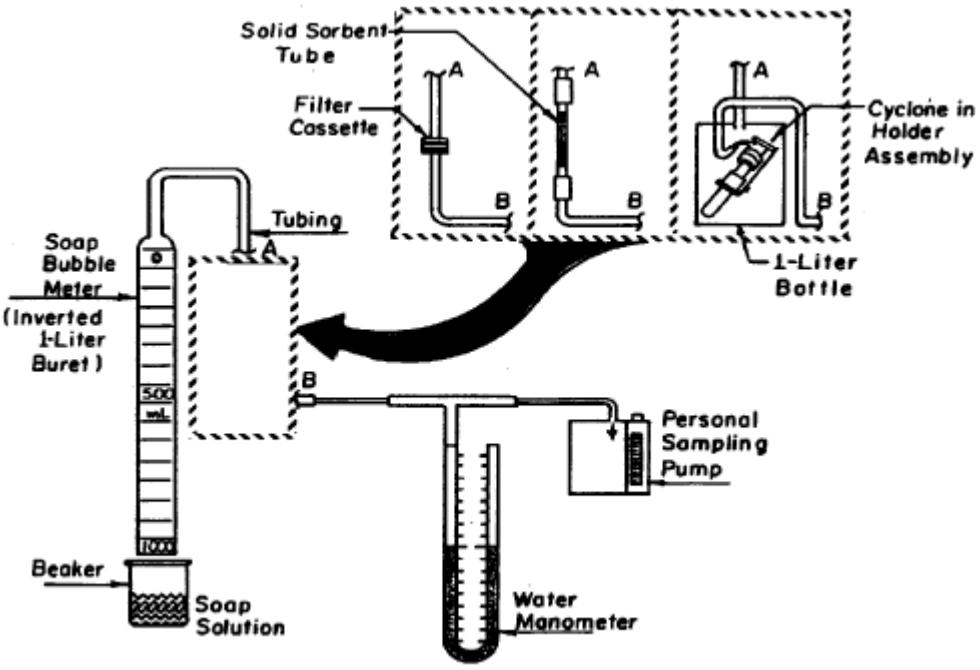

Figure 1. Calibration Apparatus

b. Sampling instructions for solid sorbent tube sampler

Use these instructions for active personal sampling (i.e., pumped sample airflow) for substances which are retained on solid sorbents such as activated charcoal, silica gel, porous polymers, etc.

1.) Calibrate each personal sampling pump at the desired flow rate with a representative solid sorbent tube in line. Use a bubble meter or equivalent flow measuring device.

2.) Break the ends of the solid sorbent tube immediately before sampling to provide an opening at least one-half of the internal diameter at each end.

3.) Connect the solid sorbent tube to a calibrated personal sampling pump with flexible tubing with the smaller sorbent section (backup section) nearer to the pump. Do not pass the air being sampled through any hose or tubing before entering the solid sorbent tube. Position the solid sorbent tube vertically during sampling to avoid channeling and premature breakthrough.

4.) Prepare the field blanks at about the same time as sampling is begun. These field blanks should consist of unused solid sorbent tubes from the same lot used for sample collection. Handle and ship the field blanks exactly as the samples (e.g., break the ends and seal with plastic caps) but do not draw air through the field blanks. A minimum of three field blanks are normally required for each batch of samples.

5.) Take the sample at an accurately known flow rate as specified in the method for the substance and for the specified air volume. Typical flow rates are in the range 0.01 to 0.2 L/min. Check the pump during sampling to determine that the flow rate has not changed. If sampling problems preclude the accurate measurement of air volume, discard the sample. Take a minimum of three replicate samples for quality control for each set of field samples.

6.) Record pertinent sampling data including location of sample, times of beginning and end of sampling, initial and final air temperatures, relative humidity and atmospheric pressure.

7.) Seal the ends of the tube immediately after sampling with plastic caps. Label each sample and blank clearly with waterproof identification.

8.) Pack the tubes tightly with adequate padding to minimize breakage for shipment to the laboratory. In addition to the sample tubes and field blanks, ship at least six unopened tubes to be used as media blanks and three additional tubes so that desorption efficiency studies can be performed on the same lot of sorbent used for sampling.

9.) Ship bulk samples in a separate package from the air samples to avoid contamination of the samples. If applicable, hazardous shipping procedures must be followed. Consult with an experienced hazardous goods shipper to determine appropriate protocol. Suitable containers for bulk samples are glass with a polytetrafluoroethylene (PTFE)-lined cap, e.g., 20-mL glass scintillation vials. It is important to consult with the laboratory before collecting bulk samples to ensure use of proper sample size and containers.

c. Sampling instructions for filter sampler

Use these instructions for personal sampling of inhalable aerosols. Methods requiring these instructions specify FILTER as the sampling method. These instructions are not intended for respirable aerosol sampling.

1.) Calibrate the personal sampling pump with a representative filter in line using a bubble meter or equivalent flow measuring device.

2.) Assemble a filter or internal capsule in a cassette filter holder. Support the filter by a cellulose backup pad or stainless steel screen. Close the filter holder to ensure that its parts mate evenly and securely to prevent leakage [Frazee and Tironi 1987]. Seal the filter holder with plastic tape or a shrinkable cellulose band.

3.) Remove the filter holder plugs and attach the filter holder to the personal sampling pump with a piece of flexible tubing. Position the filter holder in the worker's personal breathing zone, with the sampler inlet pointed downwards.

4.) Prepare the field blanks at about the same time as sampling is begun. These field blanks should consist of unused filters (or internal capsules) and filter holders from the same lot used for sample collection. Handle and ship the field blanks exactly as the samples, but do not draw air through the field blanks. Three field blanks are required for each batch of samples.

5.) Sample at the prescribed flow rate (usually 1 to 5 L/min) until the recommended sample volume is reached. Set the flow rate as accurately as possible (e.g., within ± 5%) using a calibrated flowmeter. Take three replicate samples (minimum) for quality control for each set of field samples.

6.) Observe the sampler frequently and terminate sampling at the first evidence of excessive filter loading or change in personal sampling pump flow rate. (It is possible for a filter to become plugged by heavy particulate loading or by the presence of oil mists or other liquids in the air.)

7.) Disconnect the filter holder after sampling. Cap the inlet and outlet of the filter holder with plugs. Label the sample. Record pertinent sampling data, including times of beginning and end of sampling, initial and final air temperatures, relative humidity and atmospheric pressure. Record the type of personal sampling pump used and location of the sampler.

8.) Ship the samples to the laboratory as soon as possible in a suitable container designed to prevent damage in transit. Ship bulk material to the laboratory in a chemically inert container. Never store, transport or mail bulk samples in the same container as the samples or field blanks. In addition to the samples and field blanks, ship at least four unused filters or filter capsules from the same lot for use as media blanks.

d. Sampling instructions for filter + cyclone sampler

Use these instructions for personal sampling of respirable (or thoracic) aerosols [Frazee and Tironi 1987]. Methods requiring these instructions specify CYCLONE + FILTER as the sampling method.

1.) Calibrate the pump to the rate specified by the cyclone, with a representative cyclone sampler in line using a bubble meter (or a secondary flow measuring device which has been calibrated against a bubble meter). The calibration of the personal sampling pump should be done close to the same altitude where the sample will be taken.

2.) Assemble the pre-weighed filter in the cassette filter holder. Use a conductive or static-dissipative cassette. Support the filter with a cellulose backup pad or stainless steel screen. Close firmly to prevent sample leakage around the filter. Seal the filter holder with plastic tape or a shrinkable cellulose band.

3.) Remove the cyclone's grit cap and vortex finder before use and inspect the cyclone interior. If the inside is visibly scored, discard this cyclone since the dust separation characteristics of the cyclone might be altered. Clean the interior of the cyclone to prevent reentrainment of large particles.

4.) Assemble the two-piece filter holder, coupler, cyclone and sampling head. The sampling head rigidly holds together the cyclone and filter holder. Check and adjust the alignment of the filter holder and cyclone in the sampling head to prevent leakage. Connect the outlet of the sampling head to the personal sampling pump by a 1-m piece of 6-mm ID flexible tubing.

5.) Position the cyclone assembly in the worker's personal breathing zone and attach the personal sampling pump to a belt or harness. Ensure that the cyclone hangs vertically with the inlet pointed downwards. Explain to the worker that the cyclone must not be inverted.

6.) Prepare the field blanks at about the same time as sampling is begun. These field blanks should consist of unused filters and filter holders from the same lot used for sample collection. Handle and ship the field blanks exactly as the samples, but do not draw air through the field blanks. A minimum of three field blanks are required for each batch of samples.

7.) Turn on the pump and begin sample collection. If necessary, reset the flow rate to the pre-calibrated value, using the manufacturer's adjustment procedures. Since it is possible for a filter to become plugged by heavy particulate loading or by the presence of oil mists or other liquids in the air, observe the filter and personal sampling pump frequently to keep the flow rate within ± 5% of the target flow rate. Sampling should be terminated at the first evidence of a problem.

8.) Disconnect the filter after sampling. Cap the inlet and outlet of the filter holder with plugs. Label the sample. Record pertinent sampling data, including times of beginning and end of sampling, initial and final air temperatures and atmospheric pressure or elevation above sea level. Record the type of personal sampling pump, filter, cyclone used and the location of the sampler.

9.) Ship the samples and field blanks to the laboratory in a suitable container designed to prevent damage in transit. Ship bulk samples in a separate package.

10.) Take a minimum of three replicate samples for every set of field samples to assure quality of the sampling procedures. The set of replicate samples should be exposed to the same dust environment, either in a laboratory dust chamber or in the field. The quality control samples must be taken with the same equipment, procedures and personnel used in the routine field samples. The relative standard deviation, sr,

calculated from these replicates, should be recorded on control charts and action taken when the precision is out of control.

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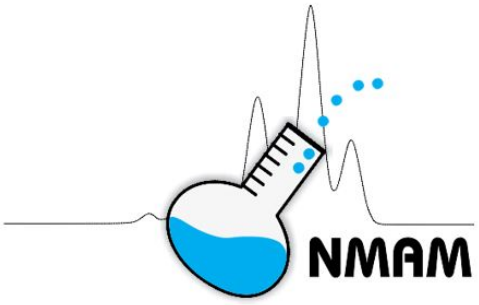

NIOSH Manual of Analytical Methods (NMAM), 5th Edition

Factors Affecting Aerosol Sampling

by Paul A. Baron, Ph.D., NIOSH

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

1 Introduction

The need for aerosol sampling is driven by research or regulatory needs to understand or quantify the properties of airborne particles in the workplace or ambient environments. The property of most common interest is the airborne concentration of particulate mass defined as the aerosol mass per unit volume of air, usually expressed in units of micrograms or milligrams per cubic meter. Alternatively, concentrations of other related properties such as surface area or number, or particle size distributions are also of interest in certain cases, especially where exposure to nanoparticles or ultrafine aerosols are involved. In many applications, airborne concentration of a certain chemical or analyte, usually expressed in terms of micrograms per cubic meter, is more important. Aerosol sampling is the process of collecting a representative sample of airborne particles of interest from the air environment by physically separating them from the sampled air of known volume. The degree to which the physically separated sample represents the in situ aerosol depends on the design of the physical separation device, often known as the aerosol sampler. Other factors that affect the representativeness of the particulate sample include environmental conditions (e.g., wind, temperature, humidity), particle characteristics (particularly if they are highly irregular or nonspherical), and subsequent analytical methods used for particle analysis. This chapter focuses mainly on the key characteristics of aerosol samplers that may influence the representativeness of the sampled aerosol. Direct-reading aerosol samplers are not discussed in this chapter.

Most samplers use size-selective inlets that conform to certain health-based conventions. The American Conference of Governmental Industrial Hygienists (ACGIH) [Vincent 1999a; ACGIH 2015], the International Organization for Standardization (ISO) [ISO 1995], and the European Standardization Organization (Comité Europeén de Normalisation, CEN) [CEN 1993] have adopted identical particle size-selective sampling conventions for inhalable, thoracic, and respirable aerosols (Figure 1). The purpose of these conventions is to provide a scientific basis for a new generation of particle size-selective occupational exposure limits (OELs) for aerosols. Such OELs can therefore be matched to the relevant sites of aerosol deposition after inhalation into the respiratory tract, and in turn to the health effects of interest in a given exposure assessment. These sampling conventions are used throughout this manual unless otherwise specified.

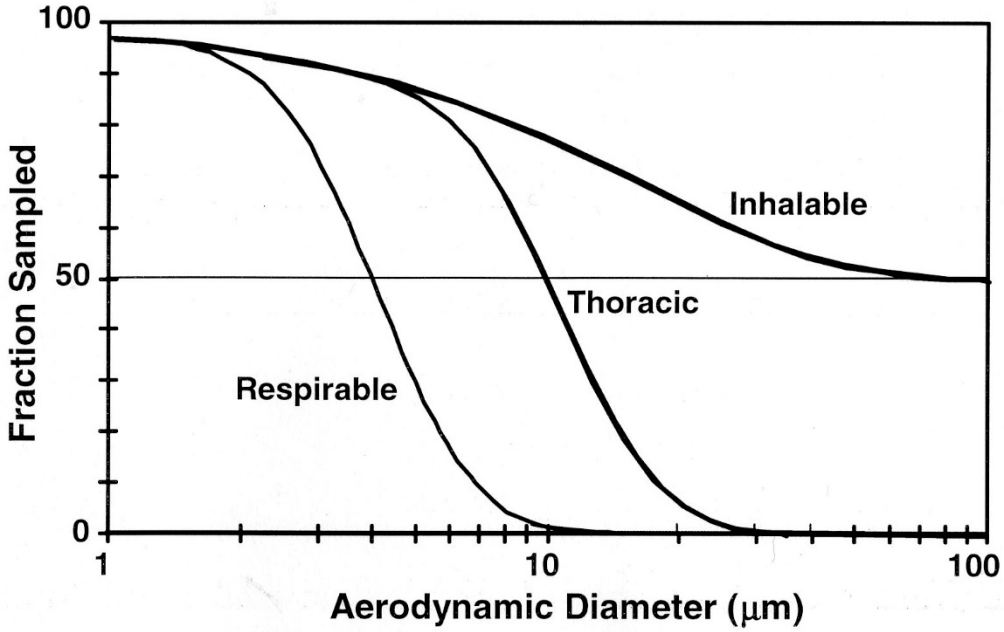

Figure 1. ISO/ACGIH/CEN sampling conventions [ISO 1995]. An ideal sampler should have a sampling efficiency curve that matches one of these curves as closely as possible under all wind directions and velocities. The 50% cut points for the respirable and thoracic conventions are 4 and 10 μm, respectively.

The criteria presented in this manual are used to determine the most appropriate aerosol sampling equipment. The type of sampling to be performed determines which criteria are important for estimating the adequacy of the sampler and determining aerosol concentration levels. For example, "total dust" samplers generally do not have a size selective particle classifier preceding the filter media and fall under the inhalable sampling convention. Alternatively, sampling for regulatory or voluntary compliance with aerosol exposure standards usually requires greater accuracy, increased efficiency, size-specific selectivity, and good analytical precision. Furthermore, regulations may require the use of a specific sampler and sampling conditions to standardize sampling results (eliminate bias) and reduce uncertainty among laboratory reports. See the chapter on measurement uncertainty and NIOSH method accuracy for further discussion on standardization and aerosol measurement error.

Open-face filter cassettes do not use constricted opening or tubing and expose the filter directly to the aerosol to minimize the losses. They provide relatively uniform particle deposition on the filter. On the other hand, closed-face filter cassettes are often necessary to connect to upstream tubing or size-selective inlets.

Over the past decades, researchers have pointed out strengths and weaknesses with several types of aerosol samplers (Figures 2A-J). Some of these samplers were adapted from existing devices used for other purposes, e.g., the 10-mm nylon cyclone and the 37-mm cassette, without the benefit of current testing technology and understanding of particle behavior.

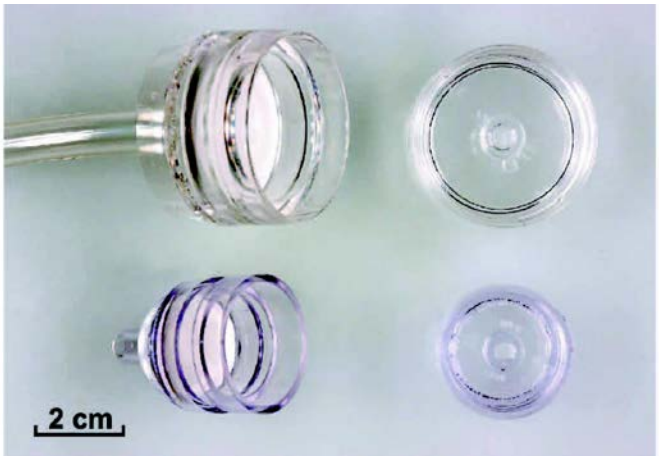

Figure 2A. 37-mm (top) and 25-mm (bottom) filter cassettes. Open faced cassettes are shown on left. Closed-faced cassettes include placement of clear piece (on right) over filter. These are shown in acrylic copolymer (clear, non-conducting) material and are more prone to electrostatic losses. Other construction materials are available, including conducting plastic. Sampling flow rates range from 0.5 to 10 L/min.

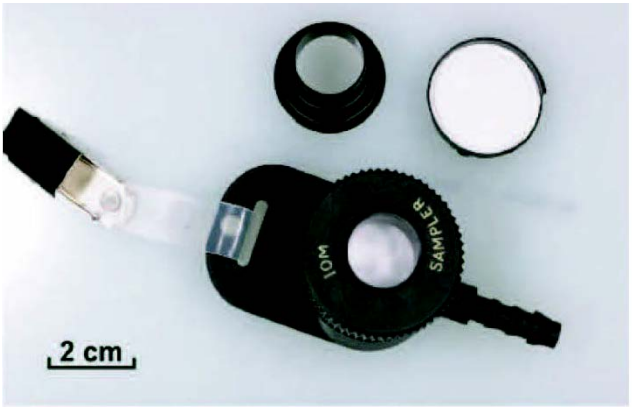

Figure 2B. IOM inhalable sampler. This is the first sampler designed specifically to match the inhalable sampling convention. The sampling cartridge is shown on the right with the inlet, filter, and support grid. All dust entering the cartridge is collected and analyzed. Sampler is made of conductive plastic and operates at 2 L/min.

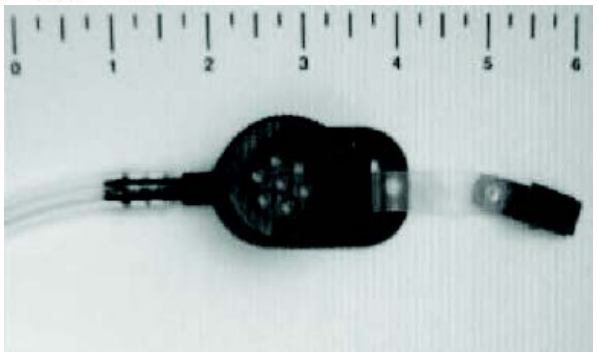

Figure 2C. Seven hole sampler used for inhalable dust sampling in the UK. Sampler is made of conductive plastic and operates at 2 L/min.

Figure 2D. Button sampler. So-named because the inlet, a hemispherical screen with ~380 µm diameter holes, resembles a large button. It was developed as an inhalable sampler with reduced wind direction response and improved filter deposit uniformity. The sampler uses metal construction and operates at 4 L/min.

Figure 2E. Asbestos sampling cassette. The long (50 mm) inlet was designed to prevent incidental contact with the filter surface and, when facing downward, acts to a certain extent as an elutriator, preventing larger particles from reaching the filter surface. It is made of conductive plastic and is operated at a flow rate between 0.5 L/min to 16 L/min.

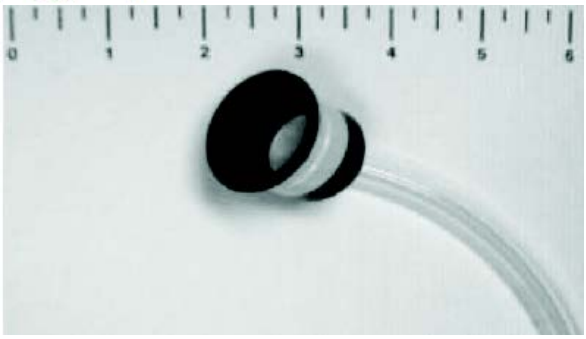

Figure 2F. Bell mouth cowl sampler. An alternative to the standard asbestos sampling cassette. The inlet is flared to reduce the effect of external air motion on sample uniformity. It is made of conductive plastic and is operated at a flow rate between 0.5 L/min to 16 L/min.

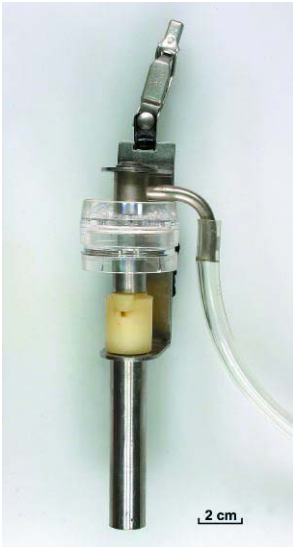

Figure 2G. Dorr-Oliver 10-mm nylon cyclone. It is used as a respirable sampler most often at 1.7 L/min. A version of this sampler is used at 2 L/min in coal mines with a 1.38 correction factor applied to the resultant mass. The holder encases body of the cyclone so that only the inlet section is visible just below the connection to the 37 mm cassette. The coal mine dust sampler version uses a cassette with an aluminum cartridge encasing the collection filter.

Figure 2H. Higgins-Dewell cyclone. This sampler was developed and used primarily as a respirable sampler in the UK. This version provides an interface directly to a 37-mm cassette. Cyclone construction is steel and operates at 2.2 L/min.

Figure 2I. GK2.69 cyclone. This cyclone was designed to match the slope of the thoracic and respirable conventions more closely than other sampling cyclones. Cyclone construction is stainless steel and operates at 4.2 L/min as a respirable sampler and 1.6 L/min as a thoracic sampler. GK4.162 RASCAL Cyclone is also available for higher flow rates of 8.5-9 L/min.

Figure 2J. Personal cascade impactor sampler (model Marple 290, Thermo Fisher Scientific). The sampler has five stages in the version shown and an additional three stages are available to provide cutpoints from 0.4 µm to 21 µm. The flap over the inlet reduces direct projection of large particles into the inlet. This sampler allows measurement of aerosol size distribution and calculation of respirable and thoracic fractions. It is constructed of aluminum and operates at 1.7 L/min.

More recently developed aerosol samplers were designed to either maximize the information gained regarding aerosol concentration levels or to minimize any inherent losses associated with the sampler design. Thus, each sampler design may have been based on some of the following criteria: inlet or aspiration efficiency, classifier accuracy, cassette assembly (bypass leakage), electrostatic losses, particle deposition uniformity, collection media stability, sampler surface losses, and sampler field comparisons. These criteria are discussed in the following sections of this chapter.

2 Inlet efficiency of the sampler

An important review of sampling theory and practice was compiled in a book by Vincent [2007]. The inlet efficiency of several samplers has been evaluated including thin-walled tubular inlets [Grinshpun et al. 1993], a cyclone [Cecala et al. 1983], an asbestos sampler [Chen and Baron 1996], total aerosol sampling cassettes [Fairchild et al. 1980], and inhalable aerosol samplers [Kenny et al. 1997; Aizenberg et al. 2001]. All samplers have an inlet efficiency, also called aspiration efficiency, which varies as a function of particle aerodynamic diameter, inlet velocity, inlet shape and dimensions, dimensions of the body it is attached to, external wind velocity, and external wind direction. The *aspiration efficiency* of an aerosol sampler can be defined as

$$A = \frac{C_S}{C_0}$$

where C_S is the concentration of particles passing directly through the plane of the sampling orifice and C_0 is the ambient concentration. This is true for aerosol samplers for which the entire amount of aerosol that enters the plane of the sampling orifice is quantified, as is the

case for the IOM sampler (SKC, Inc., Eighty Four, PA). However, it is important to note that many commercially available aerosol samplers use only the aerosol collected on the filter that is housed in the sampler, while any particles deposited on the inner surfaces upstream of the filter are disregarded. Performance of this type of sampler is therefore best characterized by its *sampling efficiency*, in which the aspiration efficiency is modified by the particle size-dependent wall losses prior to the filter. The aspiration or sampling efficiency of a particular aerosol sampler, whichever is the most relevant, expressed as a function of particle aerodynamic diameter, is the primary index of sampler performance. The overall size-dependent transmission efficiency of the sampler must match the appropriate health-based criterion (e.g., the inhalability criterion) to allow its use for a health-based assessment of personal aerosol exposure.

As an aerosol is being sampled, the large-particle trajectories are more affected by external flow fields than those of small particles. Thus, the shape, orientation, and inlet flow field will be most critical for inhalable aerosol sampler inlets; they will be less important for thoracic samplers and unlikely to be important for respirable samplers, except at very high wind velocities. The flow field near the inlet of a sampler is different when the sampler is mounted on a person (or in laboratory simulations using a mannequin) than when it is freestanding. Therefore, it has been recommended that measurement of inhalability be determined from mannequins in wind tunnels [Vincent 1999a; Kennedy et al. 1995; Kennedy and Hinds 2002; Aitken et al. 1999]. Flow field studies using mannequins in wind tunnels indicate that the air is slowed down by the body, resulting in an enrichment of large particles in the upstream side of the body [Rodes et al. 1995]. When intended for use at low wind speeds (less than about 1 m/s [200 ft/min] (representing most indoor workplaces), it may be possible to test the samplers as freestanding devices if it can be shown there is no effect from the mannequin body [CEN 1997]. However, if the sampler is to be used at higher windspeeds, which frequently occur outdoors, personal aerosol samplers should be evaluated on a mannequin in a wind tunnel [CEN 1997].

Respirable aerosol samplers generally do not have problems with inlet effects because the particles being sampled have low enough inertia and settling velocity. However, Cecala et al. [1983] found that the 10-mm nylon cyclone operated free-standing in a wind tunnel oversampled at external air velocities greater than 4 m/s when the inlet faced the wind and undersampled at 90° and 180° to the wind at velocities greater than 1 m/s. The maximum sampling error of about 40% was observed at 10 m/s. It is expected that these errors would be reduced if the sampler were located on a person, because the air velocity decreases near the body surface. It should be noted that the Cecala et al. work was conducted in the context of aerosol sampling in underground mining environments. Here, windspeeds of the magnitude quoted are not uncommon. However, in industrial workplaces more generally, windspeeds are much lower. Two surveys of a wide range of workplaces [Baldwin and Maynard 1998; Berry

and Froude 1989] revealed that actual indoor windspeeds rarely exceeded 0.2 to 0.3 m/s and more typically were less than 0.1 m/s.

The EPA PM_{10} standard for environmental sampling specifies a sampler that has a 50% cutpoint at 10.6 µm particle diameter, approximately the same as that for the thoracic sampler [Baron and John 1999]. Although the requirements for environmental PM_{10} samplers stipulate wind tunnel testing, similar work on personal PM_{10} and thoracic samplers is yet to be performed. It is expected that these samplers will be more susceptible to wind effects than respirable samplers because larger particles are more susceptible to inertial and gravitational effects.

The most extensive comparison of available inhalable aerosol samplers was that carried out under the auspices of the European Commission (EC) [Kenny et al. 1997]. Eight samplers were tested: CIP-10 (foam-based, French); 37-mm closed-face cassette (Spain and US) (Figure 2A); 37-mm open-face cassette (Sweden) (Figure 2A); PAS-6 (Netherlands); PERSPEC (Italy); GSP (Germany, sold as CIS sampler in US; BGI, Inc. Waltham MA); IOM (United Kingdom; (Figure 2B); and the Seven-Hole Sampler (United Kingdom; Casella CEL, Inc., UK) (Figure 2C). Conditions of the experiment included measurement of sampler collection efficiencies on a mannequin for aerosol particles with diameters as large as 100 µm at a wind speed of 0.5m/s, 1.0 m/s, and 4 m/s. Samplers were positioned on a mannequin rotating within a wind tunnel. The samplers were all conductive; the 37-mm cassette samplers were painted with an external conductive coating. The aerosol was, however, not neutralized. The results of this experiment indicated high inter-sampler variability, but permitted estimates of bias relative to the inhalable convention. The EC study also indicated that most samplers work reasonably well at low wind speeds (<1 m/s) for particle median diameters below 25 µm [Kenny 1995]. The study indicated that experiments of this type were difficult, expensive, and generally had poor precision. Perhaps better understanding of the flow field near the body may lead the way to improved and simplified sampler testing. Recent work suggests ways of making the wind tunnel testing of inhalable samplers simpler and less expensive, e.g., by using a compact body to simulate the chest of a mannequin [Witschger et al. 1997] and by using miniaturized mannequins and samplers that are calculated to be aerodynamically equivalent [Ramachandran et al. 1998].

The orientation and diameter of an inhalable sampler inlet may affect the collection of very large particles (generally >100 µm), since these may be thrown into the inlet as projectiles. The current definition of inhalable aerosol only covers particles up to100 µm aerodynamic diameter.

In situations where large particles can be generated (e.g., abrasive blasting, wood working, and grinding operations) excessive collection of particles up to the millimeter range is likely to

occur. There have been some attempts to modify inlets with shields to provide a barrier against the collection of large particles, but these modified inlets have not been demonstrated to provide the same agreement with the inhalable convention as the unmodified ones.

Another potential problem with inhalable samplers is the collection of passively sampled particles. Measurements when the sampler airflow is turned off indicate that IOM samplers, which pointed outward from the body and had a large inlet diameter (15-mm), can collect quite significant amounts of dust, with median values of 9 to 32 percent of the mass collected during active sampling [Lidén et al. 2000b]. Open-faced cassettes had only 2 to 11 percent of the mass passively collected. These samplers have a larger inlet (37-mm), but point downward, reducing the likelihood of particle settling onto the collection surface. The mechanism of collection is unclear, but the dust may be transported into the inlet by turbulence and deposited by settling or turbulent diffusion. How this passively collected dust modifies the amount collected during active sampling remains under investigation.

A comparison of measurements obtained with the 37-mm closed-face cassette (4-mm inlet diameter) to the IOM sampler (15-mm inlet diameter) in several workplaces gave similar results when the material on the interior walls of the 37-mm cassette were added to the analyte deposited on the filter [Demange et al. 2002; Harper and Demange 2007]. This suggests that the two samplers can have similar inlet efficiencies in spite of differences in inlet size and orientation if the median particle size sampled is not too large. Therefore, if the total aspiration (which includes the mass from filter and the wall deposits) of the IOM sampler conforms with the ISO inhalable size-selection criterion, then so does the total aspiration of the closed cassette filter. Several studies have now shown that in metals industries the total of mass from particulate filter and the wall deposit are comparable for both the closed cassette filter and the IOM samplers [Harper and Demange 2007].

3 Classifier accuracy

The theory of classifier separation is based on particle aerodynamic diameter, which is defined as the diameter of a 1 g/cm^3 density sphere having the same gravitational settling velocity as the particle in question. If the particle is markedly nonspherical or irregularly shaped, the aerodynamic diameter may depend on particle's orientation and other factors, possibly contributing to sizing errors. For example, fibers and plate-like particles settle slightly differently depending on orientation [Kulkarni et al. 2011]. Thus, the sampling conventions, based on aerodynamic diameter of particles reaching specified parts of the respiratory system, become somewhat ambiguous for these types of particles. For such nonspherical particles, further testing of classifiers to simulate particle behavior in the respiratory tract may be necessary. For instance, Maynard [1996] found that plate-like particles may orient differently in elutriators, impactors, and cyclones. This preferred orientation in a cyclone produced a

collection efficiency 15% below that estimated to occur in the respiratory system. In addition, Baron et al. [2008] showed that the overall enveloping physical size of airborne single-walled carbon nanotube (SWCNT) agglomerates is much larger than their aerodynamic size, by a factor of up to 10. Ku and Kulkarni [2015] measured both aerodynamic and mobility (or diffusion) diameters of airborne carbon nanotubes (CNTs) and other nanomaterials to show that aerodynamic diameter is smaller by a factor of 2 to 4 than mobility diameter for SWCNT and multi-walled CNT particles. These studies indicate that relevant equivalent diameters must be used to obtain reliable estimation of lung deposition fraction. Improved understanding of fiber [Esmen and Erdal 1991], nanotube [Baron et al. 2008; Ku and Kulkarni, 2015] and plate-like particle [Maynard 1996] behavior in the respiratory tract is needed to aid in development of more accurate samplers for these types of particles. The phase (i.e. liquid or solid) of the aerosol particles also influences sampling errors. Koehler et al. [2012] examined the sampling efficiency as a function of particle phase of three personal aerosol samplers, including the IOM and button sampler. They found that large liquid droplets have low transmission efficiencies through the screened inlets and that the bounce of solid particles significantly affects the aspiration efficiencies of screened inlets.

Various types of classifiers have been constructed to meet the ACGIH/ISO conventions. For example, respirable samplers have used cyclones [Caplan et al. 1977], impactors [Marple 1978; Kimura 1978; John 1994], elutriators [Lynch 1970], and porous foam [Brown 1980; Courbon et al. 1988] to remove non-respirable particles from the aerosol prior to filter collection. The technology for testing these samplers has improved in recent years through use of a real-time aerodynamic sizing instrument and resulted in quicker and more precise measurements [Baron 1993; Gudmundsson and Lidén 1998]; this technique has allowed the accuracy of these samplers to be investigated more carefully [Bartley et al. 1994]. However, a round-robin comparison of 50% cut-point measurements from six laboratories using an aerodynamic sizing instrument to test the same cyclone agreed within a range of 11% [Lidén 2000a]. Further work on the testing protocol is needed to improve interlaboratory agreement. Many current classifiers do not match the shape of the respirable convention exactly and produce biases that depend on size distribution. Two comparisons of several respirable samplers have been performed using the aerodynamic sizing technique [Chen et al. 1999b; Görner et al. 2001].

The introduction of the thoracic fraction in the ACGIH/ISO conventions has spurred interest in thoracic classifiers for certain types of aerosols, e.g., cotton dust, asbestos and sulfuric acid [Baron and John 1999]. The performance characteristics of the vertical elutriator (operated at 7.4 L/min) used for cotton dust approximately meets the thoracic definition [Robert 1979]. Laboratories in many countries perform asbestos fiber measurement using the technique of counting only fibers with diameters of 3 μm or less; this size selection was shown to be approximately equivalent to thoracic sampling [Baron 1996]. Further tests indicate that

several thoracic samplers may be appropriate for asbestos sampling [Jones et al. 2001; Maynard 1999]. Thoracic sampling is also recommended for sulfuric acid [Lippmann et al. 1987] and metal working fluids [NIOSH 1998].

Several samplers based on inertial, cyclone and foam separators have been specifically developed to meet the thoracic definition [Fabriès et al. 1989; Fang and Lippmann 1995; Mark et al. 1988; Kenny and Gussman 1997]. The CIP-10 sampler has been used for thoracic sampling in Europe [Gorner et al. 1994], but is not applicable to aerosols with a significant submicrometer fraction [Fabriès et al. 1989]. Several of these samplers have been tested to compare with the thoracic convention [Jones et al. 2001; Maynard 1999]. The GK2.69 cyclone (Figure 2I) has been used for metal working fluids [NIOSH 1998] and GK4.162 cyclone has been used for measurement of crystalline silica [Qi et al., 2015]. Several developmental samplers have also been developed. Koehler and Volckens [2013] have developed multistage regional deposition sampler that allows estimation of regional deposition of aerosol in the human respiratory system. This sampler is not suitable for gravimetric analysis but is well suited for measurement using variety of chemical analyses. A personal nanoparticle respiratory deposition sampler was developed by Cena et al. [2011] for particles smaller than 300 nm diameter, whose aspiration efficiency curves matches the fractional International Commission on Radiological Protection (ICRP) deposition curve for human respiratory tract below ~300 nm. Tsai et al. [2012] have developed a personal nanoparticle sampler which simultaneously collects both respirable and nanoparticles fraction (<100 nm aerodynamic diameter).

The PM_{10} standard for environmental sampling is very similar to the thoracic convention and impactors with a 10 μm cutoff size have been used for personal PM-10 sampling [Buckley et al. 1991]. A cascade impactor, e.g., the Andersen personal cascade impactor (Figure 2J), can be used to calculate the thoracic fraction of an aerosol. Although a thoracic sampler is commercially available (Figure 2I), further work is needed to determine its applicability for specific types of aerosol. For example, a thoracic sampler for fibers must result in a uniform deposit of the particles on the filter for accurate analysis results.

The overall accuracy of a classifier with respect to sampling in accordance with the one of the sampling conventions can be estimated using a bias map (Figure 3). The bias map displays the percent difference between the predicted mass collected by the sampler and the mass expected according to the convention as a function of the parameters of a lognormal particle diameter distribution for a range of likely workplace distributions. Such a bias map can be used for selecting a sampler for a workplace having a certain range of particle sizes or for developing samplers that agree more closely with the sampling conventions.

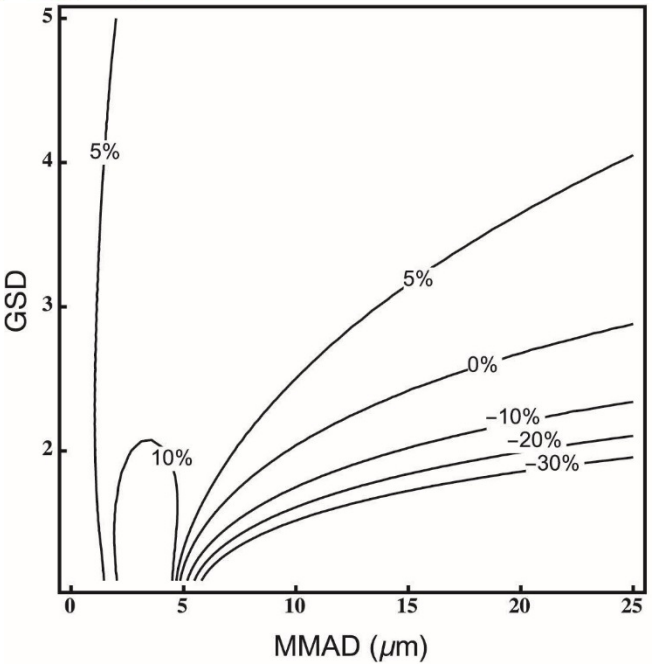

Figure 3. Bias map for the 10-mm nylon cyclone (operated at 1.7L/min) compared with the respirable convention [Courbon et al. 1988]. The contour lines represent percent bias for specific lognormal size distributions. The calculation of this map is based on laboratory measurement of cyclone penetration and can be used with field size distributions to estimate sampling bias.

The bias map in Figure 3 was created by: (a) fitting the penetration curve for the 10-mm nylon cyclone (Figure 2G) [Gudmundsson and Lidén 1998] at 1.7 L/min with a lognormal curve (a logistic curve also can be used), (b) calculating the bias between the respirable convention and the curve from the previous step for a range of lognormal size distributions, and (c) plotting the bias contour lines as a function of the size distribution mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD). The 10-mm nylon cyclone shows significant negative biases, especially at large MMADs and small GSDs, because the cyclone penetration curve drops off more rapidly with size than the curve for the respirable convention. The "best" flow rate to use in a workplace when sampling according to one of the conventions becomes a matter of judgment, depending on the size distribution typically encountered in that workplace. A cyclone that fits the convention more exactly will exhibit smaller biases throughout the entire size distribution range. Bias maps are available for several respirable samplers [Chen et al. 1999b; Görner et al. 2001]. It should be mentioned that in some cases, e.g., coal mine dust sampling, a single sampler is specified by regulation. This sampler specification eliminates the question of bias for that type of measurement.

Investigation of the effect of changing the physical dimensions of a commercial cyclone resulted in modifications that improved the match to the respirable sampling convention

[Lidén and Gudmundsson 1996]. Chen and coworkers developed a virtual cyclone that appeared to give excellent compliance with the respirable curve [Chen et al. 1999a]. It is possible to make samplers that have predicted biases less than 10% over the entire range of likely workplace size distributions. While the behavior of certain samplers, such as impactors, can be predicted theoretically, it is still important to measure penetration curves experimentally to ensure correct application of the theory. Bias maps based on these data then allow estimation of accuracy for a specific workplace application. As improved samplers are tested and become commercially available, more accurate thoracic and respirable aerosol measurement on a routine basis will be possible.

As mentioned above, several inhalable samplers were investigated in a wind tunnel to evaluate their sampling efficiency compared to the inhalable convention [Kenny et al. 1997]. Based on these data, sampler performance (maximum bias confidence limit) was ranked [Bartley 1998] and the IOM, GSP, and CIP-10 samplers were rated the best.

As interest in the new particle size-selective conventions by standards setting bodies has grown, efforts have been made to define protocols to guide the testing and validation process for available samplers. One approach was developed by the CEN [Lidén 1994; CEN 1998]. In the CEN model, for any given sampler to be tested, the first step is a critical review of the sampling process for the instrument in question. This is intended to identify factors that may influence the performance of the sampler, including particle size, windspeed, aerosol composition, filter material, etc. This is essential in the process of sampler evaluation, determining under what conditions the sampler will need to be tested. Three options are then presented for the testing of samplers: (a) the laboratory testing of samplers to compare performance with the sampling conventions, (b) the laboratory comparison of instruments, and (c) the field of comparison of instruments. Research projects have been conducted in recent years to define testing protocols (option a), funded both by the European Community and by NIOSH, to consolidate the scientific basis for such protocols and to identify improved and more cost-effective methods.

4 Sampler assembly

Some samplers are designed such that improper assembly can result in internal leakage, i.e., aerosol particles bypassing the filter. This bypass leakage has been noted in the 37-mm closed-face cassette [Frazee and Tironi 1987; Van den Heever 1994]. Although at least one study found no problem with hand assembly of these cassettes [Puskar et al. 1991], NIOSH and others have occasionally observed, after sampling black or colored dusts, streaks of dust on the filter's compression seal region or an incomplete compression mark, indicating aerosol leakage bypassing the filter. An airtight seal in these cassettes is achieved by compression of two plastic parts that must be parallel and joined with the proper force. If this seal is not

compressed with sufficient force, the vacuum behind the filter may pull the filter from the seal, especially at high flow rates. Too high a compression force results in cracking the cassette or cutting the filter, also producing leakage.

Prudence dictates that a check of cassette integrity and the seal area on each filter should be made after sampling to ensure that the cassette was properly assembled; otherwise, the sample may underestimate the actual exposure.

At least two approaches to eliminating the sealing problem with press-fitted cassettes have been taken. One was to assemble the cassette using a press. Pressing the cassette together by hand often produces misalignment of the cassette parts, resulting in bypass leakage. Frazee and Tironi [1987] designed a mechanical press that held the two cassette pieces in proper alignment, while applying just enough pressure to effect a seal, but not so much as to cause cracking of the plastic. This press was designed to allow motion of the cassette pieces to compress to a certain distance. A commercial pneumatic press (Accu-Press™, Omega Specialty, Chelmsford, MA) used a selected pressure to compress the cassette components. For additional information on bypass leakage and bypass leak test procedures see [Baron 2002]. The second approach was to redesign the cassette to provide a more positive filter seal [Van den Heever 1994]. In a well-designed sampler, opening the seal should not cause tearing and loss of the filter or collection medium during removal from the sampler.

The 37-mm closed-face cassette is usually sealed with tape or shrink bands around the outside. There is a common misconception that this seal prevents bypass leakage in the cassette. These external seals primarily cover the joint between the cassette components to prevent deposited particles on the external surface of the cassette from contaminating the sample during filter removal. The tape or shrink band also aids in holding the cassette together and preventing external air leakage. However, Puskar, et al. [1991] found that even by using this precaution, a significant amount of dust was found downstream of the filter. The authors hypothesized that this dust was deposited during filter removal.

Three other commercial samplers, the IOM (Figure 2B), the CIS, and the coal mine dust sampler (MSA, Inc., Pittsburgh, PA) use a cartridge to hold the filter. For the first two samplers, an external threaded cover applies pressure to the cartridge to ensure a good seal around the filter. This prevents twisting at the filter surface while creating positive, even contact around the filter edge.

5 Electrostatic losses

Most aerosol particles generated in workplaces have electrostatic charge levels considerably higher than the steady-state or equilibrium charge level [Johnston et al. 1985]. The

equilibrium charge (Boltzmann equilibrium) levels are usually achieved after particles are suspended in the ambient atmosphere for approximately an hour in the presence of naturally occurring atmospheric ions of positive and negative polarity. When freshly generated particles are sampled in the presence of an electric field, as when a sampler walls are highly charged [Baron and Deye 1990b], the particle trajectories can be modified to such an extent that the particles are inefficiently sampled. No electrostatically induced particle motion occurs when either the particle charge or electric field during sampling is zero. When both the sampler walls and particles are both highly charged, external force on the particles from electrical field is much greater than that caused by gravity, inertia, diffusion or other mechanisms.

Samplers can achieve a high charge level when they are electrically insulated from ground and are triboelectrically charged (i.e., by contacting or rubbing against other surfaces); this sampler charging, as well as particle charging, tends to occur more frequently at low (<20% RH) humidity levels. Certain plastic materials, such as polycarbonate, polytetrafluoroethylene, polyvinyl chloride (PVC), and polystyrene readily retain high charge levels; others, such as Tygon® or conductive silicone rubber tubing retain relatively little charge [Liu et al. 1985]. The PVC/polystyrene copolymer used in the 37-mm closed-face cassette is an excellent electrical insulator and can retain high charge levels on its surface. These charges can be incorporated in the bulk plastic during manufacture or accumulated on the surface by handling or contact with other objects; the charge levels and polarity are highly localized and variable. Such samplers can exhibit particle losses to the internal walls of the cassette and negative sampling biases [Baron and Deye 1990a]. Non-conductive plastic asbestos samplers were shown to produce large negative biases and variable results [Baron and Deye 1990a,b; Baron et al. 1994].

Conductive samplers have demonstrably lower losses when sampling charged particles. Metal samplers obviously have high conductivity. Samples collected using nylon cyclones were shown to exhibit higher variability [Almich and Carson 1974; Briant and Moss 1984] and negative biases [Briant and Moss 1984] when sampling charged dusts. However, the degree of conductivity required is not high; as long as charges can move over the sampler surface and reach equilibrium in seconds, the effect of charges transferred to the sampler is likely to be minimized. Materials with this low level conductivity (surface resistivity <108 ohms/square) are often termed "static-dissipative." Graphite-loaded plastics were developed that have adequate conductivity to distribute charges over the surface of the cassette (e.g., the 25-mm asbestos sampler). A simple test to ensure adequate conductivity of these samplers can be performed by attaching a good quality multimeter at any two points on the sampler surface. Resistance readings in the range of tens of megohms or less indicate sufficient conductivity for sampling purposes.

Some metals are coated with a thin, non-conductive layer, e.g., anodized aluminum. These coatings may retain a surface charge, but this charge will induce an opposite charge in the conductive layer beneath the surface, effectively canceling out the field produced by the surface charge. Recent measurements at NIOSH using a non-contacting electrostatic voltmeter (Model 300, Trek Inc., Medina NY) indicated that no significant external field (<50 volts) could be produced near an anodized surface by rubbing the surface with various plastics or other materials. Plastic or cellulose-based materials rubbed in a similar manner produced electrostatic potentials measured in the hundreds to thousands of volts. Thus, metals with a thin, insulating surface layer are not likely to produce significant external fields that would affect aerosol sampling.

Digestible cassette inserts or capsules, consisting of a static-dissipative plastic dome directly sealed to a filter, have been developed for metals analysis that substantially reduce the error associated with wall losses [Ashley et al. 2013].

A further electrostatic problem not specifically associated with the cassette is the use of filters made of highly nonconductive materials, such as PVC, polytetrafluoroethylene, or polycarbonate. In addition to having desirable chemical properties, these filters have the advantage of not absorbing water from atmosphere, leading to improved weight stability [Lowrey and Tillery 1979; Bowman et al. 1984; NIOSH 1994]. However, these filters can retain a high electrostatic charge level, resulting in non-uniform particle deposition and even repulsion of particles from the filter surface. Such filters are also more difficult to handle during weighing because of charge effects. Even filters that are normally more conductive, such as cellulose-based filters, can become non-conductive and exhibit non-uniform particle deposition and particle losses at very low humidity levels (<10% RH) [Chen and Baron 1995].

A treatment was developed to make filters more conductive without significantly affecting weighing accuracy or moisture absorption [Mark 1974]. In one study, it was found that applying this treatment to the filter decreased particle losses from 14% to 2% [Blackford et al. 1985]. Anti-static sprays are available that leave a temporary static-dissipative coating on surfaces.

6 Sampler deposition uniformity

Some analytical methods require that sampled particles be deposited uniformly on the filter surface. For instance, asbestos fiber analysis by microscopy requires uniform deposition of fibers on the filter for accurate results. Direct silica analysis of collected filter samples also is improved with uniform particle deposition. Classifiers using inertial or gravitational forces tend to stratify the aerosol stream. A small, high velocity inlet in a sampler, such as the 4-mm opening in the 37-mm closed-face cassette, can also result in the larger particles being

deposited in a small central area on the filter. Even sampling at high flow rates through more open inlets can cause a non-uniform deposit [Feigley et al. 1992]. This results in particle deposits that vary in uniformity as a function of particle size. Such deposition patterns are visible when sampling colored particles [Sass-Kortsak et al. 1993]. Open-pore foam classifiers may improve the uniformity of particle deposits on the filter, but have not been thoroughly evaluated [Aitken et al. 1993; Vincent et al. 1993]. Careful design of classifiers to ensure mixing of the aerosol prior to deposit on the filter may result in adequate uniformity [Fang and Lippmann 1995]. Even inhalable samplers or samplers that have no classifier may be prone to non-uniform deposits under certain conditions of sampler orientation relative to gravitational settling, orientation relative to external winds, or when sampling charged particles [Baron and Deye 1990b; Liu et al. 1985; Baron et al. 1994; Chen and Baron 1995]. Flaring the inlet of such a sampler, as in the commercial "bell-mouth cowl," (Figure 2F, Envirometrics, Charleston, SC), is one approach to improving sample uniformity under anisokinetic conditions [Feigley et al. 1992]. In another study, a sampler having an inlet screen (button sampler, Figure 2D, SKC, Inc. Eighty Four, PA) exhibited improved filter deposit uniformity when compared to a closed-face cassette [Hauck et al. 1996].

The filters in some samplers require support to prevent tearing or distortion of the filter. The support device may cause occlusion of parts of the filter surface, resulting in non-uniform particle deposits [Hook et al. 1983].

On occasion, it was observed that poorly-sized tubing connectors protruded into the 37-mm cassette and touched the filter surface. This caused all the airflow to pass through the filter adjacent to the small area of the connector opening. When undetected, this caused low sampling efficiency and pump failure because of the high pressure drop.

7 Sampler wall losses

Particle deposits on internal surfaces (i.e., wall losses) of the 37-mm closed-face cassette for several hundred field measurements were found to be large and highly variable (2 - 100% of dust collected in the cassette) [Demange et al. 1990]. Another study found only 22% of the dust on the filter, 65% on the upstream portion of the cassette, and 22% downstream of the filter [Puskar et al. 1991]. In a study of an in-line cassette of similar shape, it was found that the internal wall deposition of particles could be largely eliminated by: (a) making the cassette conductive, (b) creating an aerodynamically smooth surface having no corners for eddies to form, and (c) decreasing the diameter of the filtration area so that dust does not deposit on the filter adjacent to the upstream walls of the cassette [Blackford et al. 1985]. By incorporating these three corrective measures, the wall losses in the latter cassette were reduced from 25-30% to 5%. These losses appear to be caused by a combination of electrostatic, inertial, gravitational and diffusion mechanisms.

Another solution to the problem of not capturing 100% of the sampled particles on the filter is to use an internal capsule sealed to the filter. All the particles collected in the combined filter capsule are analyzed. The air stream entering the cassette is surrounded by the cartridge and any deposition on the walls of the capsule is retained for analysis. The IOM sampler for inhalable dust uses this approach by having a cartridge form the inlet of the sampler (Figure 2B). This approach also has been used in the in-line cassette of the coal mine dust personal sampling unit (MSA, Pittsburgh, PA) where an aluminum foil cover is crimped onto the filter. A similar cartridge was designed for the 37-mm closed-face cassette in measurements of pharmaceutical dust [Puskar et al. 1992]. Capsules made of "static dissipative" plastic for gravimetric analysis and capsules composed of cellulosic media for elemental analysis are commercially available (Accu-Cap™, Omega Specialty Instruments, Chelmsford, MA; Woodchek™, MSA Inc. Pittsburgh, PA). It is important that capsule material be compatible with the analytical method. For instance, the plastic material used in the first version of the IOM sampler cartridge (Figure 2B, SKC, Eighty Four, PA) was found to absorb milligrams of water over periods of days, making the accuracy of gravimetric measurements problematic [Smith et al. 1997; Li and Lundgren 1999; Lidén and Bergman 2001]. Demange et al. [2002] more recently demonstrated significantly improved agreement between inhalable sampling using the IOM sampler and the 37-mm cassette by including all deposits inside the cassette. This suggests that the accuracy and precision of the 37-mm cassette can be improved by including internal sampler deposits by wiping or washing, or by using an internal capsules [Ashley and Harper 2013; Harper and Ashley 2013; Andrews et al. 2016].

8 Collection media and analytical issues

Interaction of particulate filter with the sampled aerosol and the flow can lead to certain measurement errors, which are sometimes referred to as filter artifacts. These artifacts can include adsorption of gases and vapors from the air stream, the adsorption or desorption of moisture by the filter media, evaporation of volatile or semi-volatile organic matter from the filter media, and particle bounce from the filter media. All these factors can contribute to the measurement bias.

The filter medium should be compatible with the analytical method. Some analytical methods require specific filter media or properties. For instance, atomic absorption and inductively coupled plasma analyses typically require complete ashing of the filter material; organic compound analyses require that no reaction or adsorption of the compounds occur at the filter surface. Several studies have dealt with gravimetric stability of different filter types and recommended specific procedures [Lowrey and Tillery 1979; Bowman et al. 1984; NIOSH 1994; ASTM 2000; Chow 1995; Raynor et al. 2011]. Generally, plastic materials that do not absorb water (polycarbonate, polyvinyl chloride, polytetrafluoroethylene) are more weight

stable than natural cellulose-based materials; uncoated glass fiber filters also may absorb water [Lowrey and Tillery 1979; Bowman et al. 1984; NIOSH 1994; ASTM 2000; Chow 1995].

Controlled environmental conditions in the weighing room, where temperature and humidity are strictly controlled, are essential to reduce measurement bias in gravimetric analysis. In a controlled study Tsai et al. [2012] have shown that the mass of MCE membrane filters was less stable than that of the glass fiber filters in both controlled and uncontrolled environmental conditions. Also, they found that under uncontrolled conditions (where humidity and temperatures were not controlled), glass fiber filter mass was much less stable than that of PTFE and PVC membrane filters. MCE and glass fiber filters demonstrated significantly better stability under controlled conditions; whereas the PVC and especially the PTFE filters were found to be extremely stable in both controlled and uncontrolled conditions [Raynor et al., 2011]. Other non-aqueous vapors can also adsorb to the filter media or previously collected particulate deposits. However, these artifacts are typically important only for semi-volatile organic compounds.

It should be noted that weight stable materials also tend to be more highly charged, resulting in more charged particle repulsion and deposit non-uniformity. When a plastic (Tyvek®) backup pad is crimped into a cartridge together with a filter, the weight stability of the cartridge may suffer [Kogut et al. 1999]. To improve the weight stability of coal mine dust sampler cartridges, stainless steel backup pads have been used by MSHA. The IOM sampler can be purchased with either a plastic or a stainless steel cartridge. The plastic cartridge has been shown to exhibit poor weight stability and should not be used for gravimetric analysis [Smith et al. 1997; Lidén and Bergmann 2001].

Lawless and Rodes investigated the use of modern electronic balances to determine factors affecting the accuracy of gravimetric measurements and found that balance stability, balance leveling, vibration and thermal drafts, electrostatic charge reduction, positioning of the filter in the balance so that the filter did not hang over the edge of the pan, and temperature and humidity control were all important in achieving accurate results [Lawless and Rodes 2001].

Although not strictly a problem with the collection medium, the sampler construction material should not outgas vapors that can condense on the collection medium and affect the analysis. Early (circa 1970) versions of the closed-face cassette were made of a plastic called "tenite," which resulted in weight gain of the filter over time. This currently does not appear to be a problem.

Impactors have been used as samplers and, especially with cascade impactors, the deposits on the impaction stages are measured. Particle bounce from the collection substrates on the impaction plates can be severe, especially for large solid particles impacting onto a smooth

metal plate [Marple and Olsen 2011]. Bounce can also be significant for highly nonspherical, low density particles, as was shown recently for nanotubes agglomerates [Birch et al. 2011; Maynard et al. 2004; Baron et al. 2008]. Several modifications to the collection substrate are available to improve collection efficiency of each stage. These modifications should be compatible with the analytical method. Oil can be placed on the collection substrate that wicks up over collected particles and continually provides an oiled surface. To avoid the interference or contamination of particles by oil, the following scheme has been used in recent studies: a pair of cascade impactors was prepared for sampling at a given location. Oiled filters were used on every other stage of each impactor. One of the impactors was loaded with oiled filters on Stages A and C, while Stages B and D were uncoated and used to sample particles onto the substrates. The second impactor contained oiled filters on Stages B and D, while Stages A and C were used for particle sampling. This approach provided data for all four stages (plus after filter) and minimized bounce to the adjacent lower stage [Baron et al. 2008; Birch et al. 2011]. A filter or sintered metal can be used to provide a reservoir for this oil. For gravimetric analysis, this oil must have a low vapor pressure and not migrate off the collection substrate. Alternatively, grease can be used, but after the surface is coated with collected particles, additional particles are more likely to bounce. Filters have also been used as substrates and provide a convenient substrate that is somewhat better than a smooth metal surface. Selection and use of an impactor is a complex issue and has been described in reviews [Lodge and Chan 1986; Marple et al. 2001]. Accurate analysis of cascade impactor data can also be difficult and simple regression analysis of the data may not provide the best answer [Marple et al. 2001; Kandlikar and Ramachandran 1999; Cooper 2001].

9 Sampler field comparisons

Direct field comparisons of various samplers are frequently reported in the literature. Because of the typical high variability of aerosol concentrations and size distributions in workplaces, it is difficult to use these situations for accurate assessment of sampler performance. However, field studies are important to verify the overall performance of a sampler and to indicate specific sampler issues. The problems with samplers as discussed above can be highlighted with some examples observed in field studies.

a. Sampler bias affected by internal deposits

A study of wood dust sampling comparing collocated free-standing samplers indicated that an MSA cassette (having an aluminum cartridge crimped onto the filter) used as a sampler gave two times better precision and collected 2.6 to 3.5 times more dust than the standard 37-mm closed-face cassette [NACSI 1992]. Both these samplers have the same size and shape of inlet. The same study showed that the IOM sampler collected 1.3 times more dust than the MSA cassette, indicating that the particle size, inlet shape and inlet orientation are important factors in inhalable sampling. Among a number of inhalable

samplers in current use around the world, the IOM sampler appears to agree the best with the inhalable dust sampling convention [Kenny et al. 1997; Bartley 1998]. Several studies have shown that the IOM sampler collects anywhere from slightly more to 3.5 times more dust than the closed-face cassette [Vaughan et al. 1990; Burdorf et al. 1994; Notø et al. 1996; Perrault et al. 1996; Wilsey et al. 1996]. However, Demange et al. showed that for several work sites with relatively small MMAD (about 15 μm diameter), measurements from 37-mm cassettes agreed well with the IOM results if the deposits on the internal surfaces of the cassette were added to the filter analyte [Demange et al. 2002; Harper and Demange 2007]. Measurements with the 37-mm cassette are not expected to agree as well with the IOM when the particle sizes are much larger because of differences in aspiration efficiency. However, by including all aspirated material, i.e., all material entering the 37-mm cassette inlet, in the analysis, agreement with the inhalable convention can be improved.

b. Sampler precision affected by internal deposits

The issue of measurement bias from internal wall deposits in the sampler has gained increasing recognition over the past few decades [Ashley and Harper 2013]. Though it is now widely recognized that the wall deposits must be included in the analysis, many published methods have not been modified. OSHA currently recommends including wall deposits.

In a field study of lead dust, it was found that the measurements from a closed-face 37-mm cassette gave a coefficient of variation (CV) of 1.0 and 0.33 when sampling at 2 L/min and 10 L/min, respectively, while the button sampler gave a CV of 0.10 under the same conditions [Hauck et al. 1996]. The button sampler has few internal surfaces for wall deposition, suggesting that elimination of this type of loss would improve the precision of the 37-mm cassette. Demange et al. [2002] found improved precision for the 37-mm cassette data when the wall deposits were added to the analyte.

In spite of some of its drawbacks, the 37-mm cassette is likely to be used for some time. It appears that from the standpoint of improving agreement with the inhalable convention and improving precision, the inhalable sampler wall losses should be minimized through sampler design (or through use of a cartridge such as the AccuCap or in the MSA coal mine cassette) or the wall deposits should be included in the analysis.

10 Conclusions

Clearly, when proper features are incorporated in the sampler design, significant improvements in bias and precision can be achieved for some currently used aerosol samplers. Several recommendations regarding the application of these samplers are listed:

- Classifiers used to select respirable, thoracic, or other fractions should be evaluated based on bias maps obtained from experimental data and combined with particle size distributions from workplace measurements to evaluate their applicability.

- Further research and development is needed to improve sampler design to better match ACGIH/ISO conventions and reduce inter-laboratory variability in conducting aerosol sampling. It is important to report the sampler and flow rate used to allow evaluation of potential biases due to sampling. It is also important to account for wall losses to reduce overall bias and allow better comparison across different samplers and ISO standards.

- The filter cassette and fittings should be air-tight and have no bypass leakage. A pneumatic or mechanical press should be used to assemble the cassette and a leak test should be used to establish appropriate pressure and proper assembly procedures. See [Baron 2002].

- The sampler should be made of conductive or static-dissipative materials.

- Internal deposits in sampling cassettes should be included in the analysis. One approach to improving the closed-face cassette measurements is to use an internal digestible cassette insert or cartridge that collects all the sampled dust entering the cassette. The cartridge must be compatible with the analytical method. Another approach is to wipe or wash the internal surfaces of the cassette and add this material to the filter analyte.

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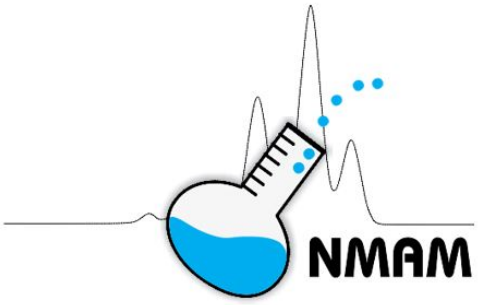

NIOSH Manual of Analytical Methods (NMAM), 5th Edition

Filter Pore Size and Aerosol Sample Collection

by William G. Lindsley, PhD, NIOSH

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

1 Introduction

Aerosol sampling filters are commonly used in industrial hygiene and environmental monitoring to collect airborne particles for analysis. The filter characteristics provided by the manufacturer frequently include the term "pore size" or "equivalent pore diameter," and pore size is also specified in many particle-sampling methods written by government agencies and standards organizations. Unfortunately, the pore size of a filter is often misunderstood, which can lead to the misinterpretation of test results and the selection of filters with much higher flow resistances than are needed for a particular application. The purpose of this article is to discuss how aerosol filters actually work and what the equivalent pore diameter really means, and then to explain how this information should be used when selecting filters and interpreting data. Much of the information and terminology presented here were drawn from Hinds [1999], Brock [1983], Lippmann [2001] and Raynor et al. [2011]. All of these sources provide a more in-depth discussion of filter theory and use and are highly recommended if more information is desired.

2 Physical structures of filters

To understand what the term "pore size" does and does not indicate for filters, we begin by looking at the physical structures of some different types of filters. Most filters used in aerosol sampling fall into one of three categories. Fibrous filters like the glass fiber filter shown in Figure 1A consist of a deep mesh of fibers with random orientations. Porous membrane filters, such as those made from mixed cellulose esters (MCE) or polytetrafluoroethylene (PTFE), have a complex structure with tortuous routes through the filter material as shown in Figures 1B and 1C. A capillary pore filter consists of a thin, smooth polycarbonate (PC) or polyethylene terephthalate (PET) film with circular pores, as shown in Figure 1D. These are also called straight-through pore filters or track-etch membrane filters (because of the manufacturing method), or Nucleopore filters after the original manufacturer.

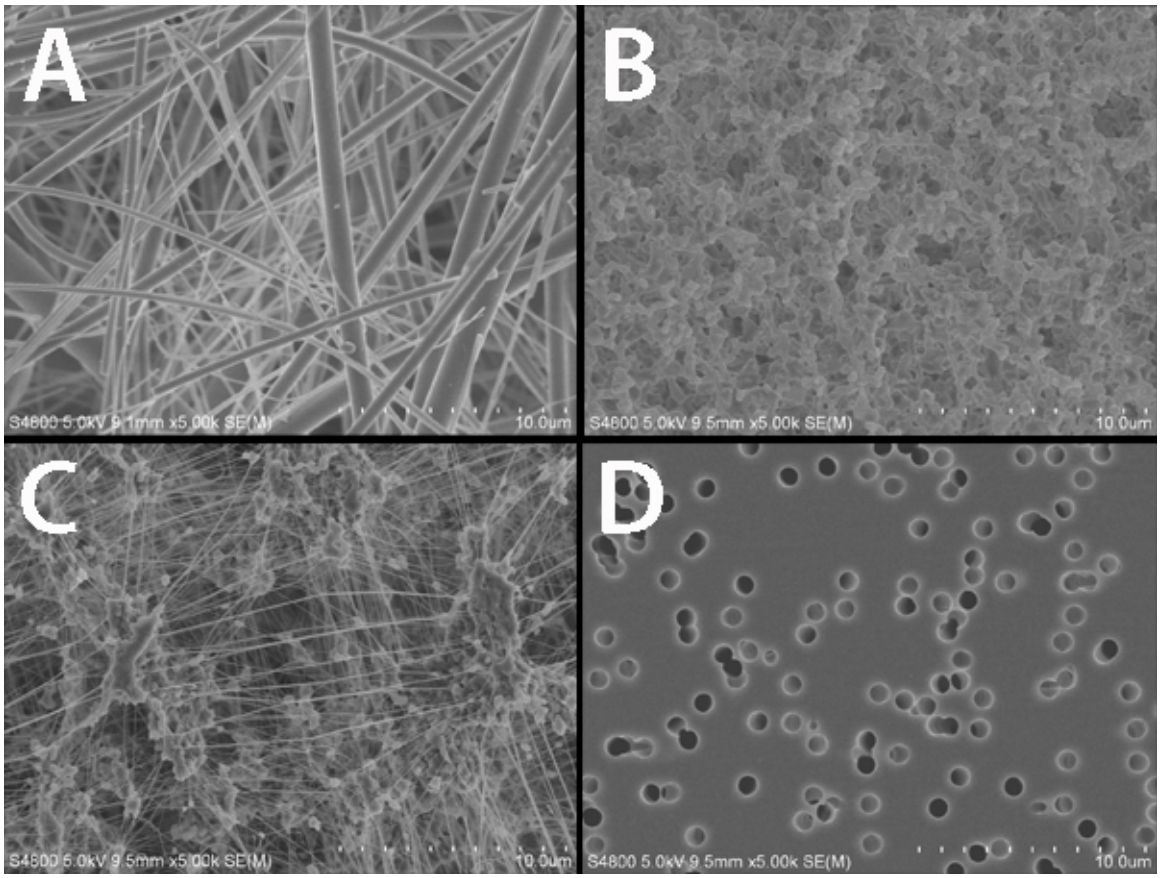

Figure 1: Scanning Electron Micrographs (SEM) of four filter types. The vertical tick marks above "10.0 µm" in the lower right-hand corner of each SEM are 1 µm apart; the entire scale is 10 µm in length.
A: Glass fiber filter with a 1-µm equivalent pore diameter.
B: Mixed-cellulose esters (MCE) filter with 0.8-µm equivalent pore diameter.
C: Polytetrafluoroethylene (PTFE) filter with 3-µm equivalent pore diameter.
D: Polycarbonate capillary pore filter with 1-µm pore size.

3 Determination of equivalent pore diameter

So what is the pore size of a filter? For the capillary pore filter, the pore size is relatively straightforward: the pores are circular and reasonably uniform and run straight through the filter material, so the pore size is the diameter of the pores. This is what many people imagine when they think of the pore size. However, the other types of filters do not have these simple pore structures. The filter material forms intricate paths, and the airstream lines twist and turn as they pass through the filter. Thus, because these filters do not have an obvious, simple dimension that characterizes their pores, an "equivalent pore diameter" is used to describe the filters. This provides a useful way to categorize filters with different sized openings and to ensure consistent performance characteristics. When a manufacturer specifies the pore size of

a filter, they are giving the actual pore diameter for capillary pore filters and the equivalent pore diameter for other types of filters.

The equivalent pore diameter is commonly measured by a "bubble-point test" [ASTM 2011]. This test is fairly simple, is non-destructive, and provides a good quality-control check for the filter. A bubble-point test works like this: Imagine that you have an ideal capillary pore filter with smooth holes that are of a uniform diameter, as shown in Figure 2. Now imagine that there is air on one side of this filter and a liquid that wets the filter on the other side. If the air pressure is low, the surface tension of the liquid will stop the air bubble from being pushed through the filter. If you slowly increase the air pressure, at some point it will be high enough to overcome the surface tension, and a visible stream of air bubbles will be produced. This pressure is called the bubble point. The pore diameter can be calculated from the bubble-point pressure with this formula [Brock 1983]:

$$D = \frac{4\gamma \cos\theta}{P} \times 10^6 \qquad \text{(Equation 1)}$$

Where:

D = pore diameter (micrometers)
P = bubble-point air pressure (Pa)
γ = surface tension of the liquid (N/m)
θ = contact angle between the liquid and the filter material

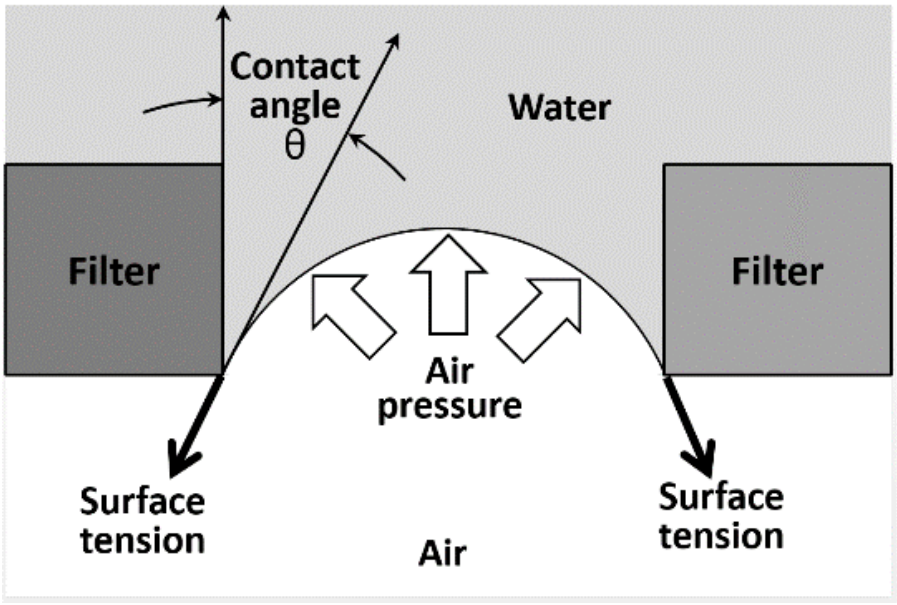

Figure 2: Principle of the bubble-point test.

Note that as the pore diameter gets smaller, more air pressure is required for air to bubble through the ideal filter (Figure 3). Thus, you could take your actual filter and see how much air pressure is needed to bubble air through it. You could then calculate the pore size of an ideal filter that requires the same amount of air pressure to form bubbles as does your actual filter using Equation 1. The pore size of an ideal filter with the same bubble point as your actual filter is the "equivalent pore diameter" of your filter.

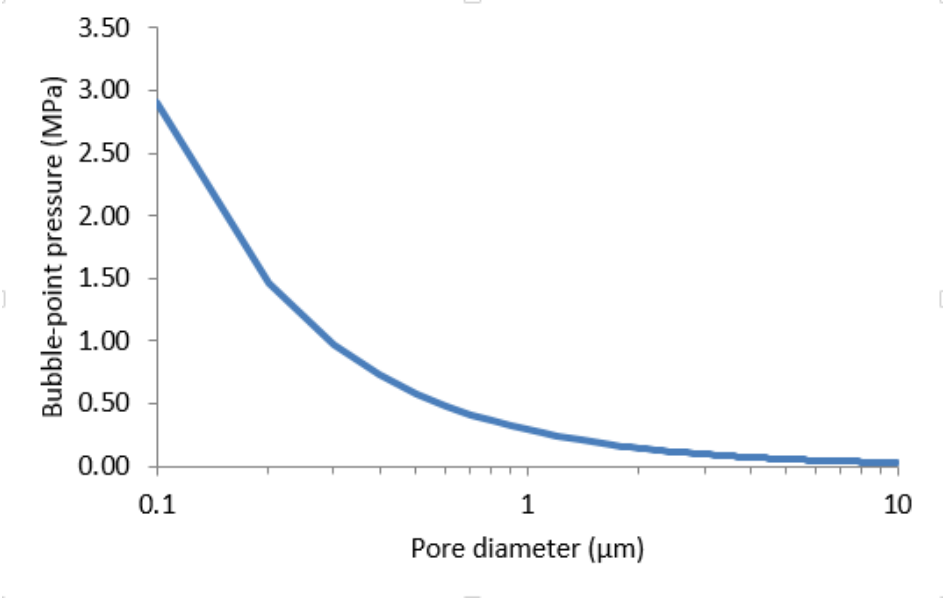

Figure 3: Pore diameter vs. air pressure for ideal filter in bubble-point test. The curve was calculated with use of water (which has a surface tension of 72.8 mN/m) as the liquid. It is assumed that the water completely wets the filter material, and thus the contact angle θ = 0°. Calculated using Equation 1.

Two things should be observed at this point. First, because less air pressure is required to push bubbles through larger openings than through smaller ones, the bubble-point test indicates the size of the largest pores in the filter, not the average pores. For this reason, the bubble-point test is useful for quality control checks of filters, since it will indicate if defects or excessively large pores are present. However, if the filter has a wide range of pore sizes, most of the pores will be smaller than the equivalent pore diameter determined by this test.

Second, the equivalent pore diameter provides a convenient reference point for describing and comparing filters of the same type, but not of different types. For example, the openings in a porous membrane filter with a 5-µm equivalent pore diameter will be somewhat larger than the openings in a porous membrane filter with a 1-µm equivalent pore diameter. However, the pore sizes of different types of filters cannot be meaningfully compared; a capillary filter with a 1-µm pore size bears little resemblance to a porous membrane filter with a 1-µm equivalent pore diameter.

4 How an aerosol filter collects particles

Now that you understand how the equivalent pore diameter is determined, let's discuss how this relates to aerosol sampling. First, we need to review how aerosol sampling filters collect airborne particles. People often assume that a filter works like a sieve—that is, that a filter is like a sheet or mesh with holes of a particular size, and that particles larger than the holes collect on the filter while particles smaller than the holes pass through it. In fact, aerosol filtration is far more complex than this simple model would suggest, and one consequence is that aerosol filters can efficiently collect particles much smaller than would be expected on the basis of the pore size of the filter.

When an airstream containing airborne particles passes through a filter, the particles are collected by five mechanisms (Figure 4):

1) *Interception:* Interception occurs when a particle moving with the airstream contacts the filter material. Intercepted particles include those that are bigger than the filter pores (sieving), and also particles that are smaller than the pores but are carried close enough to touch the surface of the filter as they follow the airstream. The closer the diameter of the particle is to the diameter of the opening in the filter, the more likely interception is to occur. Interception can be very important in the collection of fibers and other irregularly shaped aerosol particles because an elongated particle is more likely to come in contact with the filter, especially if it is sideways to the flow or if it is tumbling [Issacs et al. 2005].

2) *Impaction:* Impaction occurs when the airstream changes direction abruptly and the inertia of a particle causes it to continue in its original direction and collide with the filter material. Impaction is analogous to an insect hitting the windshield of a car driving on a highway: the air molecules can quickly change direction and move up and over the car, but the inertia of the insect causes it to change direction more slowly and impact the windshield. The likelihood that a particle will deposit by impaction increases proportionally with the density, velocity and diameter^2 of the particle. Impaction usually is most important for larger particles (around 1 μm and larger) because of their greater inertia.

3) *Diffusion*: Brownian motion causes small aerosol particles to move randomly and disperse within an airstream. If the particles collide with the filter material, they can deposit on it. Diffusion is most important for particles of around 0.1 μm and smaller.

4) *Electrostatic attraction:* Aerosol sampling filters may carry an electrostatic charge, which can attract charged airborne particles. Charged filter materials can also attract neutral particles by inducing a dipole within the particle, and charged particles can be attracted to

neutral filter materials by image forces (forces created when a charged particle induces an opposite charge in the filter material). This mechanism is especially important for electret-treated filters (filters treated to have permanent electrostatic charges).

5) *Sedimentation:* Sedimentation (or settling) occurs when particles fall onto filter materials because of gravitational forces. Sedimentation is generally significant only for very large particles, very slow flow velocities, or if the air is flowing downward into the filter. Because of this, few particles are collected by sedimentation during most workplace aerosol sampling.

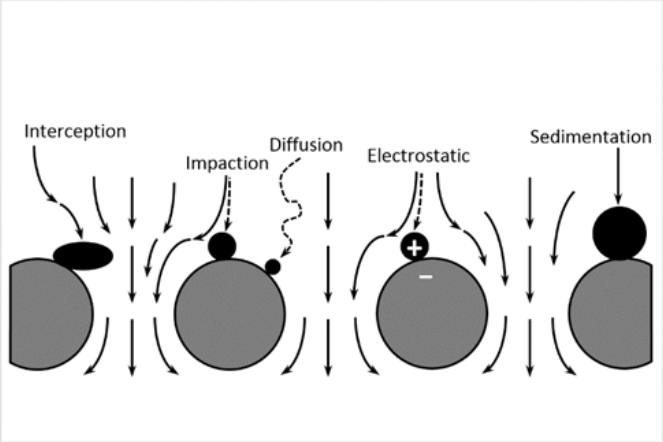

Figure 4: Aerosol particle collection mechanisms. Different types of filters have different structures but they all collect particles using the mechanisms shown here. The relative importance of the various collection mechanisms depends upon the size, shape, density and electrostatic charge of the aerosol particles and the velocity of the air flow through the filter.

An example of the collection efficiencies due to each mechanism for different aerosol particle sizes is shown in Figure 5. The effectiveness and relative importance of these mechanisms depend upon many factors. For example, a higher flow velocity favors impaction by increasing the momentum of the particles, whereas a lower velocity allows more time for particles to diffuse to the filter surface. A highly charged filter and/or aerosol will encourage electrostatic deposition. Fibers and particles with irregular shapes or branching structures are more likely to be intercepted. The filter collection efficiency remains high for nanoparticles from 10 nm down to at least 2 nm; it is thought that the collection efficiency for nanoparticles smaller than 2 nm may decrease due to thermal rebound, but this is still being investigated [Givehchi and Tan 2014; Wang and Tronville 2014].

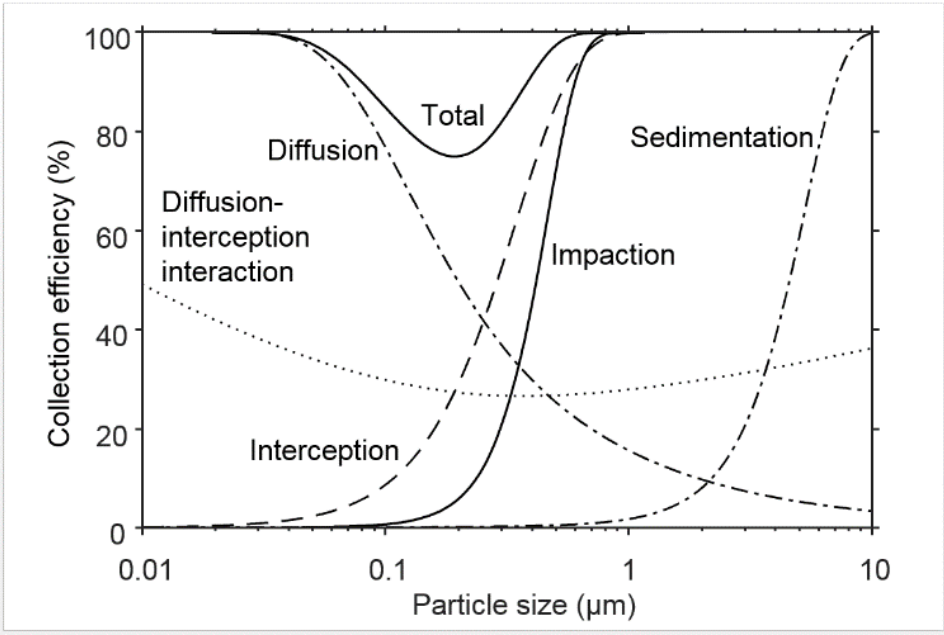

Figure 5: Theoretical collection efficiencies of aerosol particle collection mechanisms for a fibrous filter 1 mm thick with 2 µm fibers and an air velocity of 10 cm/sec. Diffusion-interception interaction is the particle collection due to an enhancement of interception by particle diffusion. The filter surface is assumed to be horizontal with air flowing downward into it, which enhances sedimentation. Total shows the collection efficiency of the filter due to all mechanisms combined. Electrostatic collection is not included because it is very difficult to model. These calculations were based on "single-fiber efficiency" for filters, which is explained in more detail in Hinds [1999]. Figure is adapted from Hinds [1999].

5 Aerosol filter efficiency and pore size

Now, with these collection mechanisms in mind, think about the structures of the different filter types shown in Figure 1. The fibrous and porous membrane filters do not have simple, well-defined pores like a sieve or a simple mesh. Instead, these filters have pathways with a broad range of sizes and a variety of irregular shapes. Thus, particles entering these filters are forced to follow a meandering path, which greatly increases the likelihood that the particles will be intercepted, impact on the filter, or diffuse onto it. For this reason, the probability that a particle will be collected by one of these filters is much higher than one might think based simply on the stated pore size (which is the equivalent pore diameter of the filters). The capillary pore filters provide a more direct pathway through the filter, but even in this case interception, impaction, and diffusion act to collect particles smaller than the sizes of the pores because of the deposition mechanisms discussed in the previous section and shown in Figure 4.

The effect of the structures of these filters and the aerosol particle collection mechanisms that we have discussed can be seen in Figure 6. This plot shows how well particles of different sizes are collected by porous membrane filters, which have tortuous flow paths with equivalent pore diameters of 0.3 and 3 µm, and capillary pore filters with pore diameters of 1 and 3 µm. Note that for all particle sizes, the collection efficiency was ≥99.7% for the 0.3-µm porous membrane filter and ≥98.4% for the 3-µm porous membrane filter, even though the test particles were much smaller than the equivalent pore diameters of the filters. The collection efficiencies of the capillary pore filters were substantially lower, but these filters were also able to collect particles much smaller than their pore sizes. This can also be seen in Figure 7, which shows submicron NaCl aerosol particles collected using a 3-µm porous membrane filter. These results clearly illustrate that the equivalent pore diameter of a filter does not indicate the size of the airborne particles that the filter will collect and that the structure of the filter has a much greater effect on the collection characteristics.

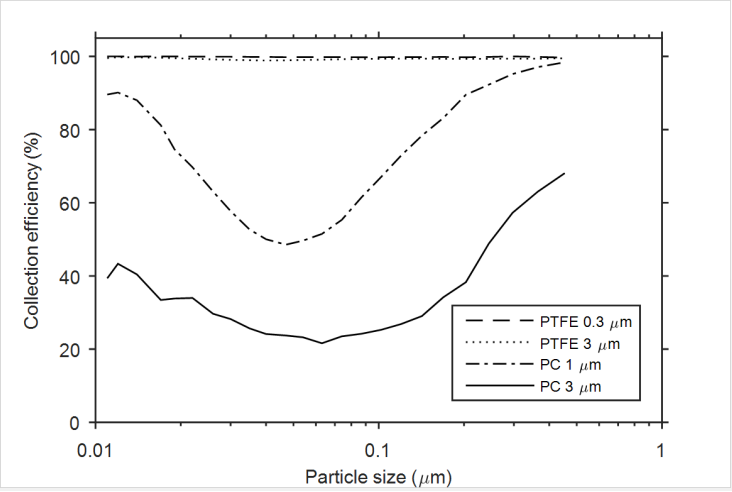

Figure 6: Aerosol particle diameter vs. collection efficiency for polytetrafluoroethylene (PTFE) porous membrane filters with 0.3-µm and 3-µm equivalent pore diameters, and polycarbonate (PC) capillary pore filters with 1-µm and 3-µm pore sizes. The differences in performance are not due to the different materials used for the filters, but rather because the porous membrane filters have tortuous paths which greatly increase the likelihood of particle deposition, while the capillary pore filters have pores that are straighter and smoother. The collection efficiency is the percentage of the particles in the airstream that are collected by the filter. The face velocity (average flow velocity of air into the filter) was 3.5 cm/s for the 0.3-µm PTFE filter and 16 cm/s for the others. The aerosol particles were NaCl. Figure is adapted from Burton et al. [2007].

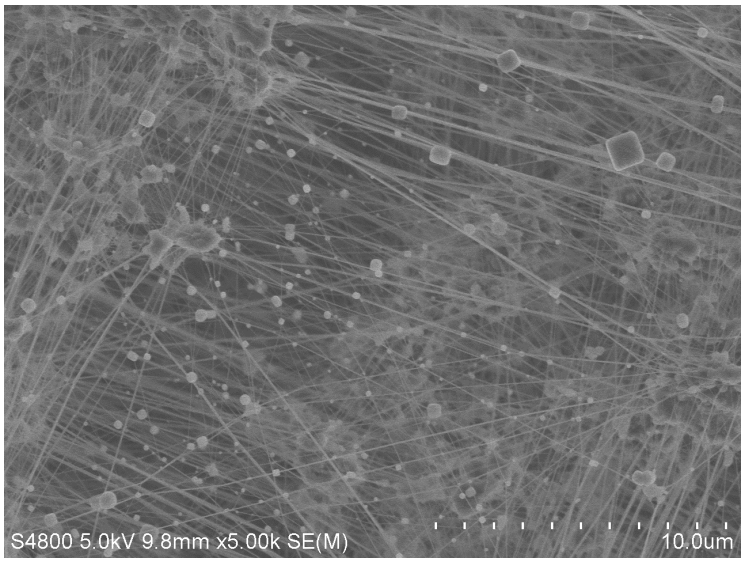

Figure 7: NaCl aerosol particles collected using a PTFE porous membrane filter with a 3-µm equivalent pore diameter at a face velocity of 8.3 cm/s. As can be seen, particles much smaller than 3 µm were captured by the filter.

It is also of interest to note that the collection efficiencies of the capillary pore filters decreased as particle size decreased down to 0.047 and 0.063 µm, and then increased as the particle sizes decreased further. This phenomenon is seen with other types of filters as well. As seen in Figure 5, this occurs because impaction decreases as the particle size decreases, which causes the overall collection efficiency curve to dip downward. However, as particles become even smaller, diffusion becomes a more important collection mechanism, and the collection efficiency increases. The particle size for which the collection efficiency is lowest is called the "most penetrating particle size", or MPPS. The MPPS for a given filter will vary depending upon the air flow rate, the electrostatic charges of the particles and the filter, the amount of particles that are deposited on the filter, and other factors [Lee and Liu 1980; Martin and Moyer 2000].

6 Significance of pore size

So why is it important to understand pore size? First, an investigator may assume incorrectly that an aerosol sample collected by a filter includes only particles larger than the stated pore size of the filter, when in fact the filter collected smaller particles as well. This can lead to a misinterpretation of test results and a misunderstanding of the actual size characteristics of the aerosol being sampled. An investigator also might wrongly try to use a filter with a particular stated pore size as a pre-filter to remove larger particles before collecting a sample; in this case, many smaller aerosol particles would be removed as well, and the true exposure to small particles could be badly underestimated.

Second, it may be mistakenly thought that two filters with the same stated pore size have the same particle collection characteristics. In fact this is not at all true for filters of different types, as seen in Figure 6: the collection efficiency of a porous membrane filter with a given equivalent pore diameter can be much higher than a capillary pore filter with the same stated pore size.

Third, a filter with a smaller pore size usually has a higher resistance to flow (and therefore a higher pressure drop across the filter) than does a filter of the same type with a larger pore size [Breuer 2012]. Thus, an aerosol sampling pump has to create a stronger vacuum to pull air at the same flow rate through a filter with a smaller pore size. If a filter with a very small pore size is selected on the erroneous belief that the small pore size is needed to collect all of the airborne particles, then the pump may not be able to reach the desired flow rate or may not be able to maintain the desired flow rate as the filter becomes loaded with particles and the flow resistance increases. This may cause the collected sample to be smaller than expected. If the sampling pump is battery powered, its running time may be greatly reduced, and the pump may even shut down prematurely.

7 Filter selection

Given all of this, what is the best way to select an aerosol filter for a particular application? The first step is to consider the purpose of the sampling and how the samples will be processed. For example, polycarbonate capillary pore filters are often used when samples are to be examined using scanning electron microscopy (SEM). Fibers are typically collected using mixed cellulose ester filters, which can be rendered transparent for counting by phase-contrast microscopy. Alkaline dusts are collected using PTFE filters, which allow for analysis by titration. For gravimetric analysis, filters that are not hygroscopic and that have stable weights, such as PVC, are needed. The characteristics of the aerosol particles to be collected also influence the choice of filter. Bioaerosols, for example, may lose viability due to damage or desiccation when collected onto filters. Liquid aerosol droplets behave in much the same manner as solid particles while airborne, but once they are collected the liquids can coat the fibers and coalesce into larger droplets, which can reduce the collection efficiency of a filter [Charvet et al. 2010; Contal et al. 2004]. In addition, oils can mask the charged regions of electret-treated filters, which can greatly reduce the collection of particles by electrostatic mechanisms [Barrett and Rousseau 1998].

The next step is to see if a recommended test method has been published for the aerosol particles of interest. Organizations such as the National Institute for Occupational Safety and Health (NIOSH), the Occupational Safety and Health Administration (OSHA), the Environmental Protection Agency (EPA), the American Conference of Governmental Industrial Hygienists (ACGIH), and ASTM International (formerly known as the American

Society for Testing and Materials) publish test methods for a variety of aerosols that include the characteristics of the filters to be used. For example, in the NIOSH Manual of Analytical Methods, Method 0600 for respirable particle sampling specifies the use of a size-selective cyclone and a "5.0-µm pore size, polyvinyl chloride filter or equivalent hydrophobic membrane filter supported by a cassette filter holder (preferably conductive.)" The NIOSH Manual of Analytical Methods also has several chapters discussing different aspects of aerosol sampling, including general considerations and factors affecting aerosol sampling, sampling bioaerosols, sampling airborne fibers, sampler wall losses, and avoiding bypass leakage in filter cassettes [NIOSH 2003; NIOSH 2014].

If a test method is not available, the collection characteristics of different types of filters can be found in reference texts such as those by Lippmann [2001] and Raynor et al. [2011]. A search of the scientific literature also can produce the results from the testing of various filters to collect different kinds of airborne particles. For example, information on the flow resistance of many types of filters and sampling tubes can be found in Breuer [2012], and Soo et al. [2016] recently tested 29 commercially available aerosol filters and reported their flow resistances and collection efficiencies. Filter manufacturers often provide data on the collection characteristics of their filters and on recommended filters for various applications. Finally, it is important to note that filter collection performance can vary with the flow rate and aerosol particle characteristics as well as the filter type and manufacturer. Thus, care should be taken when applying results from one sampling situation to a different set of conditions.

8 Conclusion

The equivalent pore diameter provides a helpful way to categorize filters and to test for consistency in filter characteristics. However, it should not be construed as an indication of the sizes of aerosol particles that will be collected by the filters. A better understanding of the meaning of the term pore size, the structures of the different types of filters, and the mechanisms by which aerosol particles are collected will help in selecting a filter for a particular application and to correctly interpret the results of aerosol sampling.

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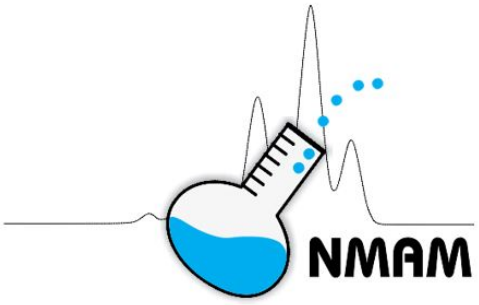

NIOSH Manual of Analytical Methods (NMAM), 5th Edition

Measurement of Fibers

by Paul A. Baron, Ph.D., NIOSH
Adapted from Baron [2001]

The NMAM team gratefully acknowledges Chen Wang, Joe Fernback and Alan Dozier for insightful review of this chapter.

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1 Introduction

Fiber-related disease has provided much of the impetus for fiber research in recent years. Asbestos has been the fiber type most commonly associated with disease. The name "asbestos" is a commercial term applied to the fibrous forms of several minerals that have been used for similar purposes and includes chrysotile, amosite, crocidolite, and the fibrous forms of tremolite, anthophyllite, and actinolite. The three primary diseases associated with asbestos exposure are asbestosis, the result of inflammation and collagen formation in lung tissue; lung cancer; and mesothelioma, an otherwise rare form of cancer associated with the lining surrounding the lungs. A current theory describing the toxicity of fibers indicates that fiber dose, fiber dimension, and fiber durability in lung fluid are the three primary factors determining fiber toxicity [Lippmann 1990].

The dose, or number of fibers deposited in the lungs, is clearly an important factor in determining the likelihood of disease. Both fiber diameter and length are important in the deposition of fibers in the lungs and how long they are likely to remain in the lungs. Figure 1 indicates some of the factors that determine fiber deposition and removal in the lungs. Fiber length is thought to be important because the macrophages that normally remove particles from the lungs cannot engulf fibers having lengths greater than the macrophage diameter.

Thus, longer fibers are more likely to remain in the lungs for an extended period of time. The macrophages die in the process of trying to engulf the fibers and release inflammatory cytokines and other chemicals into the lungs [Blake et al. 1997]. This and other cellular interactions with the fibers appear to trigger the collagen buildup in the lungs known as fibrosis or asbestosis and, over a longer period, produce cancer as well. Fiber diameter is also important because fiber aerodynamic behavior indicates that only small diameter fibers are likely to reach into and deposit in the airways of the lungs. The smaller the fiber diameter, the greater its likelihood of reaching the gas exchange regions. Finally, fibers that dissolve in lung fluid in a matter of weeks or months, such as certain glass fibers, appear to be somewhat less toxic than more insoluble fibers. The surface properties of fibers are also thought to have an effect on toxicity. Asbestos is one of the most widely studied toxic materials and there have been many symposia dedicated to and reviews of its behavior in humans and animals [Selikoff and Lee 1978; Rajhans and Sullivan 1981; WHO 1986; ATSDR 1990; Dement 1990].

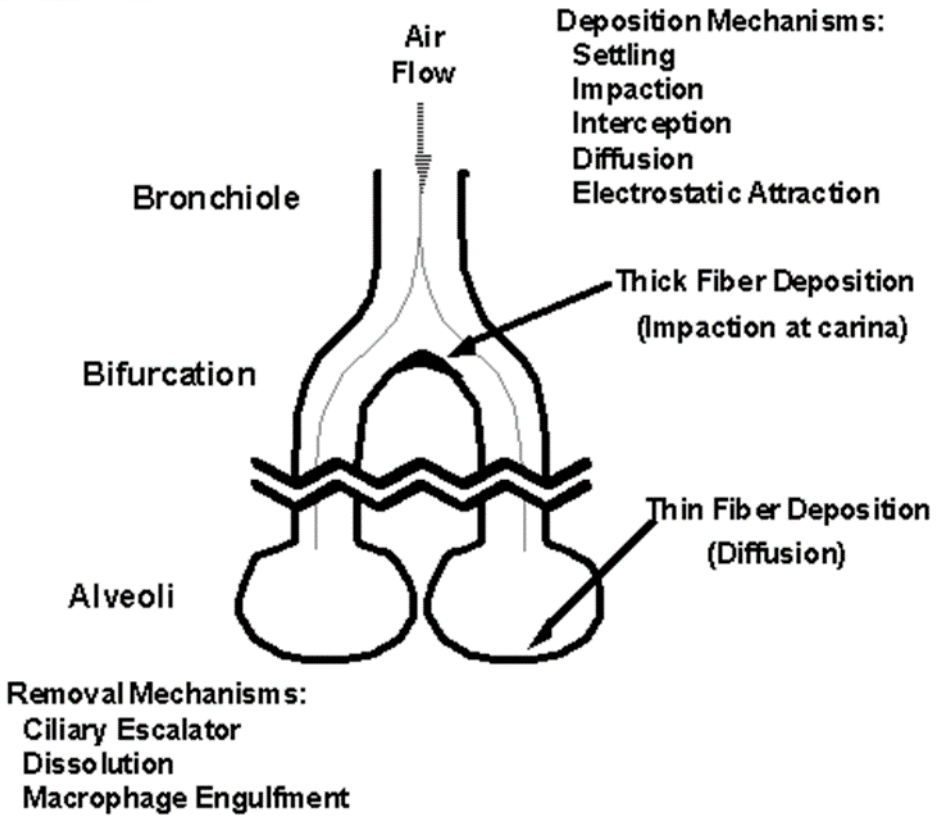

Figure 1. Schematic of mechanisms that affect fiber deposition and retention in the lungs. The deposition depends on all the indicated parameters in a complex fashion. However, larger diameter particles are affected more by gravitational settling, impaction, and interception, resulting in greater deposition further up in the respiratory tract. The saddle points, or carinae, in the branching respiratory tree are often a focal point for deposition of larger diameter fibers. Smaller diameter particles are affected more by diffusion and can collect in the smaller airways and gas exchange region (alveoli). Particle removal from the lungs is primarily effected by the cilia coating the non-gas exchange regions of the lungs; the cilia push mucus produced in the lungs and any particles trapped in the mucus out of the lung and into the gastrointestinal tract in a matter of hours or days. Some fibers are sufficiently soluble in lung fluid that they can disappear in a matter of months. Finally, white blood cells or macrophages roam the gas exchange regions and ingest particles deposited there for removal through the lymph system. Human macrophages are approximately 17 µm in diameter and can only ingest particles smaller than they are. Therefore, thin fibers are likely to deposit in the gas exchange region and, of these, the long insoluble fibers can remain in the lungs indefinitely.

Several techniques were used for asbestos measurement up until the late 1960s [Rajhans and Sullivan 1981]. Earlier than this, it was not widely recognized that the fibrous nature of asbestos was intimately related to its toxicity, so many techniques involved collection of airborne particles and counting all large particles at low magnification by optical microscopy. Thermal precipitators, impactors (konimeters), impingers, and electrostatic precipitators were all used to sample asbestos. Perhaps the primary technique in the United States (US) and the United Kingdom (UK) during this early period was the liquid impinger, in which particles of dust larger than about 1-µm aerodynamic diameter were sampled at 2.7 L/min and impacted into a liquid reservoir [Rajhans and Sullivan 1981]. After sampling, an aliquot of the liquid was placed on a slide in a special cell, particles larger than 5-µm size were counted, and the results were reported in millions of particles per cubic foot. Dissatisfaction with this approach stemmed from lack of correlation between measured particle concentration and disease in the workplace. Various indices of exposure have been developed that attempt to relate a portion of the fiber size distribution to the toxic effects. The appropriate indices for each of the asbestos related diseases as a function of fiber length and diameter (Figure 2) were suggested by Lippmann [Lippmann 1988].

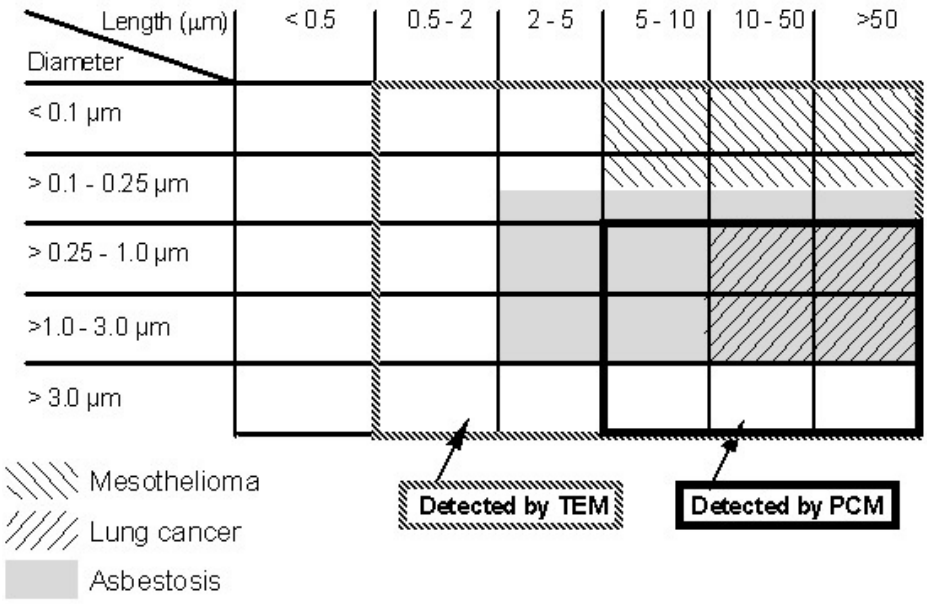

Figure 2. Comparison of proposed size ranges of asbestos fibers causing specific diseases compared with the fiber sizes detected using TEM and PCM techniques. Lung cancer and mesothelioma are more likely to occur at current occupational and environmental levels than asbestosis. PCM can cover only a portion of the total fiber distribution; PCM is used as an indicator of total exposure. TEM can cover the entire size range, but most methods emphasize one size range over another through selection of magnification and counting rules.

2 Fiber dimensions

Fibers are particles that have one dimension significantly larger than the other two. Fibers are often characterized or selected according to their aspect ratio, i.e., the ratio of the large dimension to one of the small dimensions. If no other criteria are used, then materials that might not normally be considered fibrous may contain a fraction of particles that meet the criteria for fibers. The distribution of fiber dimensions in a sample can usually be characterized by assuming a cylindrical geometry (i.e., the two small dimensions are identical) and measuring the length and diameter of individual fibers. The distribution of airborne fiber sizes generated by grinding bulk material or by mechanically releasing particles into the air often results in a two-dimensional (bivariate) lognormal distribution. Such a distribution is characterized by five parameters: the geometric mean length, the geometric mean diameter, the length and diameter geometric standard deviations, and a correlation term that relates length to diameter [Schneider et al. 1983]. In addition, several other parameters that are a function of length and diameter, such as aerodynamic diameter, can also be characterized by a lognormal distribution [Cheng 1986].

Often the discussion of fibers assumes that fibers are straight objects that can be well defined by several parameters as indicated above. However, many real-world particles are not so simple to describe. In fact, the detailed features of many fibers can aid in their identification [McCrone 1980]. Fibers are often curved, have splayed ends, or differ in other ways from a cylindrical shape. Asbestos mineral is composed of fibrils (about 0.03-µm diameter) that are packed together. This fibrillar structure is characteristic of asbestiform minerals. When the mineral is broken apart mechanically, the material separates primarily between fibrils and the resulting fibers are usually bundles of fibrils. The ends of the fibers can be broken apart, with smaller bundles or individual fibrils spread apart, yet still be part of the fiber. Fibers can be contaminated by attachment of other dust particles, creating a complex structure with aerodynamic behavior not matching that of cylindrical fibers. The complexity of fiber shapes affects all of the measurement and separation techniques described below and frequently makes it difficult to compare one method to another.

In addition to asbestos fibers, there are many types of fibrous materials being produced for commercial purposes. These include fibrous glass, mineral wool, refractory ceramic fibers, wood and other plant fibers, and synthetic organic fibers. Most of these fibers tend to have larger diameters than asbestos fibers. On the other hand, carbon nanotubes (CNTs) (<0.005um diameter) have recently been produced in small-scale commercial quantities and because of their high tensile strength, high conductivity, and other special properties, show great promise as a commercial material [Liu et al. 1998]. Unlike asbestos fibers, which have discrete lengths and diameters (i.e., aspect ratios), CNTs occur mainly as entangled particle agglomerates and may contain varying amounts of amorphous carbon and residual catalyst

metal. The complexity and variety of structures makes CNT particle counting a challenge. Measurement techniques must be tailored to the size distribution and physicochemical properties of these materials.

This review primarily relates to measurement of fibers in air. There are several techniques that address concentration of asbestos and other fibers in bulk material and measurement of mass concentration of fibers [Beard and Rook 2001]. One of these bulk methods, polarizing light microscopy, will be discussed below.

3 Phase contrasting light microscope counting (PCM)

As asbestos-induced disease became widely studied in the 1960s, cellulose-based membrane filter sampling was applied to asbestos sampling in combination with high magnification phase contrast light microscopy (PCM) for counting fibers. This technique involved collection of fibers uniformly over the surface of a cellulose ester filter, placing the filter or a segment of the filter on a microscope slide and making it transparent, and observing the fibers in the sample with a high magnification (~450X) phase contrast light microscope. Over the years, many researchers have endeavored to improve and standardize the PCM method. One researcher, Walton, discussed many aspects of this technique in a review [Walton 1982]. The high variability of the analysis results and the method's dependence on operator technique made method improvement and research difficult. The PCM method does not measure all fibers; typically only those >0.25 μm diameter are visible and counted and only those >5 μm length are counted by protocol. Therefore, the PCM method is only an index of exposure and uses the assumption that what is detected is correlated with the fibers actually causing disease (Figure 2). The PCM method does not allow identification of asbestos fibers. This is an important limitation when the method is used in settings where fiber concentrations with a significant non-asbestos fraction may occur. This should be remembered when considering some of the parameters discussed below. The aim of evaluating changes to the PCM technique may depend on whether consistency with other laboratories within a country or throughout the world is more important than making measurements that are more closely related to health effects. A number of factors which influence analysis results have been investigated, including the following:

a. Microscope-related parameters

1.) Microscope magnification

The exact level of microscope magnification depends on microscope design, but most current methods use 450X (±10%) total magnification. Pang and coworkers investigated 1250X magnification to improve fiber detectability, but this has not been adopted in any established methods [Pang et al. 1989]. Pang also investigated the effect of using lower magnification (400X) and found that counts were lower for chrysotile asbestos by 25%, but that amosite fiber counts were unaffected [Pang 2000].

2.) Phase contrast optics

This contrast enhancement technique allows detection of asbestos fibers down to about 0.25 µm diameter for chrysotile and about 0.15 µm for amphiboles. Other techniques such as dark field microscopy may offer improved detectability, but also increase the background from non-fibrous particles.

3.) Test slide to check optics

A test slide was developed to allow a check of proper alignment and magnification in the microscope [LeGuen et al. 1984]. This ensures a reasonable level of uniformity in microscope setup and operation, including the operator's visual perception. Improper setup can reduce detectability of fibers. There have also been cases where the optics were "too good," and results were obtained that were higher than the reference count.

4.) Counting area in microscope field

Some early measurements with the phase contrast microscope were made using a rectangular graticule for defining the counting area, while others were made using the entire microscope viewing area. It was found that larger viewing areas resulted in lower counts, so the Walton-Beckett graticule [Walton and Beckett 1977] was developed that nominally gave a 100-µm diameter counting area (the area is calibrated more precisely for each microscope) and has been incorporated in all current methods.

b. Sample preparation techniques

1.) Filter type

Virtually all measurements are made using 0.8-µm pore size mixed cellulose ester (MCE) filters. Some measurements are made using 1.2-µm pore size filters when sampling low concentrations to allow higher flow rate through the filter. Smaller pore size filters are used to ensure that fibers are deposited as near the surface of the filters as possible. This results in fibers ending up in the same plane so that they can be readily viewed with a minimum change of focus during fiber counting. Pore sizes

smaller than 0.8 µm are only used with line-operated pumps because of limited suction power available with personal sampling pumps.

2.) Selection of the liquid for making filter transparent

A liquid is placed on the filter that closely matches the filter refractive index, yet has an index that is as far as possible from that of the fibers being detected. Rooker et al. showed that refractive index difference between cleared filter and fibers translated directly into detectability of small diameter fibers [Rooker et al. 1982]. A viscous solution of dimethyl phthalate and diethyl oxalate mixed with cellulose filter material was commonly used in the 1970s and early 1980s. However, it did not result in a permanent sample, with crystallization of the mount and movement of fibers often occurring several days after sample preparation. Permanent slides were needed for quality assurance purposes and the sample preparation technique was also slow and required some skill. A rapid acetone-based filter clearing technique was developed that could be used safely in field situations [Baron and Pickford 1986]. After clearing, filters were coated with triacetin to surround the fibers. This resulted in a longer lasting sample (typically months to years) and is currently specified in most methods. Another technique uses a resin called Euparal to surround the fibers and results in a permanent slide preparation [Ogden et al. 1986].

3.) Filter loading

The number of fibers on the filter is usually specified to be within a certain loading range to ensure consistent counting. Cherrie et al. demonstrated using a serial dilution technique that counting efficiency was a function of concentration of fibers on the filter [Cherrie et al. 1986]. At very low filter loadings (<100 fibers/mm^2) there was a tendency to count high relative to an intermediate range of concentrations (100-1300 fibers/mm^2), where the counts were a linear function of loading. This "overcounting" was apparently due to greater visibility of fibers in a clean visual field. This effect was noted for both human counters and an image analysis system. At high filter loadings (>1300 fibers/mm^2), undercounting occurred due to overlap of fibers with other fibers and with nonfibrous particles. Most published methods indicate that optimum counting occurs within the 100-1300 fibers/mm^2 range, while some restrict the range further to less than 650 fibers/mm^2.

4.) Fiber counting rules

The basic fiber counting rules for most current methods indicate that a countable fiber should be longer than 5 µm, narrower than 3 µm, and have an aspect ratio greater than 3:1. These rules were selected because shorter fibers were difficult to detect by optical microscopy and the 3:1 aspect ratio was used to discriminate between fibrous and non-

fibrous particles in occupational settings. There has been a great deal of controversy over these rules. The use of a longer fiber cutoff, e.g., 15-20 µm, has been suggested, based on two separate arguments: first, that most asbestos fibers are relatively long and thin (with high aspect ratio) and the longer fiber cutoff would discriminate better toward fibers that were truly asbestos fibers according to mineralogical definitions [Wylie 1979]; and second, that fibers that enter the lungs are removed readily by macrophages if they are shorter than about 15 µm [Blake et al. 1997]. Longer fibers cannot readily be engulfed by macrophages, thus staying in the lungs for a long period and causing continuing fibrosis.

The aspect ratio criterion has also been questioned because many non-asbestiform particles have shape distributions that include particles with aspect ratios greater than 3:1. Since asbestos and other minerals often contain single crystal particles not in the asbestiform habit, it has been argued that these single crystals, or cleavage fragments, should not be counted. However, the Occupational Health and Safety Administration (OHSA) has supported the 3:1 minimum aspect ratio through legal precedent. The National Institute for Occupational Safety and Health (NIOSH) has noted that because of the great difficulty in differentiating whether individual high aspect ratio particles are cleavage fragments or asbestiform fibers, all such particles should be counted. These high aspect ratio particles may cause disease whether or not they are asbestiform.

Other aspects of fiber counting have been investigated, including how to count non-standard fiber shapes, overlapping fibers, overlapping compact particles on fibers, and bundles of fibers. Each of these factors can have a noticeable effect on the final count. Cowie and Crawford investigated the effect of some of these factors and estimated most of them made a difference in the final count on the order of 20% [Cowie and Crawford 1982]. Many of the methods currently in use have slight variations in their interpretation of which fibers to count and thus can contribute to variation in results between countries and organizations.

NIOSH Method 7400 contains two sets of counting rules, the A and the B rules. The A rules are used for asbestos and are consistent with counting rules in previous NIOSH methods. The A rules are required for asbestos counting by OSHA because of legal precedent in regard to the 3:1 aspect ratio rule. The A rules do not have an upper diameter limit for fibers to be counted. The B rules were introduced as an alternative to the A rules when Cowie and Crawford found that these rules agreed best with previous PCM counts, yet had improved precision [Cowie and Crawford 1982]. The B rules have been informally adopted for use with fibers other than asbestos because these rules include the upper diameter limit of 3 µm. This upper diameter limit

significantly reduces the counting of typically large-diameter fibers, e.g., glass and cellulose, which are unlikely to deposit in the lungs [Breysse et al. 1999].

c. Quality assurance schemes

1.) Sample recounts

Most methods require individual counters to recount about 10% of the field samples to ensure consistent counting procedures and alert the analyst in the case of problem samples. It is also recommended that counters have samples that are routinely recounted to ensure consistent counting within a laboratory over time.

One of the difficulties in analyzing errors made by analysts during PCM counting is that individual fields are difficult to relocate after the analyst has finished counting a slide. Differences in counts between analysts have often been ascribed to local variations in loading on the filter. Pang's development of a slide coverslip that defines counting areas on the sample solves this problem [Pang 2000]. Areas on the coverslip are vacuum coated with a thin layer of gold and platinum using an electron microscope grid as a mask. This leaves defined areas on the coverslip that can be located by grid index marks. Thus, specific fields in a sample can be readily located. Using this grid mapping approach, the location, orientation and shape of each fiber can be noted and differences in counts can be reconciled on a fiber-by-fiber basis. The coverslips have been used to study fiber counting accuracy by comparing routine counting of specified fields to counts agreed upon by a group of competent counters. It was found that the principal errors for chrysotile fiber samples were due to missing fibers close to the visibility limit, while the principal errors for amosite fiber samples were caused by incorrectly sizing fiber length near the 5-µm limit. The chrysotile samples were therefore typically undercounted (negative bias), while the amosite samples had increased variability with individual counters being biased either high or low. Both these errors can be reduced by training counters with pre-counted reference slides prepared using Pang's coverslips [Pang 2000] (Omega Specialty Instrument Co. Chelmsford MA). In addition, these reference slides can be used on a routine basis to ensure consistency in counting. These coverslips or modified versions show great promise for training analysts and perhaps for improving quality assurance schemes.

2.) Interlaboratory sample exchanges

Crawford et al. found that use of sample exchange programs was more important in ensuring agreement between laboratories than similarity in details of the counting rules [Crawford et al. 1982]. Thus, exchange of field samples between laboratories is commonly performed to improve consistency of counting. A description of several quality assurance techniques for asbestos fiber counting is described by Abell et al.

[Abell et al. 1989]. To fulfill Method 7400 requirements for an interlaboratory sample exchange, Tombes and Calpin have described a simple approach using appropriate statistical tests [Tombes and Calpin 2002].

3.) Quality check samples

In order to get agreement between laboratories within a country or internationally, several programs send out identical samples to participating laboratories to assess their relative performance [Schlecht and Shulman 1986; Kauffer 1989; Crawford et al. 1992; Arroyo and Rojo 1998]. These programs provide feedback, often tied to laboratory accreditation, which provides incentive for laboratories to ensure that their performance is similar to that of other laboratories.

d. Qualitative fiber analysis

In addition to simply counting the fibers, there are techniques available for providing at least tentative identification of fiber type; use of these techniques is commonly called differential counting. Fiber shape can be used to limit the type of fiber counted. For instance, glass fibers tend to be straighter, with smoother sides than chrysotile fibers. Polarizing light techniques can also be used to identify larger diameter (> 1 μm) fibers. These are based on the optical properties of the materials, including refractive index and crystallinity. These techniques can provide quite positive identification for the presence of certain types of fibers, but are limited in application to airborne fibers because they only work for the larger diameter fibers. These techniques are often used in analysis of bulk materials [NIOSH 1994a]. The use of identification techniques is not allowed in reporting fiber counts using Method 7400 so that the results are consistent between laboratories. Considerable confusion has been caused in the past by individual laboratories using some of these identification techniques to change the counting procedure and, hence, the final results.

Several PCM fiber counting methods have been published by national [NHMRC 1976; HSE 1990] and international organizations [Asbestos International Association 1979; WHO 1997]. Most countries have methods very similar to the ones referenced here.

e. Sampling volume for asbestos abatement applications

Sampling for asbestos after abatement requires the selection of a sampling volume so that one can have high confidence that the air meets acceptable concentration standards. The following is an example of how to calculate this sampling volume.

The approach assumes that one wishes to select sampling parameters in order to have a high degree of confidence that a target exposure standard (e.g. NIOSH REL, OSHA PEL, EPA clearance standard) is met.

Several factors need to be established in order to perform this calculation if the target exposure standard involves clearance monitoring. The U.S. Environmental Protection Agency (EPA) authorizes the use of PCM for some clearance monitoring applications and specifies that a level of 0.01 fibers/mL be met. On the method synopsis page, Method 7400 indicates that the limit of detection (LOD) for PCM analysis is 5.5 fibers/100 fields. This is based on intralaboratory variability. A major difference between Method 7400 and other analytical methods in the NIOSH Manual of Analytical Methods (NMAM) is that there is no reference method for Method 7400. Therefore, the consensus mean is the "true" value and the interlaboratory results effectively define the method accuracy. Under the heading "Evaluation of Method, B. Interlaboratory comparability," Method 7400 provides a means of calculating the confidence limits on a single analysis result (Equations 3 and 4). From Equation 3, the interlaboratory variability at the LOD is such that the upper 95% confidence limit on a measured value is 300% greater than (or 4 times) the measured value.

Using the upper confidence limit, the equation in Section 21 in Method 7400 can be used to estimate the sampling volume.

$$\frac{\frac{number\ of\ fibers}{area\ of\ 100\ fields} * total\ filter\ area}{sampling\ volume} = \frac{target\ level}{4}$$

With the appropriate values inserted, the equation becomes

$$\frac{\frac{5.5\ fibers}{0.785\ mm^2} * 385\ mm^2}{sampling\ volume} = \frac{0.01\frac{fiber}{mL}}{4}$$

Solving this equation for sampling volume gives 1080 L. This is the minimum volume that will give a result allowing a single sample to indicate compliance with the 0.01 fiber/mL limit with 95% confidence. It requires that the sample give a result less than or equal to the LOD or 5.5 fibers per 100 fields. A higher fiber count may still indicate that the concentration meets the target level, but not with the same level of confidence. This is likely to be a conservative estimate of concentration and additionally ensure compliance with the standard because the fiber concentration is low and, as indicated above, low fiber

loadings are usually overestimated. However, the background concentration of non-fibrous dust on the filter also must be low to ensure that fibers are not obscured.

f. Other techniques

Since fiber counting by human analysts produces relatively high biases and variability, several researchers have attempted to develop automated counting systems. With the increases in computer power over the last 25 years, it has been tempting to assume that fiber counting is a solvable problem and significant efforts have been made to develop such a system. The most intensive effort to produce a fiber counting system was carried out by Manchester University in collaboration with the Health and Safety Executive in the UK [Kenny 1984]. The Manchester Asbestos Program (MAP) was able to give reasonably good agreement with human counters for certain types of samples. It was used as a reference analyst for the US and UK reference sample programs for several years. Eventually, the MAP was dropped as the reference because it was not sufficiently consistent for all types of samples.

The principle problems with image analysis of asbestos fibers include: the complexity of many fiber shapes, including bundles, agglomerates, and split fibers; the fibers often go in and out of the plane of focus; the background includes many particles and other non-fibrous shapes; the phase contrast optics produces haloes around particles in the sample that can be detected as fibers; and finally, and perhaps most importantly, the contrast between the fibers and background is poor and many fibers are near the detection threshold. An evaluation of the MAP program indicated that a significant fraction of the fibers were misidentified as multiple fibers, not detected at all, and groups of compact particles or edges of large particles were detected as fibers [Baron and Shulman 1987].

Inoue and coworkers have more recently developed image analysis software using a microprocessor-based PC [Inoue et al. 1998]. Initial tests indicate that it works approximately as well as human counters. Inoue also evaluated how well human counters and the image analyzer did in detecting the same fibers in a sample and found that only about 50% of the fibers were consistently counted by all counters, so the image analysis system did approximately as well as the human counters [Inoue et al. 1999]. Further testing of the image analysis system is needed.

In addition to image analysis, optical microscopy can be enhanced using a personal computer to more easily observe the image and to mark and measure fiber dimensions, with automatic recording of the fibers counted [Lundgren et al. 1995]. This does not appear to improve the counting accuracy since the analyst still decides which fibers are to be counted.

4 Polarizing light microscopy (PLM) of bulk materials (Adapted from Baron [1993])

The asbestos fibers in bulk material can be released and become airborne when the bulk material is disturbed. For this reason, it is desirable to measure the asbestos content of bulk samples. PLM is often used to determine the percent asbestos in bulk material. The EPA [Asbestos-containing materials, 1987] has defined asbestos containing material (ACM) as material containing more than 1% asbestos using the PLM method, which effectively estimates concentration by area observed. Some confusion exists regarding the units of asbestos percentage. EPA originally indicated that the limit for ACM was 1% by mass [Asbestos-containing materials, 1987], but because of the difficulties in determining corrections for differences in material density and in determining particle volumes, the limit was changed to 1% by area as determined by the PLM method [EPA 1990b]. OSHA does not specify units for percent asbestos in its regulations [OSHA 1994].

Several PLM techniques are used for identifying fiber type as well as semi-quantifying the percent fibrous material (usually asbestos) in a sample [McCrone et al. 1978; Middleton 1979; Asbestos-containing materials, 1990; Perkins and Harvey 1993; NIOSH 1994a]. These techniques depend on particle shape, the refractive index, and other optical properties of individual particles. Many of these PLM techniques require visual observation of color in the fiber and become less reliable for fibers thinner than about 1 μm [Vaughan et al. 1981].

a. Sampling

Several procedures have been suggested for obtaining representative bulk samples of ACM in a fashion that prevents unnecessary exposure to asbestos aerosol [EPA 1985a,b; Jankovic 1985]. Representative sampling of commercial ACM materials is often problematic; these materials may vary significantly in asbestos concentration between nearby locations and even at different depths at the same location. Sampling from multiple locations and compositing samples helps improve the likelihood of obtaining a representative sample.

The material should be wetted or sealed during sample removal. A small coring device, such as a cork borer, can be used to obtain a sample from the full depth of the material. At least three samples per 1000 ft^2 of ACM should be taken [Asbestos-containing materials, 1987]. The sample should be placed in a well-sealed, rugged container. Finally, the sampled area should be repaired or sealed to minimize further fiber release.

Surface sampling has been proposed by several groups, but there is no relationship between airborne fibers and those found on surfaces [Chatfield 2000]. Therefore, surface sampling for fibers is not recommended.

b. Sample preparation analysis

Sample preparation for a PLM analysis involves grinding the material to the optimum particle size range (1-15-µm diameter) and dispersing the particles in a liquid of known refractive index on a glass slide [Perkins and Harvey 1993]. Particle size uniformity in the prepared sample is extremely important. A few large chunks of material may contain more asbestos than hundreds of much smaller particles. Friable material, i.e., that which is crumbly or can be crushed by hand, may readily release fibers and is considered more hazardous. Friable materials are generally easier to prepare for analysis than some other ACMs, such as vinyl asbestos floor tiles, which may require dissolution or ashing of the matrix material so that the fibers are separated and visible in the microscope. Before and after preparation, the sample is observed with a stereomicroscope at 10-100X magnification to evaluate sample uniformity and observe whether fibrous material is present.

Some materials that interfere with accurate fiber identification either by their similarity or by covering up the fibers can be removed by physical treatment of the sample. For instance, organic materials, such as cellulose fibers or diesel soot can be removed by low temperature, oxygen-plasma ashing [Baron and Platek 1990]. Leather fibers and chrysotile have a similar appearance and refractive index. The leather can be removed by ashing at 400°C [Churchyard and Copeland 1988].

Fiber morphology, i.e. the structure and shape of the fiber, can be used to assist in its identification. Morphology of fibers can give some indication of fiber type. For instance, chrysotile fibers tend to be curly, while amphibole fibers are straight, especially when they are shorter than 50 µm. Asbestos fibers often have frayed or split ends, while glass or mineral wool fibers are typically straight or slightly curved with fractured or bulbous ends. Many plant fibers are flattened and twisted, with diameters between 5-20 µm. Note that it is not recommended to base identification solely on morphology.

Fiber refractive index and other crystalline properties can be used to identify fiber type with reasonable certainty. Several techniques for determining these properties can be used in a polarizing light microscope. When viewed in the microscope with crossed polarizing filters, isotropic (isometric or amorphous) fibers appear consistently bright when rotated, while anisotropic (uni- or biaxial crystal structure) fibers appear bright, but disappear when rotated to their extinction angle, which is a function of crystal structure. Thus,

amorphous materials such as glass or mineral wool fibers can easily be discriminated from asbestos.

During PLM analysis, fibers are immersed in a fluid selected to have a known refractive index. When a fiber has a larger refractive index than the surrounding fluid medium, the bright halo (Becke line) around that fiber appears to move into it as the microscope focus is raised; when the fiber has a smaller refractive index, the Becke line moves out of it. Placing the fibrous material into several different refractive index fluids allows the fiber refractive index to be bracketed.

Dispersion, or refractive index change with wavelength, of a fiber can be used for identification. When particles are placed in a liquid whose dispersion is different from that of the particle, the particle may exhibit a color caused by the refraction of light. This technique requires the use of special "dispersion staining" optics. By using several refractive index liquids in series, the refractive index and the dispersion of the fiber can be established and compared with those of standard materials or published data [McCrone 1980].

Once the sample has been uniformly dispersed on a slide in the appropriate refractive index liquid, specific fiber types, e.g., asbestos, can be identified and the percent fibers estimated. Two approaches are typically used: visual comparison with prepared reference slides or pictures and point counting. When attempting to estimate whether a material is ACM (i.e., > 1% asbestos), the visual comparison technique is adequate when more than about 10% of the particles observed are asbestos. Point counting is used for lower concentration samples to provide higher accuracy [EPA 1990a]. It involves observing 400 or more randomly selected "points" (identified with a reticle crosshair) in the sample. The number of points containing asbestos is divided by the total number of points observed to give the percent asbestos. A combination of these approaches balances the analysis time and accuracy of the results [Webber et al. 1990].

PLM also can be used for qualitative analysis of air sample filters by collapsing the filter and using low temperature plasma etching of the surface to expose the fibers. Various refractive index liquids can then be placed on the etched surface to surround the fibers, allowing techniques noted above to be used [Vaughan et al. 1981]. The smallest fibers that can be identified by this method are about 1-µm diameter.

c. Accuracy

PLM analysis is primarily used for qualitative identification of fiber type. Accurate identification of asbestos and other fibers requires proper training in the crystallographic

properties of particles as well as training and familiarization with the PLM. As with fiber counting, a laboratory quality assurance program is necessary to ensure consistently accurate results. The National Voluntary Laboratory Accreditation Program (NVLAP) operated by the National Institute for Standards and Technology (NIST) inspects laboratories for proper practice as well as providing unknown samples four times a year to check their performance in fiber identification. Under a predecessor to this program, approximately 350 laboratories correctly classified 98.5% of the samples as asbestos and correctly identified the specific asbestos types in approximately 97% of the samples. A blind test of 51 laboratories resulted in 97.5% correct classifications and 79.1% correct identifications [EPA 1986]. The American Industrial Hygiene Association Proficiency Analytical Testing Program provides similar PLM audit samples to laboratories. Some common interferences for bulk analysis by PLM include sepiolite, vermiculite, and cleavage fragments of non-asbestos amphiboles.

PLM has been cast in a quantitative measurement role by the EPA requirement of determining whether a school building material meets the 1% asbestos level defining ACM. Many variables including particle size, density and shape are not adequately controlled or measured in the analysis and contribute to errors in the percent mass estimate. Thus, PLM analysis is at best a semi-quantitative technique.

Chatfield indicated that the accuracy of PLM for low concentrations of asbestos was poor and described a set of procedures that concentrated the asbestos into a weighable fraction [Chatfield 2000]. An EPA report describes, in addition to the PLM and Chatfield's gravimetry methods, a TEM and an x-ray diffraction method for bulk analysis of asbestos [Chatfield 2000]. NIOSH Method 9000 describes an x-ray diffraction method for chrysotile [NIOSH 1994c].

5 Electron microscopy

Scanning electron microscopy (SEM) has not been the focus of as much method development as either light microscopy or transmission electron microscopy (TEM). PCM found favor because of the low equipment cost and lower training level required for analysis. TEM is preferred for environmental and research studies because it offers the highest resolution and the most positive identification capabilities. TEM allows visibility of all asbestos fibers down to the individual fibrils, electron diffraction for crystal structure identification, and energy dispersive x-ray analysis for elemental measurement. SEM has intermediate resolution, with many instruments of this type not able to see all asbestos fibers. However, many modern SEMs have the capability of detecting asbestos fibrils, though contrast with background may be poor for some fiber types, especially if a high contrast substrate is not used. Energy dispersive x-ray analysis is also available for many SEMs, providing some qualitative

information of fiber type. However, since electron diffraction typically cannot be performed by SEM, this often leaves open the question of positive identification of fibers.

6 Scanning electron microscopy (SEM)

Particles are observed in the SEM when a beam of electrons is focused onto the sample surface and scanned over an area. The electrons are scattered from the surface and detected above the surface synchronously with the beam scan rate and an image of the scanned surface is created. Thus, the SEM measures the surface of particles on a substrate. The best image can be obtained on conducting objects deposited on a smooth, conducting substrate. Particles are often deposited on aluminum or carbon planchets that fit directly into the SEM or onto polycarbonate membrane (track-etched, Nuclepore®) filters. The samples are usually coated with gold or carbon to increase conductivity.

There have been some SEM methods developed for fiber counting [Asbestos International Association 1984; WHO 1985; ASTM 1996; ISO 2002]. These methods are primarily used for inorganic man-made fibers that have larger diameter fibers than can occur with asbestos. Thus, all the fibers are potentially visible using the SEM.

7 Transmission electron microscopy (TEM)

The transmission electron microscope (TEM) allows detection of particle shape and structure down to the smallest asbestos fibers (Figure 2) and can be used to determine crystal structure from electron diffraction as well as determining elemental composition from energy dispersive x-ray analysis. Although TEM analysis is potentially very powerful and accurate, the process of sample collection and preparation and details involved in sample analysis can degrade the quantitative accuracy of the technique. Several more specialized techniques, such as electron energy loss spectroscopy and secondary ion mass spectrometry, have been used for analyzing particles and can also be applied to fibers [Fletcher et al. 2001].

Airborne fiber samples for TEM analysis are typically collected onto a filter, usually a polycarbonate membrane or MCE membrane filter. For the latter filter type, the filter is chemically collapsed to form a smooth upper surface on which collected fibers are trapped. Sometimes the surface is etched using a low temperature asher to expose the fibers collected on or near the surface of the original filter. The filter is coated with a carbon film that entraps fibers exposed on the filter surface and the filter material is then dissolved away. The carbon film is transferred to a TEM grid (usually 3-mm diameter) and the sample can be placed in the TEM for analysis.

For Method 7402, the surface is not ashed because some fibers, e.g., cellulose, may be removed and give an inaccurate total fiber count [Baron and Platek 1990]. Ashing can thus affect the measurement of the asbestos fiber fraction.

The above approach to preparing MCE filters for TEM analysis is called the direct-transfer approach, since fibers are transferred to the carbon film with minimum disturbance to the way they were collected. An alternative technique is to dissolve the entire filter in liquid, ultrasonicate the suspension to disperse the particles, and deposit an aliquot of the particle suspension onto a polycarbonate filter for final transfer to the carbon film. This is called the indirect-transfer technique. With the indirect technique, the optimum particle loading of the TEM sample can be obtained and soluble particles can be removed from the sample. However, the suspension process can change the apparent size distribution of the particles and fibers by breaking apart agglomerates or even breaking apart asbestos fibers into smaller fibers or fibrils [Sahle and Laszlo 1996]. The breakup problem can be especially severe for chrysotile, causing a large increase in fiber count. Quality assurance is especially important with TEM analysis of fibers. The NVLAP program provides quality assurance accreditation for laboratories performing TEM analysis using the Environmental Protection Agency's Asbestos Hazard Emergency Response Act (AHERA) method. Note that data provided under the AHERA method, because of significant differences in counting rules, the types of structures counted as asbestos, and the size range of fibers, cannot be directly compared with counts by Methods 7400 or 7402.

The process of sample collection and preparation is a complex one that can introduce biases into the final measurement. Since only small portions of the filter are measured during TEM analysis, sampled fibers that deposit non-uniformly onto the filter due to inertial, gravitational, and electrostatic effects will be measured inaccurately [Chen and Baron 1996]. Fibers that penetrate the filter surface and are not transferred to the carbon film will be lost. If the filter is incompletely dissolved away from the carbon film, the sample will be difficult to analyze.

Many of the sources of bias and variability noted in sampling and counting by PCM also apply to TEM analysis. Fiber counting in a TEM can also introduce biases and variability in the final result. There is a tendency to use the high magnification of the TEM to look for the smallest fibers, while ignoring some of the larger ones. Even so, fibers shorter than 0.5 μm tend to be missed because they are difficult to see in the background clutter of the sample [Steel and Small 1985]. Taylor et al. found that TEM counting gave poorer precision than counting the same sample by PCM and recommended that the fraction of asbestos fibers counted by TEM be applied to the PCM count as indicated in Method 7402 [Taylor et al. 1984]. This combined PCM/TEM approach gave better precision than counting by TEM alone.

In addition to recognizing fibrous shape and structure of the several asbestos minerals, qualitative analysis of fibers by TEM primarily involves two techniques, energy dispersive x-ray analysis and electron diffraction. X-ray analysis produces responses for each of the elements (typically atomic number > 6, but is instrument dependent) present in a particle; the responses occur as peaks in an energy spectrum. Specific asbestos minerals can be identified using peak intensity ratios observed in standard samples and as specified in the method.

The crystal structure of individual fibers is evaluated using electron diffraction. Focusing the TEM electron beam on a single fiber produces a diffraction pattern consisting of a number of spots. The spot locations depend not only on the particle crystal structure, but also on the geometry of the electron beam optics and other instrumental parameters. The diffraction spot locations relative to one another give a very specific identification of crystal structure. For easily recognized minerals, such as chrysotile, the visual identification of the diffraction pattern is often sufficient. However, to identify fibers not fitting the x-ray analysis pattern for standard asbestos minerals, careful measurement, or indexing, of the diffraction spots is important.

The combination of x-ray analysis and electron diffraction gives a highly definitive identification of specific minerals. However, as with any analytical methods, there are exceptions that require greater expertise to recognize potential interferences. Some minerals that are difficult to differentiate from regulated asbestos minerals include non-regulated amphiboles and fibrous talcs. There are several established methods for analyzing fibers, especially asbestos fibers, by TEM [Asbestos-containing materials, 1987; NIOSH 1994b; ISO 1995, 1999; ASTM 1998].

8 Optical detection (light scattering)

Two types of light scattering detectors are commonly used for measuring airborne dust concentrations: the optical particle counter (OPC), which detects and counts individual particles, and the photometer (sometimes called a nephelometer), which detects the scattering from all particles in a defined detection volume. A standard OPC was used to detect asbestos concentrations in a workplace where the aerosol was primarily fibrous and good correlation with fiber counts was obtained [Rickards 1978]. A nephelometer may also be used, but may have an even greater interference from non-fibrous dusts.

The fibrous aerosol monitor (Model FM-7400, MIE, Inc. Bedford MA) used an electrostatic alignment technique by applying a field that aligns and rotates individual fibers in a laser beam. The light scattered from the fibers uniquely identified the presence of individual fibers. This allowed specific detection of fibers [Lilienfeld et al. 1979] and was even used to measure fiber length [Marijnissen et al. 1996].

Several field tests have indicated that the fibrous aerosol monitor agrees reasonably well with field measurements of fibers by phase contrast microscopy, though mostly at concentrations above ambient levels. It has been used at abatement sites to provide rapid feedback and ensure acceptable containment of airborne fibers during asbestos removal.

9 Fiber classification

Several devices have been used to measure or separate fibers by diameter. A spiral centrifuge was used to separate fibers and reference spherical particles to estimate fiber aerodynamic diameter [Stöber 1972]. It was found that the aerodynamic diameter was directly proportional to physical diameter, proportional to the square root of the fiber density, and proportional to fiber length to the $1/6^{th}$ power. For mineral fibers having a density of about 3 g/cm^3, the aerodynamic diameter was approximately three to five times the physical diameter of the fiber. Behavior of glass fibers in a cascade impactor was investigated by Burke and Esmen [Burke and Esmen 1978]. A small correction to the aerodynamic diameter was developed to take into account interception of longer fibers with the impaction surface. An inertial spectrometer was used to measure fiber aerodynamic diameter and good diameter separation was achieved [Morigi et al. 1999]. Baron and Deye developed a technique for separating fibers by length using dielectrophoresis [Baron et al. 1994; Deye et al. 1999]. This technique was also shown to be useful for measuring fiber length and diameter distributions [Baron et al. 2000].

As with most airborne dusts, fiber settling will reduce the number of larger diameter fibers in a distribution as the distance from the source of the dust increases. Esmen et al. showed that average fiber concentration in workplaces decreased exponentially with an increase of fiber diameter, indicating that the larger diameter fibers settled out more quickly than smaller diameter fibers [Esmen et al. 1979]. Cyclones, impactors and porous foam classifiers were evaluated for efficiency of removing airborne fibers not likely to deposit in the lungs [Maynard 1996].

The aerodynamic diameter of fibers is dependent primarily on fiber physical diameter and fiber density, with a minor dependence on fiber length [Baron 1996]. The diseases caused by asbestos fibers are lung diseases and so it makes sense to measure only fibers that can enter the lungs, i.e., thoracic fibers. Identical conventions for thoracic samplers have been published by ISO, ACGIH [ACGIH 2002], and CEN. Baron [Baron 1996] showed that sampling fibers with a thoracic sampler was approximately equivalent to counting only mineral fibers with a physical diameter smaller than 3 µm. Jones et al. [Jones et al. 2001] reported that there appeared to be no impediment to using a thoracic sampler for fiber sampling; they found that several samplers matched the thoracic convention, the sample collected by these samplers could be analyzed by standard methods, and that field studies indicated equivalence to the

current method. Maynard [Maynard 1999] also found that there appeared to be no variation in penetration through these samplers as a function of fiber length. The advantage to using a thoracic sampler, apart from adhering to conventional sampling practice, is that it would remove larger compact particles and fibers from the sample and result in a cleaner sample. Although current US practice does not use an upper diameter limit for asbestos fibers, such a limit is commonly used for man-made fibers. Except for the United States, all national and international organization methods use an upper diameter limit of 3 µm for fiber counting of asbestos fibers.

It is likely that thoracic sampling will eventually be in routine use for measurement of asbestos and other fibers. This approach has several advantages. It places the fiber method in line with other dust sampling conventions. It removes some of the larger particles in the sample, resulting in a cleaner sample for the analyst. It removes the need for determining fiber diameter during counting and it is consistent with previous practice of using an upper diameter limit of 3 µm for fiber counting in some methods. Thoracic sampling has the disadvantage of requiring the flow rate for a specific sampler to be fixed. This reduces the flexibility to target the loading of the filter by adjusting the flow rate. However, several classifiers can be designed to operate at selected flow rates to allow some flexibility in sampling.

10 Conclusions

The capability for measurement of fiber size distributions is available through microscopy and, to a much lesser extent, through direct-reading instrumentation. Because of differences in counting rules, resolution capability, and ability to distinguish asbestos from interfering particles or other fibers, PCM, PLM, SEM, and TEM methods often do not produce results which are directly comparable. The traditional methods of microscopy are relatively inaccurate when compared to chemical analysis methods for most other analytes because of the many sources of error in the sampling and analysis procedure. To improve laboratory-to-laboratory agreement, counter training and quality control, including the exchange of samples among laboratories and proficiency testing, are important. Implementation of training through the use of Pang's coverslips allows investigation of counting errors and potential improvement of PCM counting accuracy. Thoracic sampling could eliminate interfering particles and thereby improve measurement methods in the future.

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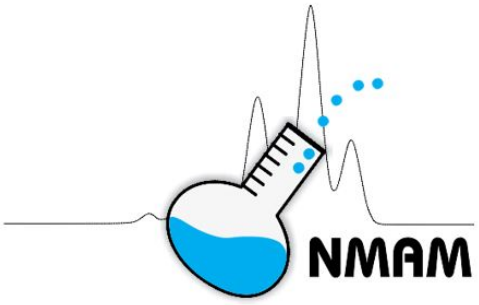

NIOSH Manual of Analytical Methods (NMAM), 5th Edition

Sampling and Analysis of Soluble Metal Compounds

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[Much of this chapter was adapted from Fairfax and Blotzer 1994; and Ashley 2001.]

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
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1 Introduction

Workplace exposure standards have been established for several soluble metals and metalloids to take into account the increased bioavailability of some metal compounds. Exposure standards for soluble compounds can be up to 500 times lower than the exposure standards for less soluble compounds for the same metal. However, there is often confusion among chemists, industrial hygienists, and laboratories over what is meant by "soluble" when the metal species, extraction fluid, or solubility conditions are not specified in the exposure standard nor in the supporting exposure standard documentation [Fairfax and Blotzer 1994]. In addition, the metals and metal compounds may interact chemically or physically with the sampling media or with each other [Ashley 2001]. Such complications can affect the stability and speciation of the metals and their compounds, and must be addressed in order to obtain meaningful results. These issues are becoming more important in workplace airborne metals exposure monitoring.

The solubility of a metal will depend on the chemical form of the metal, the fluid used to extract the metal, and the conditions under which the extraction occurs (e.g., temperature, volume, time). Unfortunately, the degree of method specificity needed to obtain measurements that are reproducible among laboratories is generally either missing or is subject to a variety of interpretations from exposure standards and supporting documentation. The need for a better definition of what is meant by the term "soluble" in relation to exposure standards was first raised in the 1990s, but as of the new millennium no significant improvement had occurred within exposure standard-setting organizations in the United States. Therefore, to meet the needs of analysts, laboratories, and laboratory clients for better definition of the analyte of interest, and to improve measurement reproducibility among laboratories, various organizations are working to achieve international consensus on extraction of soluble metal compounds. Consensus guidelines have been promulgated in an International Standard [ISO 2012a], and this will serve to fill the void and improve the situation.

2 Soluble and insoluble metal compounds

The American Conference of Governmental Industrial Hygienists and several countries (e.g., France, Germany, UK, USA) have established occupational exposure limits (OELs) for soluble metal and metalloid compounds [ACGIH 2015; IFA 2014]. Some examples of elements for which soluble OELs have been promulgated are listed in Table 1 (see Appendix for additional details). For many of these elements (e.g., Tl, Ag, Cr[VI], Ni, Pt), the OELs for the soluble compounds are lower than for the corresponding insoluble forms [ACGIH 2001; CRC 2015].

Table 1. Example metallic elements for which soluble compounds have been assigned OELs [IFA 2014; ACGIH 2015]

Aluminum – Soluble compounds, as Al
Barium – Soluble compounds, as Ba
Chromium – Water-soluble Cr[VI] compounds
Iron – Soluble salts, as Fe
Molybdenum – Soluble compounds, as Mo
Nickel – Soluble compounds, as Ni
Platinum – Soluble salts, as Pt
Rhodium – Soluble compounds, as Rh
Silver – Soluble compounds, as Ag
Thallium – Soluble compounds, as Tl
Tungsten – Soluble compounds, as W
Uranium – Soluble compounds, as U

a. Solvent

The term "solubility," as used by analytical chemists, ordinarily pertains to the dissolution of a material in pure water [CRC 2015]. The subject of water solubility of metal compounds is covered in several references [CRC 2015; ACGIH 2001; Beliles 1994; O'Neil 2006]. According to *Patty's Industrial Hygiene and Toxicology* [Beliles 1994] and the individual ACGIH Threshold Limit Value® (TLV) documentation for these metals [ACGIH 2001], the solubilities of metals and metal compounds are quite variable depending upon the solvent. Other pertinent references sustain the notion that solubility, regarding metals and their compounds, is generally identified in terms of their solubility in water [ACGIH 2001; O'Neil 2006]. The solubility and insolubility of numerous inorganic substances are presented in the Appendix. What is meant by "soluble" depends on the operational definition employed for the extraction conditions desired by the investigator.

b. Temperature

Temperature is another variable that directly affects solubility. Most current analytical methods specify deionized water, but not water temperature (some procedures call for hot water (37 °C), but others use water at room temperature). Some important questions thus arise:

1.) If using deionized water, should chemists assure that water temperature has been heated to body temperature (i.e., 37 ˚C)? For occupational exposure assessment purposes, should solubility be based upon body temperature?

2.) Should the OEL value documentation specify that analytical procedures use extraction media heated to body temperature?

3 Health effects

From a health perspective, the solubility of a metal or metal compound is not the only consideration of interest. Ultimately, the most important consideration is the extent to which such soluble metals accumulate in body fluids or target organs, leading to toxic levels of the metal ion. This is of more concern than solubility in water, acids, or alkalis per se. Further complicating the solubility issue is the fact that the term "soluble" may have different meanings among industrial hygienists and chemists. Chemists generally use the term "soluble" as defined by the CRC Handbook of Chemistry and Physics [CRC 2015]. According to the CRC Handbook, a material is considered soluble if a saturated solution in water (at 25 ˚C) contains more than 1% (m/v); any material in which 1 percent or less is dissolved is considered insoluble. Unfortunately, a material listed as insoluble, using the CRC definition, could still dissolve in body fluids and produce a significant tissue concentration which is biologically detrimental. The point is that an OEL for an "insoluble" compound may not be sufficient to protect exposed workers. When asked in an informal poll to choose a solvent in which to measure the relative solubility of metals, industrial hygienists chose, in order of preference, water, body fluids, and a petroleum solvent [Fairfax and Blotzer 1994].

a. Body fluids

When considering the biological effect of the solubility of a material, we should ideally first consider body fluids. However, body fluids vary considerably in pH. For example, the pH of the stomach is acidic, the pH in the intestine is alkaline, the pH of blood serum is approximately neutral, some macrophages are highly acidic, and the pH of saliva is slightly acidic. Furthermore, body fluids contain a variety of solutes, including salts and polypeptides (proteins). Polypeptide molecules can bind to metal ions in solution and often contain functional groups that can chelate metals. Polypeptides have strong chelating ability in body fluids and will account for the considerable difference between the solubility of a metal in body fluids versus that same metal in water. Metals, in turn, are bound to different proteins, depending upon where in the body they are located at a given time. In passing through the body, a metal ion is bound by different polypeptides. For each of them, a different reaction may be involved. Some reactions may increase or decrease the toxicity of the metal ion.

Because of the effect of proteins, pH, and other solutes in body fluids, the solubility of a metal compound in body fluids will be quite different than the metal's solubility in water [ACGIH 1987].

4 Sampling considerations

a. Filter reactivity

The filter medium used must not react with the airborne particulate collected by the sampler so as to change the chemical form of the captured sample. This can occur if a soluble compound reacts with the filter material or a contaminant therein to produce an insoluble or less soluble compound. An example of this problem has been observed with silver, where a soluble silver compound, $AgNO_3$, can react with chloride in some mixed cellulose ester (MCE) or polyvinyl chloride (PVC) filters to form AgCl, which is much less soluble in water. Thus, low recoveries of "soluble" silver will result unless an alternative filter medium, such as polytetrafluoroethylene (PTFE), is used. Another problem is illustrated by soluble forms of Cr[VI], which can react with the filter medium to form insoluble compounds and/or undergo reduction to Cr[III] and, therefore, be lost to Cr[VI] analysis. Hence, chemical compatibility issues must be investigated before samples meant for "soluble" extraction procedures are taken.

Membrane filters are appropriate for sampling aerosols for subsequent determination of soluble metal compounds. Such filters are manufactured from a variety of polymeric materials by a number of different processes. Choice of polymer material comprising the filter (e.g., MCE, PTFE, PVC) will depend on chemical reactivity issues discussed in the preceding paragraph. The metal content of the filters must be as low as possible, since it can make a significant contribution to the blank value.

5 Analytical considerations

A number of analytical methods for soluble metal compounds in occupational hygiene samples have been published by various organizations [NIOSH 1994; HSE 1998; BIA 1989; INRS 2014]. Efforts to harmonize sample preparation approaches have led to the promulgation of related consensus standards [Ashley 2015].

a. European standard

Guidance on sample preparation methods for soluble metals and metalloids in workplace air has been promulgated recently in a European Standard [CEN 2009]. In these published methods and guidelines [NIOSH 1994; HSE 1998; BIA 1989; INRS 2014], two methodologies are generally favored for the extraction of "soluble" metal species: (1) extraction in pure water, or (2) extraction in diluted (~0.1 M) hydrochloric acid (HCl). In the European Standard [CEN 2009], both strategies are given as options for the dissolution of "soluble" metals in workplace air samples. Extraction of metals and metalloids in water is meant to reflect the chemical definition of "soluble" (as mentioned above), while extraction in diluted HCl is designed to mimic the dissolution of "soluble"

metal compounds in stomach acid, which is highly acidic (pH 1). A temperature of 37 °C is recommended since this is normal body temperature.

b. Extraction solvent

A researcher in Germany [Hahn 2000] argued for the establishment of 0.1 M HCl in an operational definition for soluble metals in occupational hygiene samples and, also, specified mechanical agitation at 37 °C for two hours prior to sample analysis. An exception is made for thallium, which can form insoluble TlCl, in which case HCl is replaced by diluted nitric acid (HNO_3). (A similar problem would arise if HCl were used as the extraction acid for soluble silver compounds.) The German extraction method for several soluble metal species [BIA 1989] is consistent with the strategy outlined [Hahn 2000], which attempts to address bioavailability by choosing HCl as the extraction acid. However, in standard methods promulgated by the United States [NIOSH 1994], the United Kingdom [HSE 1998], and France [INRS 2014], deionized water is the solvent chosen in the operational definition of "soluble" for numerous metallic elements in workplace air samples. An exception to extraction in water is made for nickel [HSE 1998], where an ammonium citrate solution is specified as the leachate for soluble compounds of this element. Ammonium citrate provides buffering and chelating properties that are desirable for leaching soluble nickel compounds [HSE 1998].

c. Operational definitions

Operational definitions of "soluble" metal species have been promulgated for consumer products such as toys, paper products, paints and art materials [ASTM 2014; CEN 2013; ISO 2011]. Standard procedures for the extraction of metal compounds from consumer products are based on sample treatments in 0.07 - 0.14 M HCl (depending on the sample) for an hour at a temperature of 37 °C [Hahn 2000] or at room temperature [CEN 2013]. An ASTM International procedure (formerly the American Society for Testing and Materials) [ASTM 2014] is meant to provide an estimate of the bioavailability of several metals in art materials, using ~0.1 M HCl and extraction at body temperature.

d. Quantity of solvent

Another uncontrolled variable is the quantity of solvent used in laboratory analytical procedures for soluble metals at different laboratories. Different laboratories may (and do) use different amounts of deionized water for extraction. For example, one laboratory might use 10 mL of deionized water to extract the metal from a sample, while another lab may use anywhere from 25 to 100 mL to extract the compound. Depending upon the amount of material present in the sample, the procedure using 25 to 100 mL can dissolve a larger mass of solute than that using 10 mL. A conservative analytical method for metals used 15 mL of deionized water for extraction. This volume was chosen as a convenience

and may not bear any relationship to what the body might absorb. Thus, two identical samples could produce two different results depending on the volume of solvent and other analytical parameters. A further factor affecting solubility is the particle size distribution of the sample: smaller particles are ordinarily more easily dissolved than larger ones. Thus for two samples having the same mass, the sample comprised of small particles may be more easily dissolved than a sample having large particles.

6 ISO procedure for soluble metals and metalloids

Various procedures for the extraction of soluble metals and metalloids have been used for years, based on different operational definitions of solubility. The International Organization for Standardization, Technical Committee 146 on Air Quality, Subcommittee 2 on Workplace Atmospheres, Working Group 2 on Inorganic Particulate Matter (ISO/TC 146/SC 2/WG 2) has attempted to standardize extraction procedures for "soluble" metal compounds by offering an operational definition in terms of a sample preparation method for metallic elements in industrial hygiene measurements.

a. Bioavailability

In the 1990s, it was argued that the solubility in body fluids should be considered in the development of a new definition for soluble TLVs [Fairfax and Blotzer 1994]. But since different body fluids have different solubility characteristics (e.g., pH, salts, polypeptides), such an operational and uniform definition for "bioavailable" cannot realistically be decided. Indeed, the meaning of "bioavailability" has been debated nationally and internationally for years, and it was not deemed practicable nor defensible to attempt to operationally define solubility based on biochemical arguments. Hence, it was decided by consensus within the ISO working group (ISO/TC 146/SC 2/WG 2) to describe procedures for soluble metal compounds in terms of strictly chemical, and not biochemical, criteria [Ashley 2001].

b. Laboratory consistency

With regard to analytical methods for the extraction of soluble metals and their compounds, it was suggested that the extraction media, temperature, and extraction volume should be consistent among all laboratories [Fairfax and Blotzer 1994]. For an operational definition of "soluble" to be offered, delineation of these analytical parameters is necessary in order to fully standardize the extraction procedure for soluble metal species. Moreover, the apparatus used, as well as chemical compatibility issues, must be amply described. Matters that are outside of laboratory control, notably sampling, cannot

always be adequately influenced; however, recommendations as to sampling media, sample handling, and transport requirements should be provided to the field industrial hygienist.

c. Development of ISO procedure

The ISO working group responsible for the development of ISO 15202-2, ISO/TC 146/SC 2/WG 2, began its task in September 1995, not long after the publication of the aforementioned article [Fairfax and Blotzer 1994]. Shown in Table 2 is a list of countries that participated in voting on the technical content of the draft international standard when it was circulated for balloting, from 1996 to 2000.

Because of the various operational definitions for "soluble" metal compounds, a significant challenge was presented to the ISO working group responsible for the development of an international standard method to describe a procedure for extracting soluble metals and metalloids for subsequent atomic spectrometric analysis. Two choices were available based on the standard methods mentioned above: (1) extraction in pure water, or (2) extraction in 0.1 M HCl. It was decided by consensus of ISO delegates present at the earlier working group meetings to follow the former course, where solubility of metal compounds in occupational hygiene samples is defined in chemical terms. This decision was upheld during the later international voting process, which involved those countries listed in Table 2. Nevertheless, text within the International Standard [ISO 2012a] states that individual countries may specify alternative procedures for the measurement of soluble metal species in workplace air samples. This, then, leaves open the option to use other extraction media, such as 0.1 M HCl.

Table 2. "Participating Member"* Countries of ISO/TC 146/SC 2 (During the period of development of ISO 15202-2 [1996-2000])

Belgium	Korea	Turkey
Germany	Netherlands	United Kingdom
India	Poland	United States
Italy	Spain	
Japan	Sweden	

* "Participating," or P-Member, countries are those nations able to vote on Draft International Standards, and therefore may provide comments on the technical content of the documents during voting. "Observing," or O-Member, nations (not listed) may also offer comments and can participate in the development of ISO standards. However, in the formal ISO voting process, O-member nations can vote only on Final Draft International Standards, which allows only for editorial, and not technical, changes at this stage.

The ISO procedure for soluble metals and metalloids assumes that samples were collected using the International Standard for the collection of workplace air samples for subsequent multi-element analysis, ISO 15202-1 [ISO 2012b]. However, the choice of filter material used for the collection of samples targeted for the "soluble" metals procedure is important. Annex A of ISO 15202-1 [ISO 2012b] and Annex B of ISO 15202-2 [ISO 2012a] provide useful guidance on this subject.

The "soluble" metals procedure described in ISO 15202-2 [ISO 2012a] lists all of the elements in Table 1 except for Cr[VI] and Fe. Nevertheless, the sample preparation protocol described in this International Standard is certainly applicable to these other two metallic elements as well. The ISO "soluble" metals method [ISO 2012b] calls for treatment of collected workplace filter samples in 5 mL of deionized water (or ammonium citrate leach solution in the case of Ni) and mechanical agitation in a water bath at 37 ± 2 °C for 60 min. Undissolved material is thereafter separated from the sample solution using a suction filtration apparatus or a syringe filter, and ensuring use of filtration materials that are unreactive towards the soluble metal compounds of interest. After filtration, the sample solution is acidified with nitric acid in order to stabilize the dissolved metallic elements within the extracted sample. This test sample is then ready for analysis by ICP-AES (or ICP-mass spectrometry [ICP-MS] if very low detection limits are required). Of course other analytical techniques, e.g., atomic absorption spectrometry [Wang et al. 2000; Draper et al. 1999] or electrochemical analysis [Ashley 1994; Draper et al. 1999], can be used as analytically equivalent alternatives.

d. Method performance

The performance of soluble extraction methods has been evaluated for several soluble metal species, e.g., those of nickel, silver and hexavalent chromium. Soluble extraction and atomic spectrometric analysis of soluble nickel in cellulosic air filter samples and in bulk reference samples, using 0.1 M ammonium citrate for extraction (as part of a sequential extraction method), was ruggedized and validated both within a single laboratory and via interlaboratory trials [Zatka et al. 1992]. This ammonium citrate leaching procedure forms the basis of the ISO 15202-2 (Annex B) methodology [ISO 2012a] for soluble nickel compounds. In other research, soluble silver compounds on PTFE filters were subjected to leaching in deionized water [ISO 2012a] within opaque sampling cassettes, with subsequent analysis by ICP-MS [Drake et al. 2006]. The use of opaque samplers was necessary to prevent photoreduction of silver ions in solution, and ICP-MS was required due to the need for lower method detection limits for the soluble silver fraction in real samples. The soluble silver procedure was validated in-house by using silver nitrate spikes on PTFE filters, demonstrating >90% recoveries. Field studies were also carried out in silver refineries by using a multiport sampler, where it was found

that the soluble silver fraction was less than 2% of the mass of total silver in collected air samples [Drake et al. 2006]. In further work, the use of deionized water for leaching of soluble hexavalent chromium compounds was evaluated [Ashley et al. 2009] as part of a study to validate a standardized sequential extraction procedure for Cr[VI] preceding ion chromatographic analysis [ASTM 2013]. Laboratory experiments on soluble Cr[VI] compounds spiked onto PVC filters resulted in quantitative recoveries, yet interference from Fe[II] (if present in samples) was unavoidable. Water leaching of paint pigment samples and welding fume samples was also evaluated as part of the investigation. It was found that soluble Cr[VI] compounds were prevalent in welding fumes, but their contents were variable in the different paint pigments that were tested [Ashley et al. 2009].

7 Summary

The exposure standards for some metals vary up to a factor of 500 to take into account the increased solubility and bioavailability of some compounds. Even compounds generally considered by chemists as being "insoluble" may have sufficient solubility in body fluids to be of biological importance. Exposure standards for soluble metals such as ACGIH TLVs and other OELs are not specific with regard to extraction fluid, fluid temperature, agitation and other factors affecting solubility. Since these factors significantly affect solubility, some standardization or adoption of an operational definition is necessary if there is to be reproducibility among laboratories conducting soluble metal analyses. In some countries (e.g., nations in the European Union), the national requirements provide this specificity. In other instances, including exposure monitoring standards in the United States, formal national guidelines are not available.

Therefore, adherence to international extraction guidelines or methods such as those described in ISO standards is necessary to produce measurements that are reproducible with other laboratories, and have utility to the laboratory client when exposure standards or national guidelines are vague. ISO 15202 has the advantage over other guidelines and standards in that it has had input from more than 13 participating countries (Table 2). Thus the use of ISO 15202 is encouraged until either exposure standards or national guidelines provide better specificity.

Laboratories cannot recover soluble metal data if inappropriate sample media are used. Sample stability is a problem that must be addressed when sampling for silver (Ag), chromium (Cr) and other soluble metal compounds. Although the ISO procedure has not been validated for all soluble metal species, the standard recommends that method validation be carried out using representative soluble metal compounds for target elements. ISO 15202 provides guidance on sample media selection for soluble metals that can be a useful guide for industrial hygienists and other laboratory clients.

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9 Appendix - Solubilities of selected metals and metal compounds [Fairfax and Blotzer 1994]

Aluminum and compounds

Aluminum metal reacts with dilute hydrochloric acid, sulfuric acid, potassium hydroxide, and sodium hydroxide.

The salts of aluminum, including sodium aluminate, aluminum fluoride, aluminum chloride, and cryolite, are all soluble in water.

Arsenic and compounds

Arsenic — Insoluble in hot and cold water; soluble in nitric acid.

Arsenic trioxide and pentoxide — Soluble in cold and hot water, alcohol, alkalies, and hydrochloric acid; arsenic pentoxide is soluble in acids.

Lead arsenate — Insoluble in cold water; soluble in hot water, nitric acid, and caustic alkalies.

Calcium arsenate(s) — Insoluble in water and acids.

Sodium arsenate(s) — Very soluble in water.

Arsenic acid — Soluble in water and alcohol.

Arsenic trisulfide — Practically insoluble in water.

Barium and compounds

Barium metal — Insoluble in water; soluble in alcohol.

Most of the compounds of barium are soluble in (cold or hot) water, for example, barium chloride, barium oxide, barium acetate, and barium cyanide. Barium hydroxide is slightly soluble in water. Barium carbonate is insoluble to slightly soluble in water, and is soluble in acids.

Beryllium and compounds

Beryllium — Slightly soluble in hot water; insoluble in cold water; soluble in dilute alkalies and acids.

Beryllium oxide — Insoluble in water; soluble in some acids and alkalies.

Beryllium hydroxide — Insoluble in water; soluble in acids and alkalies.

Beryllium fluoride — Soluble in cold and hot water, alcohol, and sulfuric acid.

Beryllium sulfate — Soluble in water and concentrated sulfuric acid.

Chromium and compounds

Chromium reacts with dilute hydrochloric acid and sulfuric acid, but not with nitric acid.

Chromium metal — Insoluble in hot and cold water.

Hexavalent chromium compounds, including chromium trioxide, the anhydride of chromic acid, chromates, dichromates, and polychromates, tend to be of low solubility in water and can be subdivided into two subgroups:

1.) Water-soluble hexavalent chromium compounds include chromic acid, its anhydride, and the monochromates and dichromates of sodium, potassium, ammonium, lithium, cesium, and rubidium.

2.) Water-insoluble hexavalent chromium compounds include zinc chromate, lead chromate, barium chromate, and sintered chromium trioxide. NOTE: Depending on the reference [CRC 2015, O'Neil 2006] both calcium chromate and strontium chromate are listed as soluble and insoluble in water.

Iron and compounds

Iron, ferrous oxide, ferric oxide, and iron oxide — Insoluble in hot and cold water.
Ferric chloride, ferric nitrate, ferric sulfate, ferrous sulfate and ferrous chloride — Soluble in hot and cold water.
Ferric chloride — Soluble in ethanol, methanol, and ether.
Ferric nitrate and ferrous chloride — Soluble in ethanol and acetone.
Ferric sulfate — Sparingly soluble in ethanol; insoluble in acetone.
Ferrous sulfate — Insoluble in ethanol.

Molybdenum and compounds

Molybdenum — Insoluble in hot or cold water; soluble in nitric, sulfuric, and hydrochloric acids.
Molybdic oxide — Sparingly soluble in water; soluble in acids and alkalies.
Molybdenum disulfide — Insoluble in hot or cold water and dilute acids; soluble in hot sulfuric acid, aqua regia, and nitric acid.
Ammonium molybdate — Soluble in hot or cold water, acids, and alkalies.
Calcium molybdate — Insoluble in cold water; soluble in hot water.
Lead molybdate — Insoluble in water and alcohol; soluble in acid and potassium hydroxide.
Sodium molybdate — Soluble in hot and cold water.

Nickel and compounds

Nickel — Insoluble in hot and cold water; soluble in nitric, sulfuric, and hydrochloric acids.
Nickel oxide — Insoluble in hot and cold water; soluble in ammonium hydroxide and acids.
Nickel acetate — Soluble in cold water; insoluble in alcohol [CRC 2015]; soluble in alcohol [O'Neil 2006].
Nickel carbonate — Soluble in cold water; insoluble in hot water.

Nickel hydrates — Some forms soluble, others insoluble (in water).
Nickel sulfate — Soluble in hot and cold water.

Platinum and compounds

Platinum — Insoluble in hot or cold water and single mineral acids; soluble in aqua regia; attacked by halogens, alkali cyanides, and caustic alkalies.
Platinum forms are series of complex chloroplatinate salts that are water soluble.

Rhodium and compounds

Rhodium — Insoluble in hot or cold water; soluble in hot sulfuric acid plus hydrochloric acid; slightly soluble in acids and aqua regia.
Water-soluble rhodium compounds include rhodium trichloride, sodium chlororhodite, and rhodium carbonyl acetylacetonate.

Silver and compounds

Silver — Insoluble in water and inert to most acids; reacts readily in dilute nitric acid or hot concentrated sulfuric acid; soluble in fused alkali hydroxides in the presence of air.
Silver oxide — Soluble in hot and cold water, acids, and alkalies.
Silver acetate — Soluble in hot or cold water and nitric acid.
Silver bromide — Insoluble in hot or cold water and nitric acid.
Silver chloride — Soluble in hot water; slightly soluble in cold water and ammonium hydroxide.
Silver cyanide — Soluble in cold water, nitric acid, and ammonium hydroxide.
Silver nitrate — Soluble in hot and cold water.

Thallium and compounds

Thallium — Insoluble in hot and cold water; soluble in nitric, sulfuric, and hydrochloric acids.
Thallous oxide — Soluble in water, acids, and alcohols.
Thallic oxide — Insoluble in hot or cold water; soluble in acids.
Thallous acetate and thallic chloride — Soluble in cold water and alcohol.
Thallous bromide and chloride — Slightly soluble in water.
Thallous sulfate — Soluble in hot or cold water.
Thallous sulfide — Soluble in cold water.

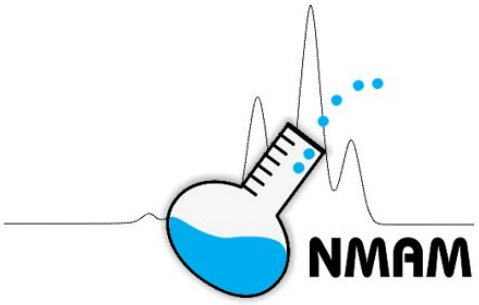
Tungsten and compounds

Tungsten — Insoluble in hot or cold water, hydrofluoric acid, and potassium hydroxide; soluble in mixtures of hydrofluoric and nitric acid; slightly soluble in sulfuric acid.
Tungsten trioxide — Insoluble in hot or cold water and acids; soluble in hot alkalies and hydrofluoric acid.

Tungstic acid — Insoluble in cold water and most acids; soluble in hot water, alkalies, hydrofluoric acid, and ammonia.
Sodium tungstate — Soluble in hot and cold water; slightly soluble in ammonia; insoluble in acids and alcohol.
Tungsten carbide — Insoluble in water; soluble in mixtures of hydrofluoric and nitric acid, and in aqua regia.
Tungsten diboride — Insoluble in hot or cold water; soluble in aqua regia.
Tungsten hexachloride — Soluble in hot water.
Tungsten oxytetrachloride — Soluble in hot or cold water.
Tungsten hexafluoride — Soluble in hot or cold water and alkalies.
Tungsten disulfide — Insoluble in cold water and in alcohol; soluble in mixtures of hydrofluoric and nitric acid.
Phosphotungstic acid — Soluble in cold water, alcohol, and ether.
Ammonium paratungstate — Soluble in water; insoluble in alcohol.

Uranium and compounds

Uranium — Insoluble in hot or cold water, alcohol, and alkali.
Uranium dioxide — Insoluble in hot or cold water; soluble in nitric acid and concentrated sulfuric acid.
Triuranium octoxide — Insoluble in hot or cold water; soluble in nitric acid and sulfuric acid.
Uranium tetrafluoride — Insoluble in cold water, dilute acids, and alkalies; soluble in concentrated acids and alkalies.



NIOSH Manual of Analytical Methods (NMAM), 5th Edition

Monitoring Diesel Exhaust in the Workplace

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Centers for Disease Control and Prevention
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1 Introduction

a. Health effects

Over a million U.S. workers (e.g., trucking, mining, railroad, construction, agriculture) are occupationally exposed to diesel exhaust [NIOSH 1988]. The widespread use of diesel-powered equipment is a recognized health concern. Exposure to diesel exhaust is associated with an increased risk of lung cancer [Attfield et al. 2012; Garshick et al. 2004; HEI 1995; IARC 2012; Silverman et al. 2012]. Diesel exhaust is pervasive, and environmental exposure is a public health concern; but workplace exposures pose higher risk because they are generally much higher than those encountered by the general population.

In 1988, the National Institute for Occupational Safety and Health (NIOSH) reported diesel exhaust as a potential occupational carcinogen and recommended that employers reduce workers' exposures [NIOSH 1998]. This recommendation was based on five independent animal studies, in which rats exposed to unfiltered exhaust showed an increased incidence of benign and malignant lung tumors [IARC 1989]. Other organizations, including the International Agency for Research on Cancer (IARC) [IARC 1989], the World Health Organization (WHO) [WHO 1996], the California Environmental Protection Agency [CalEPA 1998], the U.S. Environmental Protection Agency (EPA) [EPA 2000a], and the National Toxicology Program [NTP 2000] reviewed the animal and human evidence, and each classified diesel exhaust as a probable human carcinogen or similar designation. In 2012, based on epidemiological studies, IARC [IARC, WHO 2012] reclassified diesel exhaust as carcinogenic to humans (Group 1). In particular, a major study of U.S. miners, conducted by NIOSH and the National Cancer Institute (NCI), found increased risk of death from lung cancer in exposed workers [Attfield et al. 2012; Silverman et al. 2012].

Noncancer health effects also are associated with diesel exhaust exposure, including immunologic, respiratory, and cardiovascular effects. Diesel exhaust particles can act as nonspecific airway irritants at relatively high exposures. At lower levels, they can trigger release of mediators (cytokines, chemokines, immunoglobulins, and oxidants) of allergic and inflammatory responses [Pandya et al. 2002]. Diesel particles may promote expression of the immunologic response phenotype (Th2) associated with asthma and allergic disease and may have greater immunologic effects in the presence of environmental allergens. Internationally, the prevalence of asthma (and related hospitalizations and mortality) continues to rise in adults and children. Children may be more vulnerable than adults [Edwards et al. 1994; Weiland et al. 1994; Wjst et al. 1993; van Vlient et al. 1997]. Studies indicate children living along major trucking thoroughfares are at increased risk for asthmatic and allergic symptoms. In the United States, the number of individuals with

self-reported asthma increased by 75% from 1980 to 1994 [Mannino et al. 1998]. The immunologic evidence is consistent with results of epidemiologic studies that associate traffic-related air pollution, especially diesel exhaust particles, with an increase in respiratory diseases.

Studies have consistently found positive associations between particulate air pollution and daily mortality [Brown et al. 2000; Dockery et al. 1993; EPA 1999, 2000b; Pope et al. 1995a; Pope et al. 1995b; Pope et al. 2002; Samet 2000; Schwartz 1997; Schwartz et al. 1996]. The traditional U.S. air quality standard for particulate matter is based on particles having diameters ≤10 µm (PM10) [52 Fed. Reg. 24634 (1987)]. In 1997, EPA proposed a new standard [62 Fed. Reg. 38652 (1997)] (see www.epa.gov/airlinks/airlinks4.html) based on particles having diameters ≤2.5 µm ($PM_{2.5}$). These smaller particles originate mainly from combustion sources. The new standard was proposed because recent studies had found higher correlation between fine particle pollution and adverse health effects. In an analysis [Schwartz et al. 1996] of data from six U.S. cities, fine particles were consistently associated with increased risk of death from chronic obstructive pulmonary disease, pneumonia, and ischemic heart disease. Positive associations between fine particle pollution and hospital admissions due to respiratory and cardiovascular illness also have been found [Schwartz 1994; Burnett et al. 1995; Schwartz and Morris 1995]. Particles produced by combustion sources were implicated in these findings. In addition to asthma, chronic inhalation of diesel exhaust particles may play a role in these adverse health outcomes. Reviews on the health effects of diesel exhaust have been published [CalEPA 1998; EPA 2000a; HEI 1995, 2002; IARC 1989; IARC (WHO) 2012; NIOSH 1988; NTP 2000; Solomon et al. 1998; WHO 1996].

b. Composition

Diesel engine exhaust is a highly complex and variable mixture of gases, vapors, and fine particles. The amount and composition of the exhaust vary greatly, depending on factors such as fuel and engine type, maintenance schedule, tuning, workload, and exhaust gas treatment. The gaseous constituents have included hydrocarbons and oxides of carbon, sulfur, and nitrogen. Particulate components consisted of liquid droplets and soot particles bearing organic compounds, sulfates, metals, and other trace elements. The organic fraction (droplets and particle adsorbed) was mainly unburned fuel and oil, but thousands of compounds (e.g., aldehydes, polycyclic aromatic hydrocarbons [PAH]) have been found in the organic fraction—some of which are genotoxic [HEI 1995, 2002; IARC 1989; NIOSH 1988; WHO 1996].

c. Analyte choice: elemental carbon

Because diesel exhaust is a highly complex mixture, a surrogate of exposure must be selected. In the early 1990's, NIOSH researchers considering potential surrogates sought an overall measure of the particulate fraction because animal studies associated lung tumor induction with unfiltered diesel exhaust [IARC 1989; NIOSH 1988], and most (90% in one study) [Schuetzle 1983] of the exhaust's mutagenic potency was associated with the particulate fraction. At the time, gravimetric methods for respirable combustible and submicrometer dusts were being used in mines, but gravimetric methods lack selectivity and are not suitable for low-level (e.g., <200 μg/m^3) measurements. Methods for characterization of the soluble organic fraction of diesel particulate matter (DPM) also were available; others have since been developed. Although measurement of specific organic compounds, particularly genotoxins, may be relevant in characterizing the potential toxicity of diesel exhaust, a single compound or compound class would not reflect exposure to the particulate fraction—even if unique markers are found—because the composition of the exhaust is highly variable.

Carbon is a logical exposure surrogate for traditional diesel engines because DPM is predominantly (typically more than 80%) carbon [Japar et al. 1984; Lies 1989; Pierson et al. 1983]. However, carbon in the organic fraction (i.e., *organic carbon*, or OC) of DPM is not a selective measure because other sources of OC (e.g., cigarette smoke and other combustion aerosols, asphalt fumes) are present in many workplaces. *Elemental carbon* (i.e., carbon in the soot particle core, or EC) is a better surrogate [Birch and Cary 1996a] to monitor because it is a more selective measure of particulate diesel exhaust and still constitutes a sizable fraction (30%–90%) (see [HEI 2002], Part I, Section 1) of the particulate mass. Fine EC particles are derived primarily from the combustion of fossil fuels, and diesel engines have been major sources of these particles. Carbonaceous aerosols such as cigarette and wood smokes contain little, if any, EC [Birch 1998a; Birch and Cary 1996a]. Gasoline engines emit far less EC than diesels, so the contribution of this source is relatively small. Other sources such as coal combustion, incinerators, and tire debris can contribute to the background (environmental) levels of EC, but diesel engines were the primary emitters [Cass and Gray 1995; Sawyer and Johnson 1995]. In occupational settings, where diesel equipment is used in relatively close proximity to workers, the contribution of these remote sources is negligible, especially when EC levels are well above background. Environmental EC concentrations are typically in the 1–3 μg/m^3 range [Birch and Cary 1996a], depending on the local air pollution, while in workplaces with diesel equipment (operating), EC concentrations are generally much higher [e.g., Haney and Fields 1996; NIOSH 1992; NIOSH 1993; NIOSH 1994c; Stanevich et al. 1997; Verma et al. 1999; Whittaker et al. 1999; Zaebst et al. 1991]. Higher environmental background (e.g., 3--5 μg/m^3) has been reported for more polluted U.S. cities (e.g., Los Angeles), but the higher

EC levels were attributed to nearby diesel vehicles [Cadle and Mulawa 1990; Gray et al. 1984] (see also [Cass and Gray 1995]). At one monitoring site (Glendora, CA), examination of the data collected at 1-minute intervals revealed that emission plumes from diesel vehicles located 50 meters from the site contributed contamination up to 5 μg/m^3 above the background level [Hansen and Novakov 1990].

Carbonaceous dusts such as coal dust (EC content depends on coal rank), carbon blacks, and carbon nanomaterials contain EC, but particles in powders (dispersed as particle agglomerates) and mechanically generated dusts are much larger (generally >1 μm diameter) than combustion-based particles. Therefore, these dusts can be effectively excluded from the diesel sample on the basis of size. Only low levels of EC (≤15 μg/m^3) were found in electric-powered (i.e., nondieselized) coal mines when impactors with submicrometer cutpoints were used for air sampling [Birch and Cary 1996b]. Guidance on air sampling is discussed in a following section. In addition to selectivity, potential health effects were considered when an EC surrogate was proposed [55 Fed. Reg. 110 (1990); Birch 1991; Birch and Cary 1996a]. Diesel particles and other types of insoluble fine particles are inhaled deeply into the lungs, where they can induce an inflammatory response. Further, EC particles were shown to increase the long-term retention [Sun et al. 1982; Wolff et al. 1986] of adsorbed genotoxins and other chemical toxins because the particles have a high affinity for them [Niessner and Wilbring 1989]. The adsorbed organic fraction results from rapid cooling of the exhaust mixture, which causes enrichment of some species on the particle surface [Natusch 1978; Thrane et al. 1985; Yamasaki et al. 1982]. Enrichment by this mechanism is associated with compounds of moderate to low volatility [Thrane et al. 1985; Yamasaki 1982]. For example, PAHs having four or more aromatic rings are generally associated with particulate matter [Bjorseth and Becher 1986]; this is important because these higher-ring condensates are expected to be the most carcinogenic or mutagenic [Grimmer et al. 1983; Pott 1985]. In combination with an inflammatory response induced by the particles, genotoxic agents may promote tumorigenesis. Ultrafine particles (<0.10 μm) may pose an even greater health risk. Results of toxicological studies on solid particles having aerodynamic diameters in this size range indicate ultrafine particles are especially toxic, even those not having an organic fraction and consisting of materials considered relatively nontoxic (e.g., carbon black, titanium dioxide). In a study of rats [Donaldson et al. 2000], a 10-fold increase in inflammation was seen with exposures to ultrafine particles, relative to the same mass of fine particles. This is significant because, by mass, the majority of diesel particles are in the fine particle range, and most are in the ultrafine range by number [Kittelson et al. 2002]. Given the physical and chemical nature of EC particles emitted by diesel engines, monitoring and controlling exposures to these particles is prudent.

2 Analytical method

a. Background

A monitoring method for DPM was published as Method 5040 in the *NIOSH Manual of Analytical Methods* (NMAM). The method is based on a thermal-optical analysis technique for particulate carbon. Both OC and EC are determined, but EC is a better exposure surrogate. Rationale for selection of an EC surrogate is summarized in the previous section (*Analyte Choice: Elemental Carbon*). Method updates and an NMAM Chapter (Q) have since been published [NIOSH 1994a (1998 supplement); NIOSH 1994b (2003 supplement); NIOSH 2003] to include interlaboratory data (e.g., round robin results) and other diesel-related information obtained since its initial publication (in 1996). This 5th edition chapter is not a review of relevant literature published since the 4th edition. Its purpose is to update references and information on the following topics: classification of diesel exhaust as a human carcinogen, a study of miners exposed to diesel exhaust, results of a subsequent round robin by NIOSH investigators, and application of the Method to carbon nanomaterials. NIOSH 5040 has been used in numerous industrial hygiene surveys on diesel exhaust [e.g., Haney and Fields 1996; NIOSH 1992: NIOSH 1993; NIOSH 1994c; Stanevich et al. 1997; Verma et al. 1999; Whittaker et al. 1999; Zaebst et al. 1991], and it was applied to an epidemiological study (NIOSH/NCI) of miners [Attfield et al. 2012; Silverman et al. 2012]. Details on Method operation and performance are provided in this chapter. Exposure criteria also are discussed.

b. Instrumentation

Of the possible approaches for OC-EC analysis, a thermal-optical technique was investigated because it offered greater selectivity (pyrolysis correction for char) and flexibility (automated analysis, programmable parameter files) than previously used methods. Prior to its proposed use for monitoring occupational exposure to diesel exhaust, thermal-optical analysis (or OC-EC methods in general) had not been applied to occupational monitoring, but the technique had been routinely applied to environmental monitoring of particulate carbon air pollution.

The thermal-optical analyzer (Figure 1) has been described previously [Birch and Cary 1996a; NIOSH 1994a (1998 supplement)]. Design changes (e.g., reflectance monitoring added, software upgraded) have since been made, but the operation principle remains unchanged. OC-EC quantification is accomplished through temperature and atmosphere control. In addition, the analyzer is equipped with an optical feature that corrects for char formed through sample pyrolysis (thermal breakdown in inert atmosphere). Some samples contain components (e.g., cigarette and wood smokes) that carbonize (convert to char carbon) when the sample is heated in helium during the first part of the analysis. Like the

EC typical in fine particle pollution, char strongly absorbs light, particularly in the red/infrared region, resulting in a decrease in the filter transmittance/reflectance. Both volatile products and char are formed during the decomposition process, which may begin near 300 °C and continue until the maximum temperature (860-880 °C) is reached. Optical correction for char is made through use of a pulsed diode laser and photodetector that continuously monitor the filter transmittance/reflectance.

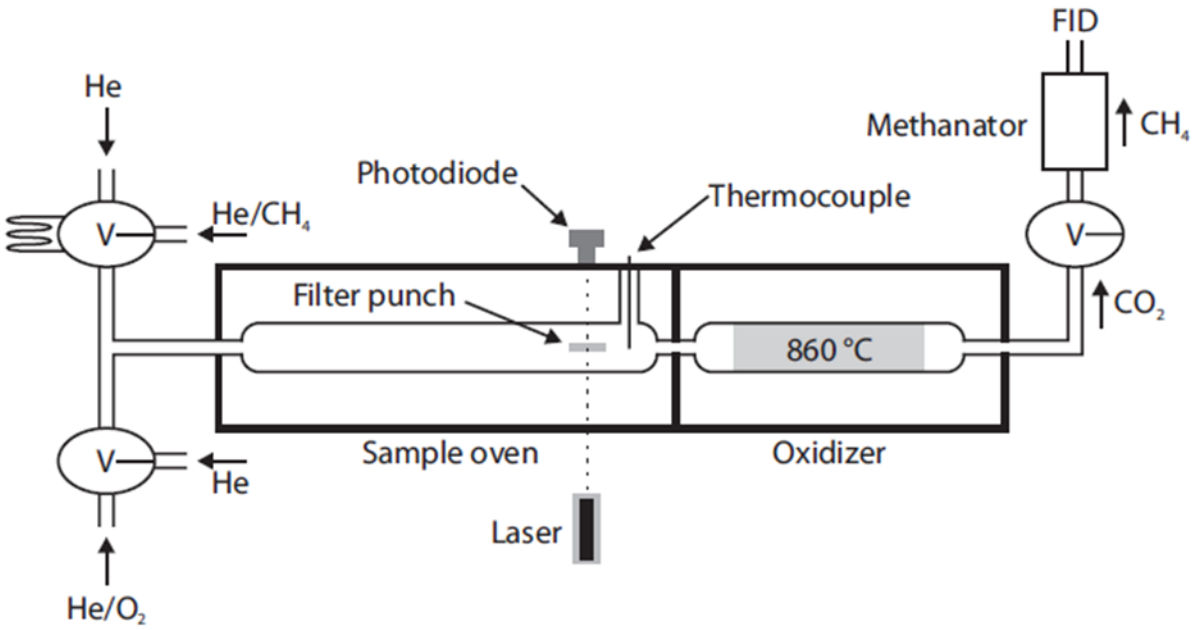

Figure 1. Schematic of thermal-optical transmittance instrument (V = valve) for determining OC and EC in carbonaceous aerosols.

In the thermal-optical analysis, a filter portion (punch) of known area (typically 1.5 cm^2) is placed in the sample oven, and the oven is tightly sealed. Quartz-fiber filters are required because temperatures in excess of 850 °C are employed. The analysis proceeds in inert and oxidizing atmospheres. In both, the evolved carbon is catalytically oxidized to carbon dioxide (CO_2). The CO_2 is then reduced to methane (CH_4), and CH_4 is quantified with a flame ionization detector (FID).

OC (and carbonate, if present) is first removed in helium, as the temperature is increased to a preset maximum (usually 850 °C or higher). If charring occurs, the filter transmittance decreases as the temperature is stepped to the maximum. After OC is removed, an oxygen-helium mix is introduced to effect combustion of the remaining carbon. As oxygen enters the oven, light-absorbing carbon is oxidized and a concurrent increase in filter transmittance/reflectance occurs. The *split* (vertical line prior to EC peak in Figure 2) between the OC and EC is assigned when the initial (baseline) value of the filter transmittance is reached. All carbon removed before the OC-EC split is considered

organic, and that removed after the split is considered elemental. If no char is formed, the split is assigned prior to removal of light-absorbing carbon. If the sample chars, the split is not assigned until enough light-absorbing carbon is removed to increase the transmittance/reflectance to its initial value. In general, char is more readily oxidized than diesel-particle EC. The delay (i.e., the transit time from sample to FID) between the laser and FID signals is considered in the split assignment. Ordinarily, the split is assigned in the oxidative mode of the analysis.

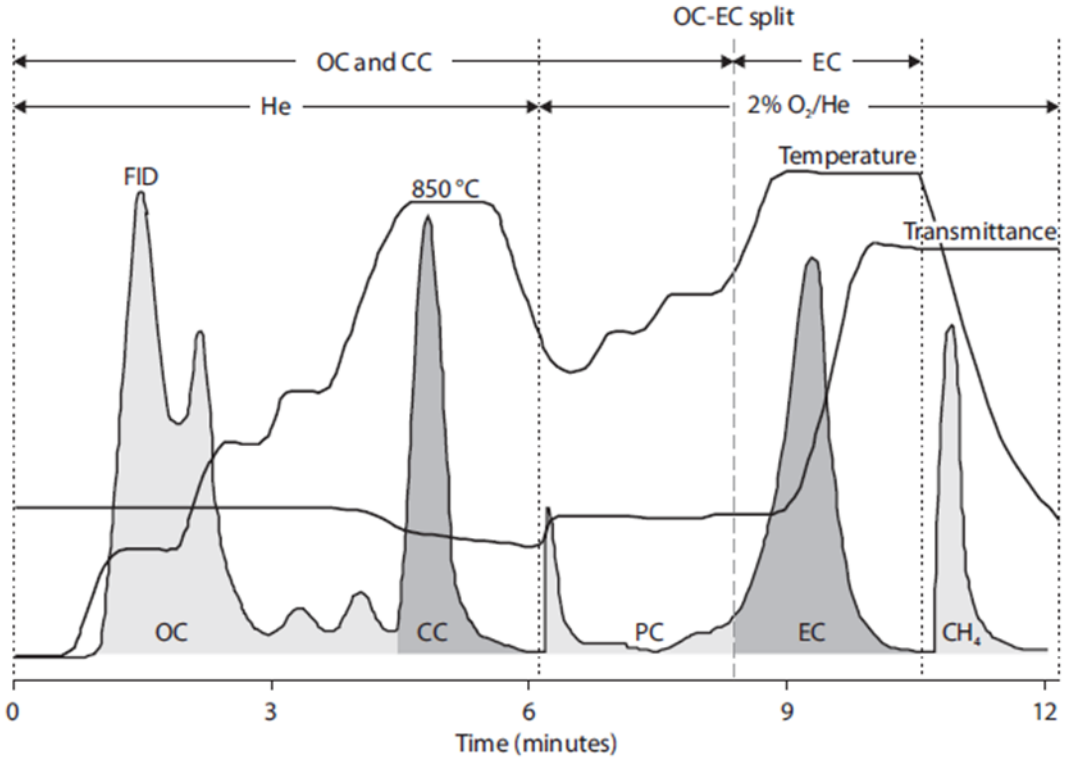

Figure 2. Thermogram for filter sample containing organic carbon (OC), carbonate (CC), and elemental carbon (EC). PC is pyrolytically generated carbon or "char." Final peak is methane calibration peak. Carbon sources: pulverized beet pulp, rock dust (carbonate), and DPM.

EC and OC results are reported in micrograms per square centimeter (μg/cm^2) of the sample deposit. The total OC and EC on the filter are calculated by multiplying the reported values by the deposit area. In this approach, a homogeneous deposit is assumed. For triplicate analyses, the precision (relative standard deviation) is normally under 5%, and it is typically 2% or better [NIOSH 1994b (2003 supplement)]. The total carbon (TC) in the sample is the sum of OC and EC. If carbonate is present, the carbon in it is

quantified as OC, unless a carbonate-subtracted value is requested. Additional details about carbonates are given in a following section.

c. Accuracy

Reference materials are not available for determining the accuracy of OC-EC measurements on filter samples of complex carbonaceous aerosols. For this reason, only the accuracy of the method in the determination of TC could be examined. No discernable differences in the responses of five different organic compounds were found. Linear regression of the data (43 analyses total) for all five compounds gave a slope and correlation coefficient (r) near unity [slope = 0.99 (±0.01), r^2 = 0.999, n = 43]. In addition to the OC standards, eight different carbonaceous materials were analyzed. Three different methods (including the thermal-optical method) were used, and laboratories reported the TC contents of the samples. The samples analyzed included DPM and other types of carbonaceous matter (coals, urban dust, humic acid). Thermal-optical results agreed well with those reported by the two other laboratories. The variability in TC results for the three laboratories ranged from about 1%–7%. These findings [Birch and Cary 1996a; NIOSH 1994a (1998 supplement)] indicate that TC is accurately quantified, irrespective of sample type.

d. Limit of detection

To estimate the method's limit of detection (LOD), a set of low-level calibration standards (ethylenediaminetetraacetic acid [EDTA]) was analyzed [Birch and Cary 1996a; NIOSH 1994a (1998 supplement)]. The standards covered a loading range from 0.23 to 2.82 µg C (or from 0.15 to 1.83 µg C per cm^2 of filter). Results of linear regression of the low-level calibration data were then used to calculate a LOD as 3 σ_y/m, where σ_y is the standard error of the regression and m is the slope of the regression line. The LOD estimated through the linear regression results was 0.24 µg C, or 0.15 µg/cm^2. This value showed good agreement with the LOD estimated as 3σ_{blank} (three times the standard deviation for blanks), which gave a value of about 0.3 µg C. The mean (n = 40) instrumental blank was 0.03 ±0.1 µg C. With a 960-L air sample collected on a 37-mm filter and use of a 1.5 cm^2 sample portion, this LOD translates to an air concentration of about 2 µg/m^3. As with all sampling and analytical methods, the LOD is a varying number that depends on the instrument, sampling parameters, and means by which the LOD is calculated.

NIOSH Method 5040 was developed for monitoring workplace exposure to DPM, especially in mines, where EC concentrations are relatively high (e.g., hundreds of µg/m^3). However, the thermal-optical technique on which 5040 is based has application to other types of carbonaceous aerosols. Thermal-optical analysis also has been applied to studies of U.S. workers exposed to carbon nanotubes and nanofibers (CNT and CNF) [Birch et al.

2011; Dahm et al. 2012; Dahm et al. 2015; NIOSH 2013]. For these studies, a lower LOD was needed because workplace concentrations of CNT/CNF are generally low. As recommended in Method 5040, a smaller (25-mm) filter and a higher flow rate were used to obtain a lower LOD (about 1 µg EC/m^3 or lower). Manual assignment of the OC-EC split also was made. Application of Method 5040 to carbon nanomaterials is discussed below (see Carbon Nanomaterials).

e. Air sampling

In the initial evaluation of the thermal-optical method, a set of laboratory-generated air samples was analyzed. A dilution tunnel equipped with a dynamometer was used for generation of diesel particulate samples. Four EC concentrations, ranging from 23 to 240 µg/m^3 (EC loadings from 2.7 to 27 µg/cm^2), were generated. The analytical results [NIOSH 1994b (1998 supplement)] indicated that the method met the NIOSH accuracy criterion [Kennedy et al. 1995]. The variance was roughly proportional to the mean concentration; therefore, the relative standard deviation (RSD) decreased with increasing concentration. The accuracy was calculated accordingly. The accuracy was ±16.7% at the lowest loading (2.7 µg/cm^2), with an overall precision (RSD) of 8.5%. On the basis of a method evaluation, the NIOSH accuracy criterion requires a confidence limit on the accuracy less than 25% at the 95% confidence level. Restated, the criterion dictates that greater than 95% of the measurements fall within ±25% of the true value at 95% confidence in the method's validation experiments. The method was considered unbiased (i.e., considered the reference method), and the overall precision reflected method accuracy. In this initial test, the sample generation and collection system was the main source of variability, not the analysis.

When only combustion-source EC is present, different samplers can be expected to give comparable EC results because particles from combustion sources are generally less than 1 µm (diameter). As such, the particles are evenly deposited on the filter and collected with the same efficiency (near 100%). To confirm this assumption, seven different sampler types (open-faced 25-mm and 37-mm cassettes; 298 personal cascade impactor [7 stages, 0.9-µm cutpoint]; 4 prototype impactors) were used to collect diesel aerosol at the loading dock of an express mail facility. The RSD for the mean EC concentration was 5.6% [Birch and Cary 1996a]. Based on the 95% confidence limit (19%; 13 degrees of freedom, n = 14) on the accuracy, results of this experiment also indicated that the NIOSH accuracy criterion [Kennedy et al. 1995] was fulfilled. The amount of EC collected (240 µg per sample) would have been equivalent to sampling an air concentration of 250 µg/m^3 for 8 h at 2 L/min. Variability in the OC results was higher (RSD = 12.3%), which is to be expected when different samplers are used to collect aerosols that contain semivolatile (and volatile) components because these can have a filter face velocity dependence.

Similar performance was obtained from collected samples in an underground molybdenum mine. Five different sampler types were used (closed-face 25-mm and 37-mm cassettes; 298 cascade impactor [7 stages, 0.9-µm cutpoint]; cyclone with filter; in-house impactor). The RSD for the EC results (mean EC = 297 µg/m^3) was 7%. The EC deposits obtained with all five sampler types were homogeneous, even when the ore deposit was visually heavier in the center of the filter (e.g., with the closed-face 37-mm cassette). Although the dust loading was higher in the center of the filter, portions taken from the center gave equivalent EC results, indicating the ore contained no EC component. The TC results for the center portions were only slightly higher, so this particular ore was mostly inorganic. EC concentrations found with three different sampler types (nylon cyclone, open-faced cassette, and impactor with submicrometer cut) also were comparable in a study of railroad workers [Verma et al. 1999].

If high levels of other dusts are present, a size classifier (e.g., impactor and/or cyclone) should be used to prevent filter overloading, particularly if the dust is carbonaceous. In the latter case, a size classifier provides a more selective measure of the diesel-source OC. It also provides a better measure of the diesel-source EC if the dust contains an EC component, which is less common. A finely ground sample of the bulk material can be analyzed to determine whether a specific dust poses potential interference [Birch and Cary 1996a]. Depending on the dust concentration, size distribution, and target analyte, an impactor may be required.

For mines, the Mine Safety and Health Administration (MSHA) recommends a specialized impactor to minimize collection of carbonates and other carbonaceous dusts [66 Fed. Reg. 5706 (2001)]. An impactor can greatly improve the selectivity of the TC measurement in some cases, but it may exclude a small amount of the DPM. Then, too, some OC interferences cannot be excluded on the basis of size (e.g., condensation aerosols, fumes, wood and cigarette smokes). If present in the sampling environment, these materials can positively bias the OC (TC) results to some degree, depending on their relative concentrations and the sampling location. Although 37-mm or 25-mm cassettes are often suitable for general industry, the required sampler depends on the sampling environment.

f. Carbonates

The presence of carbonate is indicated by a narrow peak during the fourth temperature step in helium (Figure 2). Its presence is verified by exposing a second portion of the filter to hydrogen chloride (HCl) vapor prior to analysis. When the acidified portion is analyzed, a diminished (or absent) peak during the fourth temperature step is indicative of carbonate in the original sample. (Note: Acid treatment may sometimes alter the

appearance of the EC profile in the thermogram [output signal of thermal-optical instrument], but the EC result itself should not be affected significantly.)

A desiccator containing concentrated HCl (added to the desiccator or a petri dish placed at the bottom of it) can be used to acidify the sample portions. The desiccator, or alternative vessel, should be used in a well-ventilated hood. The filter portions are placed on the desiccator tray, and the tray is placed in the desiccator. A wetted pH indicator stick can be used to check acidity. A wetted indicator stick inserted between the desiccator lid and base should give a pH near 2. Portions should be exposed to the acid vapor for about 1 hour (large particles may require more time). After acidification, the tray is placed on a clean, inert surface inside the hood. The residual acid on the portions should be allowed to volatilize in the hood for at least an hour prior to analysis.

Environmental samples typically contain little (if any) carbonate, but levels in some occupational samples can be quite high. For example, respirable dust samples collected in limestone and trona mines can contain high levels of calcium carbonate and sodium sesquicarbonate, respectively. In such cases, acidified samples give a better measure of the diesel-source OC (TC). If the carbonate loading is relatively high (e.g., carbonate carbon >10% of the TC), the difference between the TC results (before and after acidification) gives an estimate of carbonate carbon (CC). Estimation of CC by difference assumes the carbonate is evenly deposited on the filter, which may not always be the case. It also assumes that OC loss through acidification is negligible. The latter assumption is generally true for workplace samples, but depends on sample composition and loading.

Alternatively, a carbonate-subtracted OC (TC) result can be obtained through separate integration of the carbonate peak. This applies only to carbonates (e.g., calcium carbonate) that can be removed as a single peak during the fourth temperature step in helium. The carbonate of interest should be analyzed to ensure this is the case. A minor adjustment (lower) to the third temperature step may be necessary to prevent partial loss during this step. Sodium sesquicarbonate (trona) is removed over multiple temperature steps. Samples containing trona should be acidified if a carbonate-subtracted result is desired. (Note: *At elevated temperature, trona and other compounds containing sodium can etch the quartz oven wall and sample holder. An etched surface can reduce laser throughput. Avoid frequent analysis of high-sodium materials and direct contact of these materials with the oven wall and sample holder.*)

The presence of a small "peak" during the fourth temperature step is not necessarily due to carbonate. Other carbonaceous matter (e.g., char) is sometimes removed during the fourth step. Unlike carbonates, which produce a relatively sharp peak, other materials typically evolve as a small, broad peak. If determination of relatively low (e.g., CC <10% of TC)

amounts of CC is desired, a second portion of the sample should be acidified and analyzed to verify the presence of carbonate and reveal any underlying baseline features contributed by other materials. A more accurate estimate of CC can then be obtained by integrating the first (nonacidified) sample over the missing peak area (i.e., area removed through acidification).

g. Carbon nanomaterials

NIOSH Method 5040 was developed for monitoring workplace exposure DPM, as EC, but the thermal-optical analysis technique on which it is based has application to other types of carbonaceous aerosols and materials. Method 5040 has been applied to field studies on carbon nanomaterials, wherein EC was used as a measure of exposure to carbon nanotubes and nanofibers (CNT and CNF) [Birch et al. 2011; Dahm et al. 2012; Dahm et al. 2015; Fatkhutdinova et al. 2016; NIOSH 2013]. Because CNT/CNF are composed of EC, EC is a quantitative measure of airborne CNT/CNF [Birch et al. 2011; NIOSH 2013]. In 2013, NIOSH set a recommended exposure limit (REL) for CNT/CNF: an 8-hr time weighted average (TWA) of 1 μg/m^3 as respirable EC [NIOSH 2013].

For application of NIOSH 5040 to CNT/CNF, a manual OC-EC split is assigned. The larger size (μm versus nanoscale DPM) and agglomerate structure of CNT/CNF particles, combined with low air concentrations (i.e., filter loadings), make the 5040 auto-split unreliable [Dahm et al. 2015; NIOSH 2013]. Adjustments to the thermal program also may be needed depending on the material, size fraction collected, and environmental background [Birch et al. 2011; Dahm et al. 2015; Doudrick et al., 2012; NIOSH 2013]. Analysis of bulk and background samples is recommended [NIOSH 2013]. Determining the thermal profiles of bulk materials produced/processed in a given workplace, and using this information, along with results for background samples, assists manual assignment of the OC-EC split and can provide more accurate CNT/CNF measurement.

Because CNT/CNF oxidize over a range of temperatures, it is important to analyze bulk and background samples [Birch et al. 2011; Dahm et al. 2015; NIOSH 2013]. For example, Mitsui-7 MWCNT (Mitsui & Co., LTD, Tokyo, Japan), used in early NIOSH toxicity studies, is more difficult to oxidize (onset > 700 °C). A NIOSH (Cincinnati, OH, USA) laboratory normally uses a final temperature (in oxygen-helium) of 920 °C, which is adequate provided that the loading is not too high and the hold time (at final temperature) is long enough. A higher (up to about 940 °C) or lower maximum can be used, and the heating period at maximum temperature can be adjusted according to the type and amount of material analyzed. If the signal returns to baseline, EC in the sample is completely oxidized. If not (i.e., there is signal 'tailing' into the calibration peak), the final temperature can be increased and an extended period can be used. In addition to Mitsui-7

(MWCNT), some graphite products are difficult to oxidize. On the other hand, if a material is completely oxidized at 875 °C, prolonged heating at 920 °C is unnecessary. In some cases (e.g., early EC loss), a lower maximum temperature in the helium also may be appropriate [NIOSH 2003]. These changes are minor adjustments that can be made to optimize the thermal analysis.

In general, most CNT/CNF materials can be oxidized from the filter. However, there may be instances where sample oxidation is incomplete, even with holding at 920 °C (or higher) for an extended period (e.g., high loadings of graphite products or Mitsui-7). For bulks analyses, only small amounts (e.g., about 10 µg or less) of material should be analyzed, to better match the loadings of the field samples, for comparison with the bulk. If residual material (CNT) remains (post analysis), incomplete oxidation is obvious as the signal does not return to baseline and a filter deposit is visible.

Even with the aid of bulks and judicious choice of background samples, it may not be possible to exclude EC background, posing an interference problem at low CNT/CNF loadings. Also, amorphous carbon in the CNT/CNF materials may cause positive bias [NIOSH 2013]. If the oxidation rates of the amorphous carbon and CNT/CNF are sufficiently different, it may be possible to remove the amorphous material to a greater extent, but the oxidation rates may be too similar for speciation.

h. Sampling artifacts: organic aerosol

1.) Face Velocity

Quartz-fiber filters are routinely used to collect airborne particulate matter for carbon determination. Quartz filters have high collection efficiency for particulate carbon, but collection of organic aerosol is artifact prone [Cui et al. 1998; Kirchstetter et al. 2001; McDow and Huntzicker 1990; Turpin et al. 1994; Zang and McMurry 1992]. Particulate carbon (EC and nonvolatile OC) results should not depend on filter face velocity. This is true for EC, but OC (and TC) results can have a face velocity dependence due to sampling artifacts. Namely, adsorption of organic vapor can positively bias the results, while evaporative losses have the opposite effect. Although both processes may occur, studies indicate vapor adsorption is the dominant artifact [Kirchstetter et al. 2001; Turpin et al. 1994]. In one study [Turpin et al. 1994], the OC (TC) results for air samples collected at face velocities of 20, 40, and 80 cm/sec had a face velocity dependence before, but not after, correction for adsorbed vapor. Lack of dependence after correction supports adsorption as the dominant artifact. At the much lower face velocities typical of occupational monitoring (e.g., about 4 cm/sec with a 37-mm filter and 2 L/min flow rate), OC losses induced by pressure drop across the filter are expected to be minor relative to adsorption. OC sampling artifacts were

acknowledged when the thermal-optical method was proposed [55 Fed. Reg. 110 (1990); Birch 1991], but this issue was not investigated prior to publication of NIOSH 5040 because an EC surrogate was recommended. In view of the MSHA-proposed air standard for TC (proposed after 5040 publication), and the fact that both OC and EC are determined, the issue was later addressed.

2.) Adsorbed OC

Correction for adsorbed organic vapor through use of traditional blanks (media or field) may not be accurate because the amount of vapor adsorbed by them is variable [Birch et al. 1999a]. More importantly, traditional blanks collect vapor passively, while the samples collect it actively (during sampling). A more representative correction for adsorbed organic vapor can be made through use of two filters in tandem [Kirchstetter et al. 2001; Turpin et al. 1994]. The air sample is collected with a sampler containing a Teflon® or quartz upper filter and a bottom quartz filter. After sampling, the bottom filter is used to correct for adsorbed vapor. The vapor adsorbed on the bottom filter more closely represents that adsorbed on the sample filter (quartz) because both are collected actively. Use of two quartz filters is preferable to Teflon and quartz because the filter used to correct for adsorbed vapor is in the same sampler; however, the second (bottom) quartz filter may underestimate the amount of adsorbed OC relative to a quartz filter under Teflon [Kirchstetter et al. 2001; Turpin et al. 1994]. These results have been attributed to depletion of the vapor concentration by the top quartz filter, which presents a lower concentration to the bottom one. A shorter equilibration time (for partitioning between gas phase and adsorbed state) is expected with Teflon filters because they have less surface area and are more inert than quartz. Thus, less adsorption is expected on Teflon relative to quartz. Because differences in the amount of adsorbed OC have been reported for the two sampling configurations, both were examined.

Six sets of air samples were collected. Two pre-cleaned quartz-fiber filters were loaded into each of eight 37-mm cassettes. In four of these, a Teflon filter was then placed on top. The bottom quartz filters in all eight cassettes, as well as the four directly under the Teflon filters, provided measures of adsorbed OC. Filters in four additional cassettes served as passive field blanks, meaning no air was pulled through them. The second (bottom) quartz filters in the cassettes with the Teflon filters were compared to the bottom quartz filters in those having only a quartz pair. If negligible adsorption occurs on Teflon, the bottom quartz filters in the two different sampling configurations should give equivalent results. To avoid possible variability due to lot-to-lot differences, filters from the same lot were used to collect a given sample set.

3.) Portable dust chamber

A portable dust chamber [Kogut et al. 1997] designed for sampling in mines was used for sample collection. The chamber allowed simultaneous collection of up to eighteen samples. Twelve cassettes were mounted inside the chamber in a symmetrical fashion. Samples were collected on six different days, five days in a loading dock area and a sixth near an outside smokers' shelter. A diesel truck was operating in the loading dock, over different periods, on three of the days. Personal air pumps were programmed to run at 2 L/min over an 8-hour period. In one case, the pumps were stopped after 23 minutes. The short sampling period provided a low loading of diesel exhaust (a light deposit was visible) and was of interest with respect to the amount of adsorbed carbon collected in the short time frame.

Results for the six sample sets are shown in Table1 and Figure 3. The QQ2 results correspond to the bottom quartz filters in the four cassettes containing quartz pairs only. The TQQ1 results are for the four filters directly beneath Teflon filters; TQQ2 results are for quartz filters beneath the TQQ1 filters (i.e., top Teflon, middle TQQ1, bottom TQQ2). The mean carbon on the bottom quartz filters ranged from 1.35 to 3.44 μg/cm^2, and the variability (RSD) ranged from about 4% to 12% on a given day. The loading found on the two sets of bottom filters (QQ2 and TQQ2) was not statistically different, so all bottom filters were pooled in the calculation of the mean. The pooled means for the bottom quartz filters (BQ), the means for the quartz under Teflon (TQQ1), and the corresponding OC and EC loadings are plotted in Figure 3. Results for the TQQ1 filters were only slightly higher than those for the bottom quartz filters, even with the 23-minute sampling period (set 4). Thus, using a separate cassette that has a top Teflon filter appears unnecessary. Although differences between the amount of carbon adsorbed on a quartz filter under another quartz and on one beneath a Teflon filter reportedly can be significant [Kirchstetter et al. 2001; Turpin et al. 1994], these studies concerned environmental monitoring at much higher flow rates. The negligible differences reported here most likely relate to the lower flow rates and filter face velocities used.

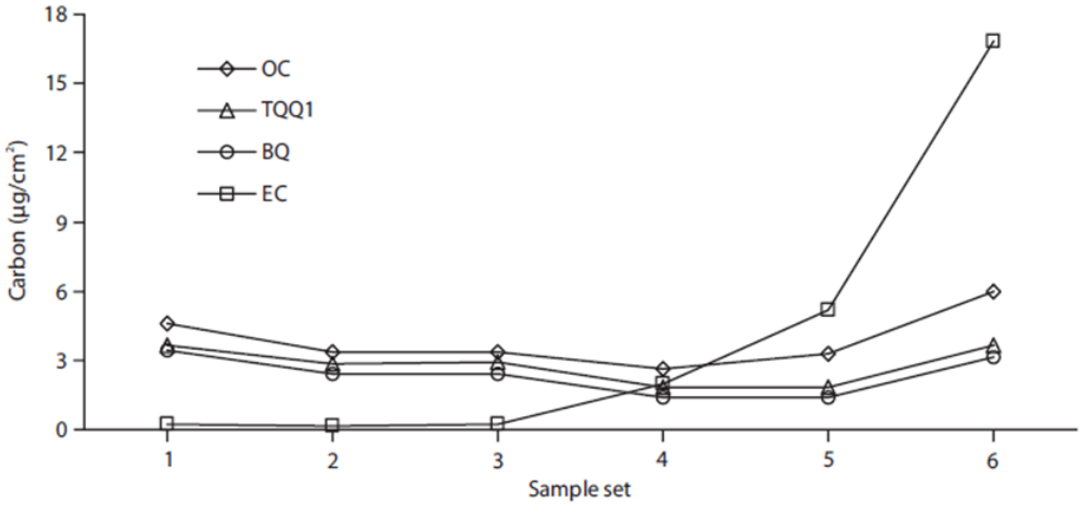

Figure 3. Results for six sets of air samples collected in two outdoor locations. OC and EC results are the means for the top quartz filters (QQ1) of quartz-filter pairs. TQQ1 is the mean carbon (total) result for quartz filters placed directly beneath Teflon. BQ is the mean carbon result for all bottom quartz filters (i.e., QQ2 and TQQ2). See text for additional details.

Table 1. Results summary for total carbon (TC, µg/cm²) from six sets of air samples collected in two outdoor locations (SD = standard deviation; RSD = relative standard deviation). See text for details.

Set	Location	QQ1 mean	QQ1 SD	QQ1 RSD (%)	TQQ1 mean	TQQ1 SD	TQQ1 RSD (%)	Bottom quartz mean, QQ2	Bottom quartz mean, TQQ2	Bottom quartz mean, pooled	Bottom quartz mean, SD	Bottom quartz mean, RSD (%)	Adsorbed fraction (%)
1	shelter	4.81	0.47	9.77	3.66	0.43	11.8	3.46	3.41	3.44	0.30	8.80	76
2	dock	3.52	0.25	7.10	2.82	0.36	12.8	2.48	2.33	2.43	0.23	9.57	80
3	dock	3.61	0.05	1.39	2.89	0.04	1.38	2.41	2.42	2.41	0.18	7.45	80
4	dock	4.59	0.18	3.92	1.79	0.24	13.4	1.41	1.36	1.38	0.09	6.46	30
5	dock	8.43	0.33	3.91	1.84	0.35	19.0	1.35	1.36	1.35	0.16	12.0	22
6	dock	22.8	0.35	1.54	3.62	0.18	4.97	3.10	3.18	3.14	0.13	4.09	16

The mean carbon loading (Table 1) on the sample filters (QQ1) was about 4 µg/cm² on four different days (sample sets 1–4). A diesel truck was operating briefly on one of these days (set 4). On two other days (sets 5 and 6), the truck was running for longer periods, as evidenced by the higher EC loadings (Figure 3). The corresponding TC loadings on these two days were about 8 µg/cm² and 23 µg/cm². Over the loading range, the amount of adsorbed OC had no dependence on the TC loading, and the OC results for the bottom quartz filters (1.35 to 3.44 µg/cm²) were higher than those for the passive field blanks (0.17 to 0.74 µg/cm²). Two of the results (sets 4 and 5) were slightly lower than the others. In one case (set 4), the sampling period (23 minutes) was shorter, but the adsorbed OC results for the bottom filters in both sampling configurations (i.e., QQ2 and TQQ2) were equivalent and comparable to the upper

quartz filters (TQQ1), below the Teflon. This implied that partitioning [Turpin et al. 1994] (between gas and adsorbed states) on the sample filters (QQ1) had reached equilibrium; thus, the lower result was not due to lack of equilibration. In large part, the results for passive blanks provided a likely explanation for the lower value. The mean blank (passive) for this set was 0.17 (±0.10) µg/cm^2, which was the lowest value obtained. Passive blank results for the other sets (excluding set 5) ranged from 0.25 (±0.07) to 0.74 (±0.14) µg/cm^2. It is not known whether the same explanation applied to set 5 because passive blanks for this set were accidentally contaminated (results voided). As in sets 1–3 and 6, set 5 was collected for an 8-hour period, but it was collected during the spring, while the other sets were collected during midsummer. Changed weather conditions may explain the lower value.

Over three days, the adsorbed OC fraction (calculated as the TQQ1 TC mean divided by QQ1 TC mean) constituted about 80% of the TC on the sample filters (QQ1). On three other days (sets 4, 5, and 6), the adsorbed OC fraction was 39%, 22%, and 16% of the total. A backup quartz filter provided a better correction for adsorbed carbon than a traditional blank would have. Traditional blanks (media and field) underestimated the adsorbed OC, causing overestimation of the true particulate OC (TC) concentration. The need for this correction, and the number of backup filters analyzed, depends on the sampling strategy and environment. The lower the OC loading, the greater the influence of adsorbed vapor on the particulate OC measurement. If the EC loading also is low, the same holds true for the TC result. Thus, when carbon loadings are low, correction for adsorbed OC is important for accurate measurement of particulate OC and TC concentrations. However, the correction addresses adsorbed vapor only—not interference of less volatile materials (e.g., components in cigarette and wood smokes, oils) collected primarily on the top filter. Depending on vapor pressure, sampling conditions (temperature, flow rate, sampling period), and filter loading, these materials also collect on the bottom filter to some extent. The bottom filter cannot correct for this interference. If high OC loadings are found on the bottom filter, less volatile OC interferences should be suspected.

i. EC oxidation in helium

In the NIOSH 5040 analysis, oxidation of original EC (as opposed to char) is sometimes seen during the last temperature step in helium, but this is generally not common. If early removal occurs, it is important to ensure that oxygen contamination is not responsible. This check can be performed by analyzing a sucrose standard solution applied to a clean, unused filter punch. Although char loss is sometimes observed with sucrose, the filter transmittance normally does not reach its initial value until after oxygen is introduced. If oxygen contamination can be ruled out, the early EC loss is most likely due to oxidants in

the sample. In our laboratory, EC loss in helium has been observed with samples from a few mines [Birch 1998b]. With these samples, the filter transmittance exceeded its baseline (initial) value during the last temperature step in helium. No sample pyrolysis was apparent, so the increase in transmittance was not caused by char loss. Moreover, analysis of sucrose standards revealed only a minor increase in transmittance in helium, and no increase was seen with samples from other mines. For these reasons, oxygen contamination was ruled out. On average, about 10% of the EC was removed at 870 °C in helium, but the carbon removed was included in the EC result because the OC-EC split was assigned when the initial transmittance was reached (in helium). Reducing the maximum temperature to 750 °C was recommended [NIOSH 1994a, 1994b] for these types of samples (i.e., *no sample charring and early splits in helium*). Early EC loss was not seen at this temperature. A lower (<750 °C) temperature may be required, depending on the sample composition. Our analytical results and precision were not affected by the early splits, but a reduced temperature was recommended in the interest of interlaboratory precision, which might be adversely affected. Interlaboratory testing was not conducted to determine if this is the case, and, if so, whether a lower temperature would improve precision.

j. Reference materials

As mentioned, a suitable reference material for OC and EC is not available. A Certified Value (17.68% g/g) for the TC mass fraction of an urban dust standard (SRM 1649a, formerly SRM 1649) was reported by the National Institute of Standards and Technology (NIST), but only Information (not Certified) Values were provided for the EC content. The EC content (as EC:TC fractions) was determined by a variety of methods. As expected, based on prior studies [Birch 1998a; Chow et al. 2001; Countess 1990; Norris et al. 1999; Schmid et al. 2001], the results were quite variable. The EC:TC fractions found by 13 methods ranged from about 7% to 52%, and the data were distributed in three clusters. Method bias was not evaluated. The reported range is too broad to use this material as an analytical standard. According to the Certificate of Analysis (1649a), the reported values may be useful for comparison with results obtained by similar methods, but this may not be the case for methods with optical corrections because filter samples are not available. Depending on its placement, bulk dust on a filter can present different optical properties, which may increase variability. Sample composition is an important consideration in the production of an analytical reference material. As is true with many standards, no single OC-EC material can be representative of all samples because there are many sources of particulate carbon and many different monitoring sites—both occupational and environmental. Production of an OC-EC reference material is further complicated by the variability between methods (SRM 1649a provides only Information Values for different methods), and the need of a filter-based material for thermal-optical methods.

Because sample components that char pose a potential interference in the determination of EC, and interlaboratory variability is greater when samples contain them, analysis of organic materials that char provides an important quality assurance check. Sucrose serves as both an analytical standard and a check of the method's char correction, but sucrose is a simple carbohydrate (a disaccharide). Air samples can contain complex particulate matter, such as wood and cigarette smokes, plant debris (cellulose), and products of biomass burning. In some cases, biomass may contribute a sizable fraction of the sample carbon. About 38% of the particulate carbon in SRM 1649a (an urban dust) is derived from biomass (see Certificate of Analysis [NIST 2001] and related publication [Currie et al. 2002]). For these reasons, a material more representative of the plant-derived components in air samples was sought.

Various plant-derived materials were examined to determine whether any would be useful as laboratory control samples. A well-characterized, stable material that chars also would be useful for proficiency testing, and it could potentially be used to produce a standard reference material. After a preliminary screening of candidate materials (e.g., agarose, alginic acid, starch, and cellulose), alginic acid was selected for further study. Alginic acid is a polysaccharide derived from sea kelp [Morrison and Boyd 1973], it has adequate solubility in water, and it forms a significant amount of char during the analysis.

To prepare a solution, about 150 mg of alginic acid (Sigma-Aldrich, St. Louis, MO) was added to a test tube containing 10 mL of purified water (ultrafiltered, type I). The tube was shaken vigorously and allowed to sit overnight at room temperature. The following day, the tube was shaken again and then centrifuged to settle the suspended material. The clear supernatant was removed and syringe filtered. Aliquots of the alginic acid solution were applied to clean filter punches. The solution was analyzed over a seven-week period. Results of these analyses are plotted in Figure 4. No evidence of solution degradation was observed. A mean carbon loading of 13.98 µg/cm^2 (RSD = 3.06%, n = 22) was obtained for 10-µL aliquots of the solution. This translates to a carbon concentration of 2.06 µg/µL. About half of the carbon in alginic acid remained on the filter as char before oxygen was introduced, but the mean EC result (0.04 ±0.06 µg/cm^2) was not statistically different from that for the media blanks (0.06 ±0.03). Therefore, the pyrolysis correction was accurate.

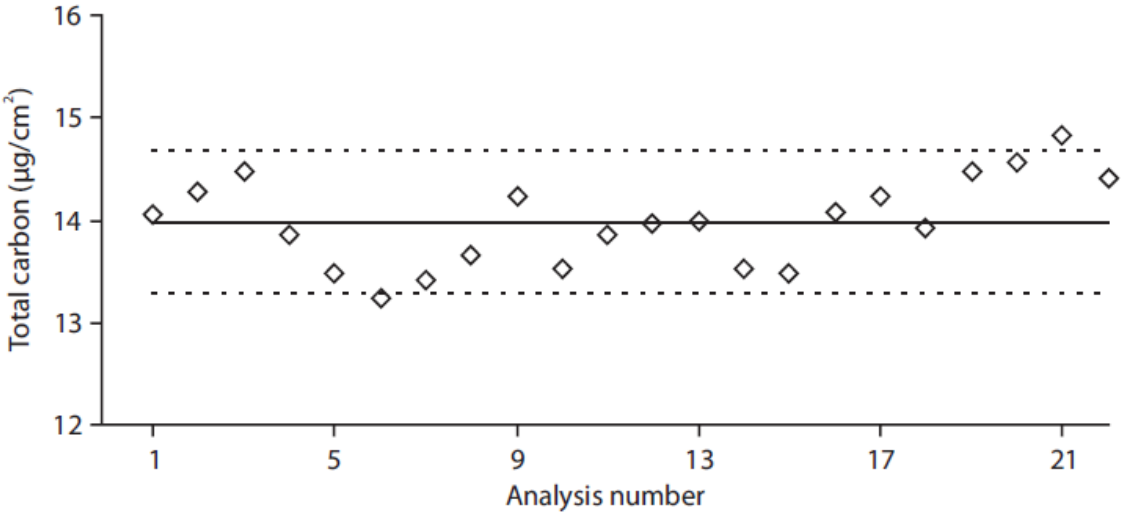

Figure 4. Results for clean punches (blanks) spiked with 10-µL aliquots of alginic acid solution. Analyses done over a 7-week period. The middle horizontal line is the mean result (13.98 µg/cm²). The upper and lower dashed lines are ±5% of the mean.

Sets of diesel soot samples spiked with the alginic acid solution also were examined. Multiple punches (1.5 cm²) were taken from a soot sample collected on an 8" x 10" filter. The punches were then analyzed before and after spiking with a 10-µL aliquot of the solution. Punches in a given set were taken from the same area of the filter to minimize variability, and the solution was applied in a consistent manner (dispersed evenly on one end of the punch where the laser penetrates it). Mean TC results for the unspiked and spiked samples are provided in Table 2. Results for three sample sets (A, B, and C) are reported. For each set, the difference between the mean results for the unspiked and spiked samples is reported; this difference is the alginic acid carbon. Based on the mean (13.98 µg/cm²) for 22 spiked blanks, recoveries of alginic acid carbon from the soot samples were 96%, 101%, and 110% (sets A, B, and C, respectively). The pooled recovery for all spiked samples was 97%.

Table 2. Recovery of alginic acid carbon (means and standard deviations, *n*=3; µg/cm²) from unspiked diesel particulate samples and samples spiked with 10-µL alginic acid solution.

Sample set	Unspiked	Spiked	Difference	Recovery* (%)
A	22.9 (1.49)	34.9 (0.66)	13.5	96
B	22.3 (0.28)	36.4 (0.65)	14.1	101
C	22.6 (0.33)	38.0 (0.80)	15.4	110
All	22.6 (0.84)	36.1 (1.32)	13.5	97

*Based on mean result (14.0 µg/cm²) for 22 analyses of spiked blank punches; analyses carried out over a 7-week period.

Table 3. Results for elemental carbon (EC; means and standard deviations, *n*=3; µg/cm²) from spiked and unspiked diesel particulate samples.

Sample set	Unspiked	Spiked	Difference
A	4.24 (0.20)	4.36 (0.42)	0.12 (0.47)
B	3.88 (0.01)	3.78 (0.12)	-0.10 (0.12)
C	4.32 (0.14)	4.43 (0.12)	0.11 (0.18)

EC results for the three sample sets are listed in Table 3. Spiked sample results for two sets (A and C) were slightly higher, while those for a third set (B) were slightly lower. Differences between the mean EC loadings on the unspiked and spiked samples were not statistically different. Thus, an accurate correction was again made for the char formed through pyrolysis of alginic acid.

k. Quality assurance

1.) NIOSH

Quality assurance (QA) procedures followed at NIOSH and NIOSH contract laboratories have included repeat analyses, analysis of OC standards, and analysis of media and field blanks. Results for repeat analyses of over 200 filter samples at a contract laboratory (DataChem Laboratories, Inc., Salt Lake City, UT) gave a pooled RSD (95% confidence) of about 4% for EC and TC, and 5% for OC [Birch et al. 1999a]. The samples were collected in mines, and some contained other carbonaceous matter such as limestone. In the analysis of OC standards, recovery was typically within 6% of the expected value [Birch et al. 1999a]. For example, the mean recovery for more than 400 sucrose standards analyzed at DataChem over a one-year period was 99.97% ±6.07%. Nearly identical results (100.33% ±5.15%, n = 462) were obtained by Clayton Laboratory Services (Novi, MI). Different sets of field blanks (41 at DataChem and 129 at Clayton) analyzed by the two laboratories also gave comparable results [Birch et al. 1999a]. Mean blank results (µg carbon per filter) were as follows: DataChem OC = 9.96 ±7.05, Clayton OC = 12.80 ±5.76; DataChem EC = –0.54 ±1.89, Clayton EC = –0.08 ±2.14; DataChem TC = 9.26 ±7.30, Clayton TC = 12.70 ±6.18.

In lieu of an OC-EC reference material, a limited confirmation of results by a second laboratory is advised. For example, our laboratory (NIOSH, Cincinnati, OH) has routinely performed repeat analyses on samples previously analyzed at a contract laboratory. As an added check, subsets of representative field samples also have been analyzed by a third laboratory. In the analysis of fifty samples (analyzed at DataChem, NIOSH, and Clayton) from mines, the pooled RSD (95% confidence) was about 6% for TC, 10% for EC, and 12% for OC [Birch et al. 1999a]. These results are consistent with those found in a previous round robin [Birch 1998a].

2.) EPA

The EPA conducted a special study [EPA 2001] as part of the QA oversight for the $PM_{2.5}$ Speciation Trends Network (STN). Samples collected as part of this network were removed from refrigerated storage eight months after they were analyzed at Research Triangle Institute (RTI, Research Triangle Park, NC). The samples were then shipped to the EPA New England Regional Laboratory (NERL, Lexington, MA) for reanalysis. Good interlaboratory agreement was reported. The acceptance criteria for the archived samples were based on filter loading (µg/cm^2). The three acceptance criteria are the following: a difference ≤1 µg/cm^2 for loadings less than 5 µg/cm^2, a relative percent difference (RPD) ≤20% for loadings from 5 to 10 µg/cm^2, and an RPD ≤15% for loadings above 10 µg/cm^2. The OC, EC, and TC data had 85%, 96%, and 93% of the interlaboratory results, respectively, within the acceptance criteria. The lower percentages for OC and TC are thought to reflect contamination of lightly loaded samples from adsorbed vapors and handling. An OC blank (passive) correction was applied but may not have been representative of the entire sample set. Additional comparison results are discussed in the next section: Interlaboratory Comparisons.

3 Interlaboratory comparisons

a. NIOSH 5040

When results of the initial method evaluation were published [Birch and Cary 1996a], an interlaboratory comparison was not possible because the thermal-optical instrument was available in only one laboratory. Interlaboratory comparisons are especially important in this type of analysis because variable results have been obtained by different OC-EC methods [e.g., Birch 1998a; Chow et al. 2001; Countess 1990; Norris et al. 1999; Schmid et al. 2001;], and a reference material is not available. After additional laboratories acquired thermal-optical instruments, a round robin comparison [Birch 1998a] was conducted. Matched sets of filter samples containing different types of complex carbonaceous aerosols were distributed to eleven laboratories. Six of the eleven analyzed the samples according to NIOSH 5040, while five used purely thermal (i.e., no char correction) methods. Good interlaboratory agreement was obtained among the six laboratories that used NIOSH 5040. In the analysis of samples containing DPM, the variability (RSD) for the EC results ranged from 6% to 9%. Only low EC fractions were found in wood and cigarette smokes. Thus, these materials pose minimal interference in the analysis of diesel-source EC. In addition, only minor amounts of EC were found in two OC standards that char: about 1% and 0.1% for sucrose and the disodium salt of ethylenediaminetetraacetic acid (EDTA), respectively. Two aqueous solutions of OC standards were included in the comparison as a check on the validity of the char correction and accuracy of the TC results. Variability (RSD) of the TC results for the two standard solutions and five filter samples ranged from 3% to 6%.

Note: *In the round-robin study [Birch et al. 1996a] discussed above, the maximum temperature in helium ranged from about 850 °C to 900 °C. Comparable results were obtained because some differences in the thermal program do not affect the results significantly (e.g., also see Chai et al. 2012). For the purpose of standardization, use of the same maximum is recommended.*

Results of other interlaboratory comparisons on NIOSH 5040 have been reported. In one study [Schauer et al. 2001], seven environmental aerosol samples were analyzed in duplicate by eight laboratories. Four samples were collected in U.S. cities, and three were collected in Asia. Variability of the EC results ranged from 6% to 21% for six samples having EC loadings from 0.7 to 8.4 µg/cm^2. Four of the six had low EC loadings (0.7 µg/cm^2 to 1.4 µg/cm^2). The variability of the OC results ranged from 4% to 13% (OC loadings ranged from about 1 to 25 µg/cm^2). Results for TC were not reported, but the variability reported for the OC results should be representative of that for TC because the samples were mostly OC (75% to 92%). For another comparison [Chai et al. 2012], matched-filter sets with known OC–EC contents were generated and distributed to six laboratories. In this study, the maximum temperature in helium varied from 650 °C to 850 °C, but good agreement between the participating laboratories was found. Results indicated a uniform carbon distribution for the filter sets. Relative standard deviations for mean TC, OC, and EC results for seven laboratories were less than 10%, 11%, and 12% (respectively). Except for one EC result (RSD = 16%), RSDs reported by individual laboratories, for TC, OC, and EC, were under 12%. The method of filter generation is generally applicable and reproducible. Depending on the application, different filter loadings and types of OC materials can be employed. Matched filter sets can be used for determining the accuracy of OC–EC methods, which are operational.

b. Other methods

1.) Thermal methods

Different thermal methods have given consistent agreement for TC, but OC-EC results have been quite variable [Birch 1998a; Chow et al. 2001; Countess 1990; Norris et al. 1999; Schmid et al. 2001]. The degree of variability depends on the sample type. In general, there is greater disagreement among methods when samples contain materials that char [Birch 1998a; Countess 1990; Schmid et al. 2001] (e.g., wood and cigarette smokes). Methods that employ a lower maximum temperature and/or do not correct for char obtain results that are positively biased relative to NIOSH 5040 [Birch 1998a]. When a lower temperature (typically 550 °C) is used, less thermal breakdown of refractory organic components (and possibly carbonates) may occur. This, as well as lack of char correction, can positively bias the EC results. In the round robin study [Birch 1998a] discussed above, three laboratories employed four purely thermal

methods that specified a maximum in nitrogen (not helium) of about 550 °C. Unlike the NIOSH 5040 results, these laboratories reported high EC contents for the two OC standards (about 52% for sucrose and 70% for EDTA). Similar findings (i.e., positive bias) for thermal methods having no char correction were obtained in another international round robin [Schmid et al. 2001].

In contrast to round-robin results obtained previously [Birch 1998a], relatively good agreement was found in a comparison [Birch et al. 1999b] between NIOSH 5040 and a thermal method, ZH 1/120.44, used in Germany [Dahmann 1997; ZH 1/120.44]. The comparison was limited to two laboratories. Method ZH 1/120.44 specified a 550 °C maximum in nitrogen. The other European laboratories that participated in the previous round robin [Birch 1998a] used variations of this method. In the European laboratories, nitrogen was used as the inert gas, and carbon determination was based on coulometric titration of carbon dioxide. For the comparison [Birch et al. 1999b], samples were obtained in a mine where diesel equipment was being operated. The samples had a much higher EC content (about 50%) than did the round robin samples. No charring was noted in the thermograms, and only a minor amount of carbon was removed above 550 °C. Although differences in the OC-EC results were again seen, they were minor relative to those obtained in the round robin [Birch 1998a]. The mean EC fractions (EC:TC) found with methods ZH 1/120.44 and NIOSH 5040 were 0.53 (σ = 0.19) and 0.46 (σ = 0.15), respectively. This relatively minor difference in the reported fractions is attributed to the different thermal programs employed.

2.) IMPROVE method

Another thermal-optical method, called the IMPROVE (Interagency Monitoring of Protected Visual Environments) method [Chow et al. 1993], also was included in the NIOSH 5040 round robin [Birch 1998a]. Relatively good agreement between NIOSH 5040 and the IMPROVE method was obtained, although the IMPROVE EC was consistently higher. The carbon analyzers used for the two methods are based on similar measurement principles, but they differ with respect to design and operation. For example, the optical correction in NIOSH 5040 is based on filter transmittance, whereas that for the IMPROVE method is reflectance based. When the intercomparison study was conducted, the instrument (Sunset Laboratory, Inc., Forest Grove, OR) used for NIOSH 5040 incorporated a pulsed diode laser (670 nm) and photodetector positioned on opposite sides of the filter, while the Desert Research Institute (DRI, Reno, NV) instrument employed for the IMPROVE method used a quartz tube and fiber optic to measure helium–neon laser light (632.8 nm, unmodulated) reflected from the filter surface. In addition to instrumental differences, NIOSH 5040 specifies a higher maximum temperature (typically 850 °C or higher) in helium than the IMPROVE method (550 °C). As discussed in the preceding section, a

higher temperature is used to better remove refractory OC components and carbonates. In the NIOSH 5040 analysis, the transmittance of some samples continues to decrease as the temperature is stepped to 850 °C, indicating further carbonization above 550 °C. Additional thermal breakdown and charring result in lower EC results because char correction is larger, and volatile pyrolysis products are released to a greater extent. Although environmental samples contain only small amounts (if any) of carbonate, levels in some workplaces (e.g., mines, construction sites) can be relatively high. Collection of carbonate can be prevented (or minimized) through use of an impactor [66 Fed. Reg. 5706 (2001)].

Results of two other comparisons [Chow et al. 2001; Norris et al. 1999] between NIOSH 5040 and the IMPROVE method have been reported. In one [Chow et al. 2001], the NIOSH 5040 EC was typically less than half the IMPROVE EC; however, a Sunset Laboratory instrument was not used. Instead, samples were analyzed with a DRI instrument, by running two different thermal programs [Chow et al. 2001]. Because differences in instrument design affect the OC-EC results to varying degrees, depending on sample type, the results reported for NIOSH 5040 (emulated on a DRI instrument) may not be representative of those obtained with a Sunset Laboratory instrument. Adjustment of the temperature program, according to another method's specifications, does not necessarily produce the same results as that method. For example, lower EC results [Birch 1998a] were obtained with a Sunset Laboratory instrument when a sucrose standard was analyzed according to the temperature program specified for a method used in Europe. No pyrolysis correction was made, and the total analysis time was shorter, yet the EC result was much lower (about 3 µg with the Sunset instrument and 11 µg with a different instrument).

When the NIOSH 5040 thermal program was used on a DRI instrument, the filter transmittance reportedly exceeded its initial value before the addition of oxygen [Chow et al. 2001]. In an audit by a CARB (California Air Resources Board) laboratory, the same problem was seen with a DRI instrument, but not a Sunset Laboratory instrument [EPA 2003]. Char loss was extensive when the NIOSH 5040 program was used on a DRI instrument. Again, the filter transmittance exceeded its initial value in helium, but the split point was not assigned until after oxygen was introduced. These results contrast with those obtained by our laboratory and others, and such behavior was not seen in another comparison [Norris et al. 1999]; however, that comparison (and the CARB audit) was a direct comparison of the two methods (i.e., samples were analyzed with both Sunset and DRI instruments). Only 2 of 52 samples analyzed by Sunset Laboratory showed an increase in transmittance before the addition of oxygen, and the OC-EC split was near the point where oxygen was added [Norris et al. 1999]. Both samples had low carbon loadings (OC = 4.0 µg/cm^2, EC = 0.6 µg/cm^2,

OC = 3.3 µg/cm^2, EC = 0.5 µg/cm^2) and were thought to be wood-smoke dominated. As pyrolysis was evident, the increase in filter transmittance was attributed to char loss. Comparable EC results would have been obtained if the char had not been removed until after oxygen was added, because char is assigned to the OC fraction. In the NIOSH 5040 analysis of organic compounds (e.g., sucrose), partial char loss in helium sometimes occurs. The varying degree of loss may relate to differences in filter purity.

4 Occupational exposure criteria (U.S.)

In 1995, the American Conference of Governmental Industrial Hygienists (ACGIH) proposed a Threshold Limit Value (TLV®) for diesel exhaust [ACGIH 1995] (see Notice of Intended Changes for 1995–1996). A TLV of 150 µg of submicrometer particulate matter (mass) per cubic meter of air was proposed. Four years later, a value of 50 µg/m^3 was proposed [ACGIH 1999]. An EC-based standard was later proposed, because EC is a demonstrated exposure marker and can be accurately quantified at low levels [ACGIH 2001a]. A TLV-TWA (time-weighted average) of 20 µg EC per cubic meter of air was recommended [ACGIH 2001b]. By comparison, the proposed TLV was high relative to an environmental standard supported by the California Office of Environmental Health Hazard Assessment (OEHHA). The California OEHHA classified particulate emissions from diesel-fueled engines as a toxic air contaminant (TAC) and supported 5 µg/m^3 as the chronic inhalation reference exposure level (REL) [CalEPA 1998]. Because EC is a fraction of the diesel particulate emissions, the difference between the two air standards is greater than four fold, with the magnitude of the difference being dependent on the EC fraction of the diesel particulate mass. For example, if EC constituted 40% of the mass, the proposed TLV would be ten times higher than the OEHHA REL.

An exposure limit for DPM has been promulgated for metal and nonmetal mines, but there currently are no limits for other occupational settings (ACGIH withdrew a proposed limit [ACGIH 2003] for DPM [as EC] from its Notice of Intended Changes [NIC] list in 2003 and placed it under study). An EC (or TC) standard, rather than submicrometer particulate mass, would simplify interpretation of the analytical results because the target analyte and exposure standard would be the same. This would eliminate the problem of extrapolation (to submicrometer mass), which is not straightforward and introduces unacceptable error. As discussed previously, OC interferences are a problem with TC measurements; variable EC content is a problem when measuring EC. If EC concentrations are high and samples are relatively free of OC contaminates, the TC concentration is a reasonable measure of the diesel particulate mass, and the EC:TC ratio is representative of the EC fraction of the mass. However, this situation is uncommon outside of mines. In general industry, EC and OC levels are normally much lower. And when EC levels are low, the EC:TC ratios are not reliable estimates of the EC fraction of DPM because OC interferences can skew the ratios low and

increase variability in the apparent ratio. In such cases, TC is an inaccurate measure of the diesel particulate concentration.

Exposures in the mining industry are of particular concern because diesel particulate concentrations in mines [63 Fed. Reg. 17491 (1998); 63 Fed. Reg. 58103 (1998); 66 Fed. Reg. 5706 (2001)] have sometimes exceeded 2 mg/m^3, which is one thousand times higher than a typical environmental level. In its final rule [66 Fed. Reg. 5706 (2001)] on metal and nonmetal mines, MSHA proposed an interim exposure standard of 400 µg TC per cubic meter of air. Five years after publication of the rule, a final standard of 150 µg TC per cubic meter was to apply. In response to a legal challenge, MSHA initiated a limited new rulemaking [67 Fed. Reg. 60199 (2002)] to revise certain provisions of the final rule. Among other amendments, MSHA agreed to propose a change of exposure surrogate from TC to EC. Comments on appropriate interim and final limits for EC were requested in the new rulemaking. MSHA exposure standards consider health risks and technical and economic feasibility, based on available engineering controls and their cost.

5 Summary

NIOSH 5040 is based on a thermal-optical analysis technique for particulate carbon. Its intended application is assessment of workplace exposure to particulate diesel exhaust, but thermal-optical analysis has been routinely applied to environmental carbonaceous aerosols. Both OC and EC (and TC as OC + EC) are determined by the method. For reasons discussed in this chapter, EC was selected as an exposure surrogate for diesel exhaust. Over 30 epidemiological studies are consistent in finding a positive association between exposure to diesel exhaust and lung cancer, but many studies lack quantitative exposure data. Accurate monitoring methods are necessary for quantifying the exposure risks.

The thermal-optical instrument incorporates an optical feature that corrects for the char formed during the analysis of some materials. The EC results of purely thermal methods show positive bias when samples contain such materials. Although minimal charring has been observed with most diesel soot samples from mines, workplace (and environmental) air often contains components that carbonize. Depending on the workplace and thermal protocol, these components can be significant contributors to the measured EC. For this reason, an analytical protocol that maximizes removal of OC components (and carbonates) and corrects for the char formed through thermal decomposition is important. In the NIOSH 5040 analysis, the transmittance/reflectance of some samples continues to decrease as the temperature is stepped to 850 °C (and higher) in helium, which indicates incomplete carbonization at the lower temperatures used in some methods. Partial char loss may occur in helium at higher temperature, but removal of original EC is less common. Good interlaboratory agreement between OC-EC results has been obtained by laboratories using

NIOSH 5040. Because a certified reference material is not currently available, confirmation of results by a second laboratory using NIOSH 5040 is advised, particularly when samples char during the analysis because interlaboratory results for these types of samples are typically more variable. Organic materials that char are useful as quality control samples. Accurate pyrolysis correction was obtained in the NIOSH 5040 analysis of an alginic acid solution spiked onto blank filters and diesel soot samples. Sucrose has traditionally been used as a check on the method's char correction, but other materials are needed that are more representative of the complex components in air samples.

To ensure data quality, participation in proficiency testing among laboratories involved in major studies also is advised. Several commercial laboratories offer the NIOSH 5040 analysis, and many instruments have been used globally for environmental and occupational monitoring. Method standardization is critical if results obtained by different laboratories are to be compared. Interlaboratory studies are useful in exposing differences among methods, but standards need to be included to identify method biases. Results of such comparisons must be interpreted with a clear understanding of each method's limitations.

Continued research is needed to better assess the potential health effects of diesel exhaust and other types of fine/ultrafine particle pollution. Although the organic compounds associated with DPM have potential health effects, those traditionally measured are not unique to diesel exhaust. Nevertheless, characterization of this fraction may be useful in assessment of exposure risks, particularly if compounds enriched in diesel relative to other particulate emissions can be used as indicators of mutagenic potency (e.g., specific nitro-PAH). This information also may identify engine types and operating conditions that produce higher emission rates of genotoxic compounds.

As reasoned previously [Birch and Cary 1996a], regardless of whether the potential adverse health effects of diesel particles are due to their tiny, carbonaceous cores, adsorbed compounds, or a combination of both, monitoring and control of the particulate component are necessary if the effects are particle related. In most workplaces, diesel engines are the primary source of fine-particle EC. Other combustion sources may contribute to environmental levels of EC. These sources may be relevant from an emission control perspective, but if the potential toxicity of the particles is similar, their origin is not relevant from a health perspective.

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NIOSH Manual of Analytical Methods (NMAM), 5th Edition

Glossary of Abbreviations, Definitions and Symbols

Compiled by Kevin Ashley, Ph.D., NIOSH

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

Terms & Definitions

A

AAS - Atomic absorption spectrometry

Absorption Barrier - Any exposure surface that may retard the rate of penetration of an agent into a target. Examples of absorption barriers are the skin, respiratory tract lining, and gastrointestinal tract wall (cf. exposure surface). [Source: Zartarian V, Bahadori T, McKone T [2005]: Adoption of an official ISEA glossary. J Expo Anal Environ Epidemiol *15*:1–5.]

Acceptable Range (biological) - The range of values of a biological monitoring analyte that would be expected in workers with exposure to the chemical agent in the workplace at or below regulatory or recommended levels. These ranges are often method-specific. [Adapted from: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

Accuracy –

1. The degree of agreement between a measured value and the accepted reference value. In this manual, accuracy is calculated from the absolute mean bias of the method plus the overall precision, $\hat{S}_{rT}$ at the 95% confidence level. For an individual measurement, it includes the combination of precision and bias [Source: NIOSH [1977]: Documentation of the NIOSH Validation Tests. DHEW (NIOSH) Publication No. 77-185.]

2. Measure of confidence in a measurement. It is a qualitative term referring to whether there is agreement between a measurement made on an object and its true (target or reference) value. [Source: NIST/SEMATECH e-Handbook of Statistical Methods; Gaithersburg, MD: National Institute of Standards and Technology, http://www.itl.nist.gov/div898/handbook/]

3. The ability of a method to determine the "true" concentration of the environment sampled. Accuracy describes the closeness of a typical measurement to the quantity measured although it is defined and expressed in terms of the relative discrepancy of a typical measurement from the quantity measured. The special sense of accuracy for a method is embodied in the following definition and criterion: The accuracy of a method is the theoretical maximum error of measurement, expressed as the proportion or percentage of the amount being measured without regard for the direction of the error that is achieved with 0.9 probability by the method. [Source: NIOSH [1995]: Guidelines for air sampling and analytical method development and

evaluation. By Kennedy ER, Fischbach TJ, Song R, Eller PM, Shulman SA. DHHS (NIOSH) Publication No. 95-117, http://www.cdc.gov/niosh/docs/95-117/pdfs/95-117.pdf.]

4. The degree of conformity of a value generated by a specific procedure to the assumed or accepted true value. It includes both precision and bias. [Source: ASTM [2014]. D1356, Standard terminology relating to sampling and analysis of atmospheres. West Conshohocken, PA: ASTM International]

ACGIH - American Conference of Governmental Industrial Hygienists

Acute Exposure - A contact between an agent and a target occurring over a short time, generally less than a day. Note: Other terms, such as "short-term exposure" and "single dose," are also used. [Source: Zartarian V, Bahadori T, McKone T [2005]: Adoption of an official ISEA glossary. J Expo Anal Environ Epidemiol *15*:1–5.]

Aerosol –

1. Airborne particles and the gas (and vapor) mixture in which they are suspended. Note: The airborne particles can be in or out of equilibrium with their own vapors. [Source: CEN [2011]. EN 1540, Workplace atmospheres – terminology. Brussels: European Standards Commission.]

2. Dispersion of solid or liquid particles in a gaseous medium. [Source: ASTM [2014]. D1356, Standard terminology relating to sampling and analysis of atmospheres. West Conshohocken, PA: ASTM International.]

Agent - A chemical, biological, or physical entity that contacts a target. [Source: Zartarian V, Bahadori T, McKone T [2005]: Adoption of an official ISEA glossary. J Expo Anal Environ Epidemiol *15*:1–5.]

Analyte –

1. Substance or chemical constituent that is determined in an analytical method [Source: CEN [2011]. EN 1540, Workplace atmospheres – terminology. Brussels: European Standards Commission.]

2. A specific chemical moiety being measured, which can be intact drug, biomolecule or its derivative, metabolite, and/or degradation product in a biologic matrix. [Source: FDA [2001]. Guidance for industry - bioanalytical method validation, http://www.fda.gov/downloads/Drugs/Guidances/ucm070107.pdf.]

Ashing - The decomposition, prior to analysis, of organic matrix constituents of the sample and sampler. The most common ashing techniques are solvent, acid, or alkali dissolution; alkaline fusion; and oxidation using either low-temperature oxygen plasma or muffle furnace. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

ASV - Anodic stripping voltammetry

Atmospheric Concentration - The quantity of a constituent substance per unit volume of air [Adapted from definition of 'concentration' in: ASTM [2014]. D1356, Standard terminology relating to sampling and analysis of atmospheres. West Conshohocken, PA: ASTM International.]

Atmospheric Deposition - The transfer of an atmospheric constituent to a surface due to gravity or another mechanism, or the material which is transferred [Adapted from definition of 'deposition' in: ASTM [2014]. D1356, Standard terminology relating to sampling and analysis of atmospheres. West Conshohocken, PA: ASTM International.]

Atmospheric Dispersion - The most general term for a system consisting of a constituent suspended in air [Adapted from definition of 'dispersion': ASTM [2014]. D1356, Standard terminology relating to sampling and analysis of atmospheres. West Conshohocken, PA: ASTM International.]

AW - Atomic weight

B

B - Media blank result for a single-section sampler (e.g., sorbent tube.)

B_b - Media blank result for back section of a sampler.

B_f - Media blank result for front section of a sampler.

Background Level - The amount of an agent in a medium (e.g., water, soil) that is not attributed to the source(s) under investigation in an exposure assessment. Background level(s) can be naturally occurring or the result of human activities. (Note: Natural background is the concentration of an agent in a medium that occurs naturally or is not the result of human activities.) [Source: Zartarian V, Bahadori T, McKone T [2005]: Adoption of an official ISEA glossary. J Expo Anal Environ Epidemiol *15*:1–5.]

Bias –

1. A systematic (nonrandom) deviation of the method average value or the measured value from an accepted value. [Source: ASTM [2014]. D1356, Standard terminology relating to sampling and analysis of atmospheres. West Conshohocken, PA: ASTM International.]

2. Difference between the average measured mass or concentration and reference mass or concentration expressed as a fraction of reference mass or concentration. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

3. An estimate of a systematic measurement error [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

Bioaerosol - An aerosol consisting of (a) biological agent(s). Note: Airborne dusts of organic origin, for example, cotton dust, flour dust and wood dust, are not considered to be bioaerosols and are therefore not covered by this definition [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

Bioavailability –

1. The rate and extent to which an agent can be absorbed by an organism and is available for metabolism or interaction with biologically significant receptors. Bioavailability involves both release from a medium (if present) and absorption by an organism. [Source: Zartarian V, Bahadori T, McKone T [2005]: Adoption of an official ISEA glossary. J Expo Anal Environ Epidemiol *15*:1–5.]

2. The extent to which a chemical substance to which the body is exposed (by ingestion, inhalation, injection, or skin contact) reaches the systemic circulation, and the rate at which this occurs. It is recognized that the bioavailability (for gastrointestinal absorption) of, for example, both essential and non-essential metals, depends on various factors including the composition of the diet and the type of the chemical compound and its state of dispersion. For instance, the absorption of lead and cadmium is increased if the food is deficient in calcium or iron [Source: ILO/IPCS. Glossary of terms on chemical safety (after WHO, 1979), http://www.ilo.org/legacy/english/protection/safework/cis/products/safetytm/glossary.htm]

Biological Agent - One of a number of agents such as bacteria, viruses, fungi and other micro-organisms or parts of them and their associated toxins, including those which have

been genetically modified, cell cultures or endoparasites which are potentially hazardous to human health. Note: Dusts of organic origin, for example, cotton dust, flour dust and wood dust, are not considered to be biological agents and are therefore not covered by this definition. [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

Biological Matrix - A discrete material of biological origin that can be sampled and processed in a reproducible manner. Examples are blood, serum, plasma, urine, feces, saliva, sputum, and various discrete tissues. [Source: FDA [2001]. Guidance for industry - bioanalytical method validation, http://www.fda.gov/downloads/Drugs/Guidances/ucm070107.pdf.]

Biological Monitoring –

1. The measurements of the absorption of an environmental chemical in the worker by analysis of a biological specimen for the chemical agent, its metabolites or some specific effect on the worker. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

2. The periodic examination of biological specimens (in accordance with the definition of monitoring). It is usually applied to exposure monitoring but can also apply to effect monitoring. [Source: ILO/IPCS. Glossary of terms on chemical safety (after WHO, 1979), http://www.ilo.org/legacy/english/protection/safework/cis/products/safetytm/glossary.htm]

Biomarker of Effect/Response - A measurable biochemical, physiologic, behavioral, or other alteration in an organism that, depending on the magnitude, can be recognized as associated with an established or possible health impairment or disease [Source: National Research Council of the National Academies (NRC) [2006]. Human Biomonitoring for Environmental Chemicals. Washington DC: The National Academies Press, http://www.nap.edu/catalog/11700/human-biomonitoring-for-environmental-chemicals.]

Biomarker of Exposure (e.g., Biological Indicator of Exposure) **-** A chemical, its metabolite, or product of an Interaction between a chemical or some target molecule or cell that is measured in and organism, such as humans [Source: National Research Council of the National Academies (NRC) [2006]. Human Biomonitoring for Environmental Chemicals. Washington DC: The National Academies Press, http://www.nap.edu/catalog/11700/human-biomonitoring-for-environmental-chemicals.]

Biomarker of Susceptibility - An indicator of an inherent or acquired ability of an organism to respond to exposure to a specific chemical substance. Such an indicator may be the result of

a genetic factor, nutritional status, lifestyle, or life stage that affect susceptibility to a chemical exposure. This kind of biomarker can be used to distinguish susceptible individuals or groups; for example, a cytochrome phenotype. [Source: U.S. Environmental Protection Agency (EPA) [2016]. Defining pesticide biomarkers, http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/defining-pesticide-biomarkers.]

Biomonitoring - A method used to assess human exposure to chemicals by measuring a chemical, its metabolite, or a reaction product in human tissues or specimens, such as blood and urine. [Source: National Research Council of the National Academies (NRC) [2006]. Human Biomonitoring for Environmental Chemicals. Washington DC: The National Academies Press, http://www.nap.edu/catalog/11700/human-biomonitoring-for-environmental-chemicals.]

Blank - See Field blank, Media blank, and Reagent blank.

Blank Sample - Unused collection substrate, taken from the same batch used for sampling, processed so as to measure artifacts in the measurement (sampling and analysis) process. [Source: CEN [2005]. EN 14902, Ambient air quality — Standard method for the measurement of Pb, Cd, As and Ni in the PM_{10} fraction of suspended particulate matter. Brussels: European Standards Commission.]

BP - Boiling point, °C.

Breakthrough Volume - Volume of air that can be passed through a sampler before the gas or vapor exceeds the capacity of the sampler. [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

Breathing Zone - The space around a worker's face from where he or she takes his or her breath. For technical purposes a more precise definition is as follows: A hemisphere of radius 0.3 m extending in front of the human face, centered on the midpoint of a line joining the ears; the base of the hemisphere is a plane through this line, the top of the head and the larynx. The definition is not applicable when respiratory protective equipment is used. [Source: CEN [2011]. EN 1540, Workplace atmospheres – terminology. Brussels: European Standards Commission.]

C

C –

1. Concentration of gaseous, liquid, or solid substance in air, mg/m^3;

2. Acceptable ceiling concentration (for a specified maximum time of exposure)

when applied to personal permissible exposure limits.

Calibration Graph - Plot of analytical response vs. known mass or concentration of analyte.

CAS # - Chemical Abstracts Service Registry Number.

CE - Collection efficiency, expressed as a decimal fraction.

Chemical Agent - Chemical element or compound on its own or admixed as it occurs in the natural state or as produced, used, or released, including release as waste, by any work activity, whether or not produced intentionally and whether or not placed on the market. [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

Chronic Exposure - A continuous or intermittent long-term contact between an agent and a target. (Other terms, such as "long-term exposure," are also used). [Source: Zartarian V, Bahadori T, McKone T [2005]. Adoption of an official ISEA glossary. J Expo Anal Environ Epidemiol. *15*:1-5.]

49 CFR 171-177 - Title 49 (Transportation), Code of Federal Regulations. U. S. regulations governing shipment of hazardous materials.

Conc. - Concentrated; concentration

Concentration –

1. A general term referring to the quantity of a material or substance contained in unit quantity of a given medium. [Source: ILO/IPCS. Glossary of terms on chemical safety (after WHO, 1979), http://www.ilo.org/legacy/english/protection/safework/cis/products/safetytm/glossary.htm]

2. The quantity of a substance contained in a total unit quantity of sample. [Source: ASTM [2014]. D1356, Standard terminology relating to sampling and analysis of atmospheres. West Conshohocken, PA: ASTM International.]

Control (biological) - A value or group of values of a biological monitoring parameter collected from workers with little or no occupational exposure to the specific chemical agent. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

C_v - Concentration of gaseous substance in air, parts per million (V/V). In this manual, C_v is referred to NTP such that $C_v = (C \times 24.46)/MW$.

Cumulative Exposure - The sum of exposures of an organism to a pollutant over a period of time. [Source: EPA [1997]: EPA Terms of Environment – Glossary of Exposure Assessment Related Terms: A Compilation. Prepared by the Exposure Terminology Subcommittee of the IPCS Exposure Assessment Planning Workgroup for the International Programme on Chemical Safety Harmonization of Approaches to the Assessment of Risk from Exposure to Chemicals, 2001.]

CV – See S_r : Estimate of the relative standard deviation, equal to S (sample standard deviation) divided by the mean of a series of measurements. A measure of precision; previously referred to as CV (coefficient of variation). [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

D

D - Density, g/cm^3

DE - Desorption efficiency; fraction of known quantity of analyte recovered from spiked solid sorbent media blank. DE may be a function of loading, and should be determined by the chemist for each lot of solid sorbent used for sampling, in the concentration range of interest. Plot (mass recovered minus average media blank)/ mass added vs. (mass recovered minus average media blank). [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

Detector - The part of the monitor that sees and/or measures and/or quantifies and/or ascertains the dimensions, quantity, or concentration of the gas or vapor of interest. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

D_s - Stokes diameter.

Detection Limit - See LOD; MDL. Lowest amount of an analyte that is detectable with a given confidence level. Note: The detection limit can be calculated as three times the standard deviation of blank measurements. This represents a probability of 50% that the analyte will not be detected when it is present at the concentration of the detection limit. [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

Diffusive Sampler –

1. Device which is capable of taking samples of gases or vapors from the atmosphere at a rate controlled by a physical process such as gaseous diffusion through a static air layer or permeation through a membrane, but which does not involve active movement of air through the sampler. [Source: ASTM [2014]. D1356, Standard terminology relating to sampling and analysis of atmospheres. West Conshohocken, PA: ASTM International.]

2. Passive sampler that collects gases or vapors at a rate governed by diffusion through a static air layer and/or permeation through a membrane. [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

Dose –

1. The amount of agent that enters a target after crossing an exposure surface. If the exposure surface is an absorption barrier, the dose is an absorbed dose/uptake dose (see uptake); otherwise it is an intake dose (see intake). [Source: Zartarian V, Bahadori T, McKone T [2005] Adoption of an official ISEA glossary. J Expo Anal Environ Epidemiol, *15*:1-5.]

2. The amount of a chemical administered to an organism. [Source: ILO/IPCS. Glossary of terms on chemical safety (after WHO, 1979), http://www.ilo.org/legacy/english/protection/safework/cis/products/safetytm/glossary.htm]

Dosimeter - An instrument to measure dosage; many so called dosimeters actually measure exposure rather than dosage. [Source: EPA [1997] EPA Terms of Environment – Glossary of Exposure Assessment Related Terms: A Compilation. Prepared by the Exposure Terminology Subcommittee of the IPCS Exposure Assessment Planning Workgroup for the International Programme on Chemical Safety Harmonization of Approaches to the Assessment of Risk from Exposure to Chemicals, 2001.]

Dosimetry - Process or technology of measuring and/or estimating dosage. [Source: EPA [1997] EPA Terms of Environment – Glossary of Exposure Assessment Related Terms: A Compilation. Prepared by the Exposure Terminology Subcommittee of the IPCS Exposure Assessment Planning Workgroup for the International Programme on Chemical Safety Harmonization of Approaches to the Assessment of Risk from Exposure to Chemicals, 2001.]

E

ECD - Electron capture detector

EPA - U.S. Environmental Protection Agency

Est - Estimated

Exposure -

1. Contact between an agent and a target. Contact takes place at an exposure surface over an exposure period. [Source: Zartarian V, Bahadori T, McKone T [2005]. Adoption of an official ISEA glossary. Jour Expo Anal & Environ Epidemiol, *15*:1–5.]

2. The amount of an environmental agent that has reached the individual (external dose) or has been absorbed into the individual (internal dose, absorbed dose). [Source: ILO/IPCS. Glossary of terms on chemical safety (after WHO, 1979), http://www.ilo.org/legacy/english/protection/safework/cis/products/safetytm/glossary.htm]

3. (By inhalation) Situation in which a chemical agent or biological agent is present in the air that is inhaled by a person. [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

Exposure Assessment -

1. The process of estimating or measuring the magnitude, frequency and duration of exposure to an agent, along with the number and characteristics of the population exposed. Ideally, it describes the sources, pathways, routes, and the uncertainties in the assessment. [Source: Zartarian V, Bahadori T, McKone T Adoption of an official ISEA glossary. J Expo Anal Environ Epidemiol, *15*:1–5.]

2. The quantification of the amount of exposure to a hazard for an individual or group [Source: ILO/IPCS. Glossary of terms on chemical safety (after WHO, 1979), http://www.ilo.org/legacy/english/protection/safework/cis/products/safetytm/glossary.htm]

Exposure Concentration - The exposure mass divided by the contact volume or the exposure mass divided by the mass of contact volume depending on the medium. [Source: Zartarian V, Bahadori T, McKone T [2005]: Adoption of an official ISEA glossary. J Expo Anal Environ Epidemiol, *15*:1–5.]

Exposure Route - The way an agent enters a target after contact (e.g., by ingestion, inhalation, or dermal absorption). [Source: Zartarian V, Bahadori T, McKone T [2005]: Adoption of an official ISEA glossary. J Expo Anal Environ Epidemiol, *15:*1–5.]

F

F - Fiber(s)

FID - (Hydrogen-air) flame ionization detector

Field Blank –

1. A sample (or sampler) handled exactly the same as the field samples, except no air is drawn through it. Used to estimate contamination in preparation for sampling, shipment and storage prior to measurement, but not actually subtracted from sample readings (see media blank). [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

2. Blank (sample) that is transported to the sampling site, but not used for sample collection. Discussion: A field blank is loaded in the sampler, where applicable, and returned to the laboratory in the same way as a sample. The results from the analysis of field blanks are used to identify contamination of the sample arising from handling in the field and during transport. [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

FPD - Flame photometric detector

FTIR - Fourier transform infrared spectroscopy

G

GC - Gas chromatography

GFAAS - Graphite furnace atomic absorption spectrometry

GPO - U.S. Government Printing Office, Washington, DC 20402

H

Hemolysis - Rupture of red blood cells. [Adapted from Webster's English dictionary online, http://www.merriam-webster.com/]. Discussion: hemolysis may occur due to improper collection and handling of whole blood samples.

HGAAS - Hydride generation atomic absorption spectrometry

Hydrolysis - Chemical process of decomposition involving the splitting of a bond and the addition of the hydrogen cation and the hydroxide anion of water [Source: Webster's English dictionary online, http://www.merriam-webster.com/]

HPLC - High performance liquid chromatography

I

IC - Ion chromatography; ion-exchange chromatography

ICP-AES - Inductively coupled plasma - atomic emission spectrometry, also called ICP.

Internal Capsule - Air sampler insert consisting of a plastic housing (with an air inlet) attached to a membrane filter. Discussion: The internal capsule is fabricated so as to fit inside the body of the sampling device (e.g., closed-face cassette sampler), enabling capture of airborne particles within the housing / filter construct. [Adapted from: Harper M, Ashley K [2013]: Acid-soluble internal capsules for closed-face cassette elemental sampling and analysis of workplace air. J Occup Environ Hyg *10*:297-306.]

Interference Equivalent - Mass or concentration of interfering substance (interferant) which gives the same measurement reading as unit mass or concentration of substance being measured. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

Interferent - Constituent of the (air) sample or other aspect of the sampling or analytical procedure having an adverse effect on the accuracy of the measurement. Note: Interferents can include components of sampling or analysis equipment, reagents, etc. [Source: ISO

[2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

IR – Infrared

L

LAQL - Lowest analytically quantifiable level; see LOQ.

LC - Liquid chromatography

LOD –

1. Limit of detection (detection limit); smallest amount of analyte which can be distinguished from background. A good estimate for unbiased analyses, with media blanks not distinguishable from background, is three times the standard error of the calibration graph for low concentrations, divided by the slope (instrument reading per unit mass or per unit concentration of analyte). [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

2. The lowest concentration of an analyte that the bioanalytical procedure can reliably differentiate from background noise. [Source: FDA [2001]. Guidance for industry - bioanalytical method validation, http://www.fda.gov/downloads/Drugs/Guidances/ucm070107.pdf.]

3. The smallest amount, or lowest concentration, of a given substance that a given procedure will detect [Source: ILO/IPCS. Glossary of terms on chemical safety (after WHO, 1979), http://www.ilo.org/legacy/english/protection/safework/cis/products/safetytm/glossary.htm]

LOQ - Limit of quantitation; mass of analyte equal to 10 times the standard error of the calibration graph divided by the slope; approximately the mass of analyte for which relative standard deviation, S_r, equals 0.10. [Source: NIOSH [1995]: Guidelines for air sampling and analytical method development and evaluation. By Kennedy ER, Fischbach TJ, Song R, Eller PM, Shulman SA. DHHS (NIOSH) Publication No. 95-117, http://www.cdc.gov/niosh/docs/95-117/pdfs/95-117.pdf.]

Limit of Quantification - Synonymous with limit of quantitation, LOQ. Mass of analyte equal to 10 times the standard error of the calibration graph divided by the slope;

approximately the mass of analyte for which relative standard deviation, S_r, equals 0.10. [Source: NIOSH [1995]: Guidelines for air sampling and analytical method development and evaluation. By Kennedy ER, Fischbach TJ, Song R, Eller PM, Shulman SA. DHHS (NIOSH) Publication No. 95-117, http:/www.cdc.gov/niosh/docs/95-117/pdfs/95-117.pdf.]

LTA - Low temperature (oxygen plasma) ashing

M

MCE; MCEF - Mixed cellulose ester; Mixed cellulose ester membrane filter

MDL - Method detection limit; mass of analyte equal to 3 times the standard error of the calibration graph divided by the slope; approximately the mass of analyte for which standard deviation, S_r, equals 0.03. [Source: NIOSH [1995]: Guidelines for air sampling and analytical method development and evaluation. By Kennedy ER, Fischbach TJ, Song R, Eller PM, Shulman SA. DHHS (NIOSH) Publication No. 95-117, http://www.cdc.gov/niosh/docs/95-117/pdfs/95-117.pdf.]

Metabolite –

1. A substance produced directly by a biotransformation of a chemical. For example, phenol in urine is a metabolite of benzene and is representative of benzene absorption in the worker. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

2. A substance resulting from chemical transformation in an organism. [Source: ILO/IPCS. Glossary of terms on chemical safety (after WHO, 1979), http://www.ilo.org/legacy/english/protection/safework/cis/products/safetytm/glossary.htm]

Microbiome - The complete genetic content of all the microorganisms that typically inhabit a particular environment, especially a site on or in the body, such as the skin or the gastrointestinal tract. [Source: Medical Dictionary online, http://www.online-medical-dictionary.org/]

Measurement Range - Range of substance, in mass per sample, from the LOQ (or from 10 times the LOD, if LOQ is not known) to an upper limit characteristic of the analytical method, e.g., the limit of linearity or the mass at which precision of the method starts to become worse than S_r = 0.1. [Source: NIOSH [1995]: Guidelines for air sampling and analytical method development and evaluation. By Kennedy ER, Fischbach TJ, Song R, Eller PM, Shulman SA.

DHHS (NIOSH) Publication No. 95-117, http://www.cdc.gov/niosh/docs/95-117/pdfs/95-117.pdf.]

Media Blank - An unexposed sampler, not taken or shipped to the field, used for background correction of sample readings or for recovery studies. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

MP - Melting point, °C

MS - Mass spectrometry

MW - Molecular weight

N

Nanoparticle - Material with all three dimensions in the size range from approximately 1 nm to 100 nm [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

NIOSH - National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Public Health Service, U. S. Department of Health and Human Services.

Normal Range (biological) - The range of values for an analyte of interest in biological monitoring that would be expected in workers without exposure to the environmental chemical agent in the workplace. Note: Normal ranges are often method-specific. [Adapted from: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

NTIS - National Technical Information Service, Springfield, VA 22161.

NTP - Normal temperature and pressure, 25 °C (298 K) and 101.33 kPa (760 mm Hg), at which the molar volume of an ideal gas is 24.46 L.

O

OSHA - Occupational Safety and Health Administration, U. S. Department of Labor.

P

P –

1. Peak (maximum permissible instantaneous) concentration;

2. Pressure, in kPa, at which sampling pump is calibrated or when air sample was taken.

PAH - Polynuclear aromatic hydrocarbons; PNAH

PCM - Phase contrast microscopy

PEL - OSHA PEL; OSHA permissible exposure limit, expressed as ppm or mg/m^3 (of a substance in air).

Personal Exposure Monitor - Device used to measure an individual's personal exposure to environmental contaminants or other stressors. A device worn on or near the contact boundary that measures concentration [Source: Zartarian VG, Ott WR, Duan N [1997]. A quantitative definition of exposure and related concepts. J Exposure Anal Environ Epidemol *7*(4):411-437. and EPA [1997] EPA Terms of Environment – Glossary of Exposure Assessment Related Terms: A Compilation. Prepared by the Exposure Terminology Subcommittee of the IPCS Exposure Assessment Planning Workgroup for the International Programme on Chemical Safety Harmonization of Approaches to the Assessment of Risk from Exposure to Chemicals, 2001.]

Personal Sampler - Sampling device, attached to a person that collects gases, vapors, or airborne particles in the breathing zone for the purpose of measuring exposure to chemical agents and/or biological agents. [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

PID - Photoionization detector

Plasma, blood - The clear supernatant from whole blood collected with anticoagulants. Discussion: Blood is collected, mixed with the anticoagulant and centrifuged to separate the plasma from red blood cells. [Adapted from Medical Dictionary online, http://www.online-medical-dictionary.org/.]

PLM - Polarized light microscopy

Pool (biological) - A combination of biological specimens (i.e., urine or serum) from many workers that is used to prepare small aliquots to be run with each batch of analyses. NOTE: The analyte must be stable in the biological matrix and under the storage conditions used. Discussion: Aliquots of these pools are analyzed with each batch of samples and the data are used to develop quality control charts. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

Precision –

1. The relative variability of measurements on replicate samples about the mean of the population of measurements. Discussion: Precision is expressed by the relative standard deviation of a series of measurements, and reflects the ability of a method to replicate measurement results. [Source: NIOSH [1995]: Guidelines for air sampling and analytical method development and evaluation. By Kennedy ER, Fischbach TJ, Song R, Eller PM, Shulman SA. DHHS (NIOSH) Publication No. 95-117, http://www.cdc.gov/niosh/docs/95-117/pdfs/95-117.pdf.]

2. The repeatability or reproducibility of individual measurements expressed as standard deviation, S, or relative standard deviation, S_r (q.v.). See Accuracy. [Source: NIOSH [2003]. Glossary of abbreviations, definitions, and symbols. In: NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113, http://www.cdc.gov/niosh/docs/2003-154/pdfs/glossary.pdf.]

3. The closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogenous sample under the prescribed conditions. [Source: FDA [2001]. Guidance for industry - bioanalytical method validation, http://www.fda.gov/downloads/Drugs/Guidances/ucm070107.pdf.]

Proficiency Testing - Any interlaboratory testing program where stable specimens are sent to participating laboratories for analysis. Discussion: Results from all participating laboratories are compared, pooled, and tabulated by the testing program operator with the purpose of improving laboratory performance. [Adapted from Medical Dictionary online, http://www.online-medical-dictionary.org/.]

PTFE - Polytetrafluoroethylene

PVC - Polyvinyl chloride

Q

Q - Sampling flow rate, L/min

Quantification Range - The range of concentrations, including upper and lower quantification limits (ULOQ and LLOQ, respectively), that can be reliably and reproducibly quantified with accuracy and precision through the use of a concentration-response relationship. [Source: FDA [2001]. Guidance for industry - bioanalytical method validation, http://www.fda.gov/downloads/Drugs/Guidances/ucm070107.pdf.]

R

Reagent Blank - All reagents used in sample preparation, in the same quantities used to prepare blank and sample solutions. Note: The reagent blank is used to assess contamination from the laboratory environment and to characterize background from the reagents used in sample preparation. [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

Recovery, R -

1. Fraction recovered (see DE); previously associated with Analytical Method Recovery (AMR), a term which is no longer preferred. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

2. The extraction efficiency of an analytical process, reported as a percentage of the known amount of an analyte carried through the sample extraction and processing steps of the method. [Source: FDA [2001]. Guidance for industry - bioanalytical method validation, http://www.fda.gov/downloads/Drugs/Guidances/ucm070107.pdf.]

Relative Standard Deviation (RSD) - Quotient of standard deviation over the mean; See S_r and Precision.

Repeatability - The variation in measurements taken under the same conditions. [Adapted from: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

Reproducibility - A measure of the precision of a method under the same operating conditions on the same sample over short period of time. [Adapted from ASTM [2014].

D1356, Standard terminology relating to sampling and analysis of atmospheres. West Conshohocken, PA: ASTM International.]

Respirable Dust - Dust deposited in the non-ciliated portions of the lungs. Discussion: Respirable dust is measured by using a respirable sampler when the respirable fraction of airborne dust is of interest. [Adapted from ISO [1995]. ISO 7708 Air quality — particle size fraction definitions for health-related sampling.' Geneva: International Organization for Standardization.]

R_f **-** In thin-layer chromatography, the ratio of distance travelled by the analyte from point of application to that of the solvent front.

RF - Radio frequency

Rotameter - A device, based on the principle of Stoke's Law, for measuring rate of fluid flow, consisting of a tapered vertical tube having a circular cross section, and containing a float that is free to move in a vertical path to a height dependent upon the rate of fluid flow upward through the tube. [Source: ASTM [2014] D1356, Standard terminology relating to sampling and analysis of atmospheres. West Conshohocken, PA: ASTM International.]

RTECS - Registry of Toxic Effects of Chemical Substances (NIOSH)

Ruggedness Test - Partial or complete analysis of variance using experiments in which operational parameters of a sampling and measurement method are varied within a small range to determine their effect on overall variance [Source: Youden W, Steiner EH [1975]: Statistical manual of the AOAC, Arlington, VA: Association of Official Analytical Chemists.]

S

S **–**

1. Estimate of the standard deviation;

2. Specific mass, particles/mg.

S_b **-** Estimate of the standard deviation of media blank

S_r **-** Estimate of the relative standard deviation, equal to S divided by the mean of a series of measurements. A measure of precision. Equivalent to CV (coefficient of variation).

$\overline{S}_r$ - Pooled relative standard deviation

$\widehat{S}_{rT}$ - Estimate of overall precision including pump error

Sample Dissolution - The process of obtaining a solution containing the analyte(s) of interest from a sample. This may or may not involve complete dissolution of the sample. [Source: ASTM [2010]. D7035, Standard test method for determination of metals and metalloids in airborne particulate matter by inductively coupled plasma atomic emission spectrometry (ICP-AES). West Conshohocken, PA: ASTM International.]

Selectivity -

1. The ability of a bioanalytical method to measure and differentiate the analytes in the presence of interfering components that may be expected to be present. These could include metabolites, impurities, degradants, or matrix components. [Adapted from Medical Dictionary online, http://www.online-medical-dictionary.org/.]

2. Extent of independence of a measuring procedure from interferences. [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

Screening Test (biological) - An easily performed method, often relatively non-specific, to assess worker exposure to a class of compounds by use of biological monitoring. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

SEM - Scanning electron microscopy

Sensitivity –

1. The slope of the calibration curve. If the curve is in fact a 'curve', rather than a straight line, then of course sensitivity will be a function of analyte concentration or amount. If sensitivity is to be a unique performance characteristic, it must depend only on the chemical measurement process, not upon scale factors. [Source: Currie LA [1995] Nomenclature in evaluation of analytical methods including detection and quantification capabilities. Pure & Appl Chem *67*(10):1699-1723.]

2. The smallest change in the measured analyte concentration that will produce a reproducible change in a monitor's readout. [Source: NIOSH [2012]. NIOSH Technical report: Components for evaluation of direct-reading monitors for gases and vapors. DHHS (NIOSH) Publication No. 2012-162, http://www.cdc.gov/niosh/docs/2012-162/pdfs/2012-162.pdf.]

Serum - The clear supernatant from whole blood collected without anticoagulants, allowed to clot (30 minutes) and centrifuged to separate serum from the clotted blood. Serum does not contain clotting factors. [Adapted from Medical Dictionary online, http://www.online-medical-dictionary.org/.]

Sorbent Tube - Sorbent or a support impregnated with reagent, through which sampled air passes. Note: Some sorbent tubes are intended for use as active samplers and some as passive samplers. [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

Spike - A known mass of analyte added to a sampler for the purpose of determining recovery (analyst spikes), or for quality control (blind spikes). Also see DE. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

Sp. gr. - Specific gravity. Relative to water at the same temperature.

Spot Sample (urine) - Urine sample collected at a specified time. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

STEL - Short-Term (15-min) Exposure Limit.

T

T - Retention time, min

t –

1. Temperature, °C;

2. Time, min.

T_c **-** Temperature, degrees kelvin (K), at which sampling pump was calibrated

TEM - Transmission electron microscopy

TLC - Thin-layer chromatography

TLV - Threshold limit value, listed in TLVs® and BEIs®, Threshold Limit Values for Chemical Substances and Physical Agents and Biological Indices (American Conference of Governmental Industrial Hygienists, Cincinnati, OH, 2015; updated annually).

T_s - Temperature, kelvins (K), at which air sample was taken

TWA - Time-weighted average; the concentration of a chemical or biological agent in the atmosphere, averaged over the reference period. [Adapted from: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

U

Ultrafine Particle - Particle with a nominal diameter (such as geometric, aerodynamic, mobility, projected-area or otherwise) of 100 nm or less, produced as a by-product of a process such as welding and combustion. [Source: ISO [2015]. ISO 18158 Workplace air – terminology. Geneva: International Organization for Standardization.]

Uncertainty - A limited knowledge of the agreement between data, information, or outcomes relative to an unknown truth. The uncertainty of a measurement is the parameter associated with the result of a measurement that characterizes the dispersion of the values that could reasonably be attributed to the measurand (the quantity being measured). [Source: Taylor BN, Kuyatt CE [1994]. NIST Technical note 1297, Guidelines for evaluating and expressing the uncertainty of NIST measurement results. Gaithersburg, MD, National Institute of Standards and Technology (NIST).]

User Check - An evaluation of a written procedure for clarity and accuracy in which an independent laboratory analyzes a small number of spiked samples following a draft sample preparation and analysis exactly as written and reviews the draft method for clarity. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

UV – Ultraviolet

V

V - Volume of air sample, in L, as taken at the sampling site, corrected if necessary for rotameter calibration at a different temperature and pressure:

$$V = (flow\ rate)(time)\left(\frac{P_c T_s}{P_s T_c}\right)^{0.5}$$

Validated Method - A Method which meets or exceeds certain sampling and measurement performance criteria; see for example, the criteria given in Chapter ME [Source: NIOSH [2016]. Development and evaluation of methods. In: NIOSH Manual of analytical methods, 5th ed. DHHS (NIOSH) Publication No. 2014-151, http://www.cdc.gov/niosh/nmam.]

Validation - Process of evaluating the performance of a measuring procedure and checking that the performance meets certain pre-set criteria. Discussion: Performance characteristics to be considered include confirmation of identity, selectivity/ specificity, limit of detection, limit of quantification, analytical recovery, working and linear dynamic ranges, accuracy, measurement repeatability, measurement reproducibility, ruggedness, and robustness. [Source: CEN [2011]. EN 1540, Workplace atmospheres – terminology. Brussels: European Standards Commission.]

Vapor –

1. The gaseous phase of matter that normally exists in a liquid or solid state [Source: ASTM [2014]. D1356, Standard terminology relating to sampling and analysis of atmospheres. West Conshohocken, PA: ASTM International.]

2. Gas phase of a substance in a state of equilibrium or disturbed equilibrium with the same substance in a liquid or solid state below its boiling or sublimation point [Source: CEN [2011]. EN 1540, Workplace atmospheres – terminology. Brussels: European Standards Commission.]

V_m - Volume of 1 mole of ideal gas at the specified temperature and pressure (e.g., 24.45 L at 25 °C and 1 atmosphere).

VOL-MAX - Maximum recommended air sample volume, L, based on sampler capacity or other limitation, at the OSHA PEL

VOL-MIN - Minimum recommended air sample volume, L, based on an atmosphere at the OSHA PEL concentration and collecting a mass of substance which is equal to the LOQ. See also Working range.

VP - Vapor pressure

W

W - Mass of analyte found on an exposed single-section sampler (e.g., membrane filter)

W_b - Mass of analyte found on the back section of an exposed sampler

W_f - Mass of analyte found on the front section of an exposed sampler

Working Range - Range of air concentrations, in ppm or mg/m^3, at specified air sample volume, extending from the LOQ to a maximum determined by sampler capacity or measurement considerations. [Source: NIOSH [1994]. NIOSH Manual of analytical methods (NMAM), 4th ed. DHHS (NIOSH) Publication No. 94-113.]

X

XRD - X-ray diffraction

XRF - X-ray fluorescence

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METHODS

PARTICULATES NOT OTHERWISE REGULATED, TOTAL 0501

DEFINITION: total aerosol mass | CAS: NONE | RTECS: NONE

METHOD: 0501, Issue 1 | **EVALUATION: FULL** | **Issue 1: 8 May 2015**

OSHA: 15 mg/m^3, total dust (inert or nuisance dust; particles not otherwise regulated) [1]
NIOSH: no REL
For other OELs and guidelines: See references [2,3]

PROPERTIES: Contains no asbestos and less than 1% quartz

SYNONYMS: Nuisance dusts; particles not otherwise specified (PNOS)

SAMPLING

SAMPLER: INTERNAL CAPSULE (tared 37-mm, 2- to 5-µm PVC filter melded to PVC housing) in 37-mm 2-piece cassette

FLOW RATE: 1 to 2 L/min

VOL-MIN: 17 L @ 15 mg/m^3
-MAX: 333 L @ 15 mg/m^3

SHIPMENT: Routine

SAMPLE STABILITY: 28 days minimum

BLANKS: Minimum of 2 field blanks per batch

ACCURACY

RANGE STUDIED: 0.1 to 4 mg per sample

BIAS: 0.058 [4]

OVERALL PRECISION ($\hat{S}_{rT}$): 0.059 [4]

ACCURACY: ± 15.5%

MEASUREMENT

TECHNIQUE: GRAVIMETRIC (INTERNAL CAPSULE WEIGHT)

ANALYTE: Airborne particulate material

BALANCE: 0.001 mg sensitivity; use same balance before and after sample collection

CALIBRATION: National Institute of Standards & Technology Class S-1.1 weights or ASTM Class 1 weights

RANGE: 0.25 to 5 mg per sample

ESTIMATED LOD: 0.075 mg per sample

PRECISION ($\bar{S}_r$): 0.031 @ ≈2 mg per sample [4]

APPLICABILITY: The working range is 2.5 to 50 mg/m^3 for a 100-L air sample. This method is nonspecific and determines the 'total' dust concentration to which a worker is exposed.

INTERFERENCES: Moisture and static electricity can affect gravimetric measurements. Humidity control and minimization of static effects are addressed in this procedure.

OTHER METHODS: The method is similar to Method 5100 for carbon black [5]. This method is preferred over 0500, Issue 2 [6]. OSHA method PV2121 describes a similar procedure (but for respirable sampling) using an alternative sampler design [7].

EQUIPMENT:

1. Sampler: Internal capsule, 37-mm polyvinyl chloride (PVC), 2- to 5-µm pore size membrane or equivalent hydrophobic filter attached to PVC housing and supporting pad in 37-mm 2-piece cassette filter holder
   NOTE: The cassettes should be fabricated so as to ensure complete sealing of the internal capsule after sample collection.
2. Personal sampling pump, 1 to 2 L/min, with flexible connecting tubing
3. Microbalance, capable of weighing to ±0.001 mg
4. Static neutralizer, e.g., ^{210}Po; replace no more than nine months after the production date
5. Tool for handling internal capsules, e.g., forceps (preferably plastic)
6. Environmental chamber or room for balance (e.g., 20 °C ± 1 °C and 50% ± 5% RH)

SPECIAL PRECAUTIONS: None.

PREPARATION OF INTERNAL CAPSULES BEFORE SAMPLING:

1. Equilibrate the PVC filter capsules in an environmentally controlled weighing area or chamber for at least 24 hours.
   NOTE: An environmentally controlled chamber is desirable, but not required.
2. Place backup pads in filter cassette bottom sections.
3. Weigh the filter capsules in an environmentally controlled area or chamber. Record the internal capsule tare weight, W_1 (mg).
   a. Zero the balance before each weighing.
   b. Handle the filter capsule with forceps. Pass the internal capsule over an antistatic radiation source. Repeat this step if the capsule does not release easily from the forceps or if it attracts the balance pan. Static electricity can cause erroneous weight readings.
4. Assemble the filter capsules in the filter cassettes and close firmly so that leakage around the internal capsule will not occur. Place a plug in each opening of the filter cassette. Place a cellulose shrink band around the filter cassette, allow to dry and label the cassette with indelible ink.

SAMPLING:

5. Calibrate each personal sampling pump with a representative sampler in line.
6. Sample at 1 to 2 L/min for a total sample volume of 17 to 333 L. Do not exceed a total filter capsule loading of approximately 5 mg total dust. Take two to four replicate samples for each batch of field samples for quality assurance on the sampling procedure.

SAMPLE PREPARATION:

7. Wipe dust from the external surface of the filter cassette with a moist paper towelette to minimize contamination. Discard the paper towelette.
8. Remove the top and bottom plugs from the filter cassette. Equilibrate for at least 24 hours in the balance room.
9. Using forceps, open the cassette and remove the internal capsule gently to avoid loss of dust or damage to the capsule.

CALIBRATION AND QUALITY CONTROL:

10. Zero the microbalance before all weighings. Use the same microbalance for weighing filter capsules before and after sample collection. Calibrate the balance with National Institute of Standards and Technology Class S-1.1 or ASTM Class 1 weights.
11. Process laboratory blanks, spiked QC samples and field blanks at a minimum frequency of 1 per 20 field samples. Internal capsules used for QC samples should come from the same lot. Spiked QC samples, loaded with 0.25-4 mg of material per internal capsule, should be prepared using weight-stable material such as Arizona Road Dust [8].

MEASUREMENT:

12. Weigh each capsule, including field blanks. Record the post-sampling weight, W_2 (mg). Record anything remarkable about a capsule (e.g., overload, leakage, wet, torn, etc.).

CALCULATIONS:

13. Calculate the concentration of total particulate matter, C (mg/m^3), in the air volume sampled, V (L):

$$C = \frac{(W_2 - W_1) - (B_2 - B_1)}{V} 10^3 \quad , \text{mg/m}^3$$

where: W_1 = tare weight of capsule before sampling (mg)
W_2 = post-sampling weight of sample-containing capsule (mg)
B_1 = mean tare weight of blank capsules (mg)
B_2 = mean post-sampling weight of blank capsules (mg)

EVALUATION OF METHOD:

Lab testing was carried out using blank internal capsules and with capsules spiked with 0.1 – 4 mg of NIST SRM 1648 (Urban Particulate Matter) and Arizona Road Dust (Air Cleaner Test Dust) [4]. Precision and accuracy data are given on page 0501-1. Weight stability over 28 days was verified for both blanks and spiked capsules [4]. Independent laboratory testing on blanks and field samples have verified long-term weight stability as well as sampling and analysis uncertainty estimates [4,8].

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METHOD WRITTEN BY: Kevin Ashley, Ph.D., NIOSH/DART.

VINYL ACETATE 1453

$CH_3CO_2CHCH_2$ MW: 86.09 CAS: 108-05-4 RTECS: AK0875000

METHOD: 1453, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 August 1994
Issue 3: 15 March 2013

OSHA: None
MSHA: None
NIOSH: Ceiling 4 ppm (15 min)
OTHER OELs: [1,2]

PROPERTIES: Liquid; BP 72.7 °C; d 0.934 g/mL @ 20 °C; VP 11.8 kPa (89 mm Hg) @ 20 °C; vapor density (air = 1) 3.0

SYNONYMS: Acetic acid, vinyl ester; acetic acid, ethenyl ester; Vinyl A monomer; ethylene ethanoate; 1-acetoxyethylene; ethenyl acetate; vinyl acetate monomer; vinyl ethanoate.

SAMPLING

SAMPLER: SOLID SORBENT TUBE (carbon molecular sieve; 160 mg/80 mg)

FLOW RATE: 0.05 to 0.2 L/min

VOL-MIN: 1.5 L @ 4 ppm
-MAX: 24 L

SHIPMENT: Routine

SAMPLE STABILITY: At least 30 days @ 5 °C

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 3.7 to 46 mg/m^3 (24-L sample) [3]

BIAS: -0.04

OVERALL PRECISION ($\hat{S}_{rT}$): 0.064

ACCURACY: 14.1%

MEASUREMENT

TECHNIQUE: GAS CHROMATOGRAPHY, FID

ANALYTE: Vinyl acetate

DESORPTION: 1.0 mL 95:5% (v/v) methylene chloride/methanol

INJECTION VOLUME: 1 µL

TEMPERATURE -INJECTION: 210 °C
-DETECTOR: 260 °C
-COLUMN: 35 °C, 5 min; 5 °C/min to 50 °C; hold 1 min

CARRIER GAS: Helium, split flow 21.0 mL/min

COLUMN: Capillary, fused silica, 30 m x 0.32 mm, coated internally with 1 µm film (5% phenyl) methylpolysiloxane

CALIBRATION: Standard solutions of vinyl acetate in 95:5% (v/v) methylene chloride/methanol

RANGE: 3 to 1120 µg per sample

ESTIMATED LOD: 1 µg per sample

PRECISION ($\bar{S}_r$): 0.040

APPLICABILITY: The working range is 0.02 to 13.1 ppm (0.07 to 46 mg/m^3) for a 24-L air sample. The method is sensitive enough for ceiling measurements.

INTERFERENCES: Vinyl acetate that is not stabilized or has been depleted of inhibitor can polymerize. Any substance collected with the vinyl acetate that is capable of reacting with it is a potential interference. Acids, bases, free radical initiators, etc., are capable of reacting with vinyl acetate during and after air sampling.

OTHER METHODS: This method is an update for NMAM 1453 first issued on August 15, 1994 [4]. This method is adapted from OSHA Method No. 51 [5] and NIOSH 1453 Issue 2 and replaces NIOSH method P&CAM 278 [6].

REAGENTS:

1. Vinyl acetate*, 99% purity, inhibited with 3 – 22 ppm hydroquinone.
2. Methanol*, distilled in glass.
3. Methylene chloride*, distilled in glass.
4. Desorption solvent, 95%/5% (v/v) methylene chloride/methanol.
5. Helium, purified.
6. Hydrogen, prepurified.
7. Air, filtered, compressed.
8. Calibration stock solution, 74.7 mg/mL. Add 400 µL vinyl acetate into a 5-mL volumetric flask and dilute to volume with methanol.

   *See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: glass tube, 7 cm long, 6-mm OD, 4-mm ID, flame-sealed ends with plastic caps, containing two sections of carbon molecular sieve, (front = 160 mg, back = 80 mg) separated by a 2-mm urethane foam plug. A silylated glass wool plug precedes the front section and a 3-mm urethane foam plug follows the back section. Pressure drop across the tube at 1 L/min airflow must be less than 25 mm/Hg. Tubes are commercially available.
2. Personal sampling pump, 0.1 to 0.2 L/min, with flexible connecting tubing.
3. Gas chromatograph with flame ionization detector (GC-FID), column (page 1453-1) and data collector.
4. Vials, 2-mL, with PTFE-lined caps.
5. Syringe, 10-µL and other sizes as needed.
6. Volumetric flasks, 2- and 5-mL.

SPECIAL PRECAUTIONS: Methylene chloride is an irritant, can be absorbed through the skin, and is a potential occupational carcinogen [7]. Vinyl acetate can irritate the eyes, nose, and throat. Vinyl Acetate is flammable in air (percent by volume): lower, 2.6%; upper, 13.4% [8]. Vinyl acetate can become unstable if the polymerization inhibitor decreases to unsafe levels [8]. Methanol is flammable and a dangerous fire and explosion risk. It is moderately toxic by ingestion and inhalation. Wear appropriate protective clothing and work with these compounds in a well ventilated hood.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Break the ends of the sampler immediately before sampling. Attach sampler to personal sampling pump with flexible tubing.
3. Sample at an accurately known flow rate of 0.1 to 0.2 L/min for a total sample size of 1.5 to 24 L.
   NOTE: If high concentrations are expected, multiple samplers may need to be used to collect over an 8 hour period (collect two 4-hour samples for example) in order to not exceed the capacity of the sorbent tube
4. Cap the samplers. Pack securely for shipment.

SAMPLE PREPARATION:

5. Place the front sorbent section along with the glass wool plug in a separate vial from the back sorbent section of the sampler. Discard the foam plugs.
6. Add 1.0 mL of 95:5% (v/v) methylene chloride/methanol to each vial. Cap each vial.
7. Allow to stand 30 min with occasional agitation.

CALIBRATION AND QUALITY CONTROL:

8. Calibrate daily with at least six working standards.
   a. Add 400 µL vinyl acetate to methanol in a 5-mL volumetric flask and dilute to the mark. This is the stock calibration solution. Use serial dilutions, as needed, to obtain the desired concentration range.

b. Analyze with samples and blanks (steps 11 and 12).
c. Prepare calibration graph (area vs. µg/mL).

9. Determine desorption efficiency (DE) at least once for each lot of sorbent used for sampling in the range of interest (step 8). Prepare three tubes at each of five levels plus three media blanks.
   a. Remove and discard back sorbent section of a media blank sampler.
   b. Inject a known amount (2 to 20 µL) of a standard mixture of vinyl acetate directly onto front sorbent section with a microliter syringe.
      NOTE: Inject no more than 20 µL onto the sorbent. Dilute stock solution as appropriate.
   c. Cap the tube. Allow to stand overnight.
   d. Desorb (steps 5 through 7) and analyze with working standards (steps 11 and 12).
   e. Prepare a graph of DE vs. µg vinyl acetate recovered.
10. Analyze three quality control blind spikes and three analyst spikes to ensure that the calibration graph and recovery graph are in control.

MEASUREMENT:

11. Set gas chromatograph according to manufacturer's recommendations and to conditions given on page 1453-1. Inject sample aliquot manually using solvent flush technique or with autosampler.
    NOTE: If peak area is above the linear range of the working standards, dilute an aliquot of the desorbed liquid with desorption solvent, reanalyze, and apply the appropriate dilution factor in calculations.
12. Measure the peak area of the vinyl acetate signal.

CALCULATIONS:

13. Determine the mass, µg (corrected for DE) of vinyl acetate found in the sample front (W_f) and back (W_b) sorbent sections, and in the average media blank front (B_f) and back (B_b) sorbent sections.
    NOTE: If $W_b > W_f/10$, report breakthrough and possible sample loss.
14. Calculate concentration, C, of vinyl acetate in the air volume sampled, V (L):

$$C = \frac{(W_f + W_b) - (B_f + B_b)}{\mathrm{V}}, mg/m^3$$

NOTE: µg/L ≙ mg/m^3

EVALUATION OF METHOD:

This method was validated originally by the Organic Methods Development Branch, OSHA Technical Center, Salt Lake City, UT, over the range 187 to 710 µg per sample using Ambersorb® XE-347 as sorbent. Breakthrough studies at 70% RH, sampling an atmosphere of 150 mg/m^3 at 0.19 L/min, indicated a tube capacity of approximately 9 mg of vinyl acetate [5].

This media is no longer available and is replaced with Carboxen® 564 carbon molecular sieve tubes (OrboTM-92 or equivalent tubes). Using OrboTM-92 media, the average desorption efficiency for samples in this range was 98.5%. Recoveries from samples stored for 30 days at 5 °C were 90 to 110% for samples spiked at 187 and 747 µg per sample. The pooled coefficient of variation obtained from replicate determinations of analytical standards in this range was 0.020 [3,9].

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METHOD REVISED BY:

3rd Issue (2013) Y. T. Gagnon and P. F. O'Connor, CDC/NIOSH, Cincinnati, Ohio.
2nd Issue (1998) Y. H. Yoon, Ph.D. and J. B. Perkins, DataChem Laboratories, Inc., Salt Lake City, Utah.
1st Issue (1994) A. A. Grote, CDC/NIOSH, Cincinnati, Ohio.

NITROAROMATIC COMPOUNDS 2005

(1) Nitrobenzene: $C_6H_5NO_2$	MW: (1) 123.11	CAS: (1) 98-95-3	RTECS: (1) DA6475000
(2) *o*-Nitrotoluene: $CH_3C_6H_4NO_2$	(2) 137.14	(2) 88-72-2	(2) XT3150000
m-Nitrotoluene:		99-08-1	XT2975000
p-Nitrotoluene:		99-99-0	XT3325000
(3) 4-Chloronitrobenzene: $C_6H_4ClNO_2$	(3) 157.56	(3) 100-00-5	(3) CZ1050000

METHOD: 2005, Issue 4 **EVALUATION:** FULL **Issue 1:** 15 August 1990
Issue 4: 4 March 2016

OSHA: Table 1
NIOSH: Table 1

PROPERTIES: Table 1

SYNONYMS: (1) Nitrobenzol, oil of mirbane; (2) *o*-Methylnitrobenzene, 2-Methylnitrobenzene, 2-Nitrotoluene *m*-Methylnitrobenzene, 3-Methylnitrobenzene, 3-Nitrotoluene *p*-Methylnitrobenzene, 4-Methylnitrobenzene, 4-Nitrotoluene; (3) *p*-Chloronitrobenzene, 1-Chloro-4-nitrobenzene, 4-Nitrochlorobenzene, PCNB, PNCB

SAMPLING

SAMPLER: SOLID SORBENT TUBE (silica gel, 150 mg/75 mg)

FLOW RATE: (1) and (3) 0.01 - 1 L/min;
(2) 0.01 to 0.02 L/min

	(1)	(2)	(3)
VOL-MIN:	10 L	1L	1L
-MAX:	150 L	30L	150L

SHIPMENT: routine

SAMPLE STABILITY: 30 days @ 0 °C [1]

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: Table 1

BIAS: Table 1

OVERALL PRECISION ($\hat{S}_{rT}$): Table 1

ACCURACY: Table 1

MEASUREMENT

TECHNIQUE: GAS CHROMATOGRAPHY, FID

ANALYTE: nitrobenzene, nitrotoluene isomers, 4-chloronitrobenzene

DESORPTION: 1 mL methanol in ultrasonic bath for 30 minutes mL acetonitrile

INJECTION VOLUME: 1 µL

TEMPERATURE
-INJECTION: 250 °C
-DETECTOR: 300 °C
-COLUMN: 80 °C, 1 min, 8 °C/min to 180 °C

CARRIER GAS: He, 2.5 to 3.0 mL/min

COLUMN: capillary, 30 m x 0.53-mm ID; µm film crossbonded 5% diphenyl 95% dimethylpolysiloxane

CALIBRATION: analytes in methanol

RANGE: Table 1

ESTIMATED LOD: Table 1

PRECISION ($\bar{S}_r$): Table 1

APPLICABILITY: The working ranges for a 30-L air samples are 0.396 to 1.92 ppm (1.98 to 9.60 mg/m^3) for nitrobenzene; 0.346 to 1.73 ppm (1.97 to 9.86 mg/m^3) for *o*-nitrotoluene; 0.344 to 1.72 ppm (1.96 to 9.81 mg/m^3) for *m*-nitrotoluene; 0.303 to 1.52 ppm 1.73 to 8.67 mg/m^3) for *p*-nitrotoluene; and 0.308 to 1.54 ppm (1.98 to 9.92 mg/m^3) for 4-chloronitrobenzene [1,2].

INTERFERENCES: Any compounds with retention times similar to the analytes of interest will interfere. During sampling, high humidity may greatly decrease breakthrough volume

OTHER METHODS: This method is an update of NMAM 2005, Nitrobenzenes, issued 15 August 1994, which combined and replaced methods S217, S218, and S223 [2,3].

REAGENTS:

1. Methanol, HPLC chromatographic grade.
2. Nitrobenzene*, reagent grade.
3. *o*-,*m*-,*p*-nitrotoluene isomers,* reagent grade.
4. 4-chloronitrobenzene*, reagent grade.
5. Calibration stock solution, 500 µg/mL. Prepare each analyte in methanol.
6. Helium, purified and filtered.
7. Hydrogen, purified and filtered.
8. Air, purified and filtered.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: silica gel sampling tube; glass tube, 7 cm long, 6-mm OD, 4-mm ID, flame-sealed ends with plastic caps, containing two sections (front=150 mg; back=75 mg) of 20/40 mesh silica gel separated by a 2-mm urethane foam plug. A silylated glass wool plug precedes the front section and a 3-mm urethane foam plug follows the back section.
2. Personal sampling pump, 0.01 to 1 L/min, with flexible connecting tubing.
3. Gas chromatograph, FID, integrator and column (page 2005-1).
4. Autosampler vials, glass, 2-mL, with PTFE-lined crimp caps.
5. Volumetric flasks, 10-mL.
6. Pipets, 5-mL and 3-mL, with pipet bulb.
7. Syringes, 10-µL, 100-µL, and 1-mL.
8. Ultrasonic bath.

SPECIAL PRECAUTIONS: These analytes are severe poisons and irritants. Prevent contact with eyes, skin, or clothing by wearing eye protection, chemically resistant gloves, and a lab coat. Avoid inhalation. Nitrobenzene and *m*-nitrotoluene are absorbed through contact with skin and can cause methemoglobinemia [5,6]. 4-Chloronitrobenzene is a carcinogen. Methanol is highly flammable.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Break the ends of the sampler immediately before sampling. Attach sampler to personal sampling pump with flexible tubing.
3. Sample at an accurately known flow rate between 0.01 and 0.2 L/min for nitrotoluene isomers. Use a flow rate of 1 L/min or less for nitrobenzene and 4-chloronitrobenzene. Note the maximum and minimum sample volumes on page 2005-1.
4. Cap both ends of the sampler. Pack securely for shipment.

SAMPLE PREPARATION:

5. Place the front (include the glass wool plug) and back sorbent sections of each sample tube in separate vials. Discard the foam plugs.
6. Add 1.0 mL of methanol to each vial. Attach crimp cap securely to each vial.
7. Allow to desorb 30 min in an ultrasonic bath.

CALIBRATION AND QUALITY CONTROL:

8. Calibrate daily with at least six working standards to cover the analytical range of the method. If necessary, additional standards may be added to extend the calibration curve.
   a. Add known amounts of calibration stock to methanol in 10-mL volumetric flasks and dilute to the mark.
   b. Analyze together with samples and blanks (steps 11 and 12).
   c. Prepare calibration graph (peak area vs µg analyte).
9. Determine desorption efficiency (DE) at least once for each lot of silica gel used for sampling in the calibration ranges (step 8).
   a. Prepare three tubes at each of five levels plus three media blanks.
   b. Inject a known amount of calibration stock solution directly onto the front sorbent section of each silica gel tube with a microliter syringe.
   c. Allow the tubes to air equilibrate for several minutes, then cap the ends of each tube and allow to stand overnight.
   d. Desorb (steps 5 through 7) and analyze together with standards and blanks (steps 11 and 12).
   e. Prepare a graph of DE vs µg analyte recovered.
10. Analyze three quality control blind spikes and three analyst spikes to ensure that the calibration graph and DE graph are in control.

MEASUREMENT:

11. Set gas chromatograph according to manufacturer's recommendations and to conditions given on page 2005-1. Inject a 1-µL sample aliquot manually using the solvent flush technique or with an autosampler.
    NOTE: If peak area is above the linear range of the working standards, dilute with methanol, reanalyze and apply the appropriate dilution factor in the calculations.
12. Measure peak areas.

CALCULATIONS:

13. Determine the mass, µg (corrected for DE) of analyte found in the sample front (W_f) and back (W_b) sorbent sections, and in the average media blank front (B_f) and back (B_b) sorbent sections.
    NOTE: If $W_b > W_f/10$, report breakthrough and possible sample loss.
14. Calculate concentration, C, of analyte in the air volume sampled, V(L):

$$C = \frac{W_f + W_b - B_f - B_b}{V}, mg/m^3$$

NOTE: µg/mL≅mg/m^3

EVALUATION OF METHOD:

The 3rd issue update of this method included the use of capillary column chromatography (Rtx™-5 Amine) that lowered the LOD/LOQ values, a lower 5-level desorption efficiency study, and a 30-day storage stability study for each analyte [1]. The method evaluation data for these compounds are listed in Table 2. Methods S217, Nitrobenzene, and S218, 4-nitrochlorobenzene, were initially issued on November 21, 1975 [4]. Method S223, *o*-nitrotoluene was issued on December 19, 1975 [4]. The analytes *m*-nitrotoluene and *p*-nitrotoluene were added on May 15, 1984 [3]. In the original method development work, sample tube capacity, or breakthrough, was determined as 5% of the generated atmosphere concentration as measured in the effluent of the sample tubes. Capacity was measured at >2.8 mg/sample for nitrobenzene; >2.5 mg/sample for nitrotoluene isomers; and >2.2 mg/sample for 4-chlorobenzene [2].

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METHOD WRITTEN BY:

Stephanie M. Pendergrass, NIOSH

TABLE 1. General Information

Chemical	OSHA PEL	NIOSH REL	Physical Properties	Method Evaluation
Nitrobenzene	1 ppm (5 mg/m^3) (skin)	1 ppm (5 mg/m^3) (skin)	Colorless oily liquid, almond odor; d=1.196 g/mL @ 20 °C; MP 6 °C; BP 210- 211 °C; VP=37 Pa (0.30 mm Hg) @ 20 °C	Full
o-Nitrotoluene	5 ppm (30 mg/m^3) (skin)	2 ppm (11 mg/m^3) (skin)	yellowish liquid; d=1.163 g/mL @ 20 °C; MP -4 °C; BP 222 °C; VP=20 Pa (0.15 mm Hg) @ 20 °C	Full
m-Nitrotoluene	5 ppm (30 mg/m^3) (skin)	2 ppm (11 mg/m^3) (skin)	liquid; d=1.157 g/mL @ 20 °C; MP 16 °C; BP 232 °C; VP=20 Pa (0.15 mm Hg) @ 20 °C	Partial
p-Nitrotoluene	5 ppm (30 mg/m^3) (skin)	2 ppm (11 mg/m^3) (skin)	yellow crystals; d=1.163 g/mL @ 20 °C; MP 52 °C; BP 238 °C; VP=17 Pa (0.12 mm Hg) @ 20 °C	Partial
4-Chloro-nitrobenzene	0.16 ppm (1. mg/m^3) (skin)	Ca* (skin)	yellow crystals; d=1.298 g/mL @ 20 °C; MP 83 °C; BP 242 °C; VP=28 Pa (0.2 mm Hg) @ 30 °C	Partial

* - Cancer suspect agent

TABLE 2. Method Summary

Chemical	Range Studied (mg/m³)	$\hat{S}_{rT}$	Bias	Accuracy (±%)	Analytical Range	LOD (µg/ sample)	$\bar{S}_r$	Desorption Efficiency (%)	30-Day Storage (% Rec)
Nitrobenzene	1.98-9.60	0.0590	0.0186	12.3	2 to 598	0.6	0.12	98.7	100.2
o-Nitrotoluene	1.97-9.86	0.0142	-0.120	21.1	3 to 582	0.8	0.028	98.2	101.2
m-Nitrotoluene	Not studied	nd[b]	nd	nd	3 to 579	1.0	0.042	97.5	99.4
p-Nitrotoluene	Not studied	nd	nd	nd	9 to 511	2.6	0.061	96.9	99.4
4-Chloro-nitrobenzene	1.98-9.92	0.1034	0.0869	27.3[c]	8 to 595	2.5	0.063	100.3	97.6

[a]30-L air sample
[b] Not determined
[c] Exceeds the NIOSH accuracy criterion of ± 25% at the 95% confidence level

Disclaimer: Mention of any company or product does not constitute endorsement by NIOSH. In addition, citations to websites external to NIOSH do not constitute NIOSH endorsement of the sponsoring organizations or their programs or products. Furthermore, NIOSH is not responsible for the content of these websites. All web addresses referenced in this document were accessible as of the publication date.

CHLOROACETIC ACID 2008

$ClCH_2COOH$ MW: 94.50 CAS: 79-11-8 RTECS: AF8575000

METHOD: 2008, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 May 1989
Issue 3: 15 March 2016

OSHA: None
NIOSH: None

PROPERTIES: solid; MP 61 to 63 °C; BP 189 °C; VP 0.1 kPa (0.75 mm Hg) @ 20 °C; flash point 126 °C; lower explosive limit in air 8% v/v

SYNONYMS: chloroethanoic acid; monochloroacetic acid

SAMPLING

SAMPLER: SOLID SORBENT TUBE (silica gel, 100 mg/50 mg)

FLOW RATE: 0.05 to 0.2 L/min

VOL-MIN: 1 L @ 0.25 ppm
-MAX: 100 L

SHIPMENT: routine

SAMPLE STABILITY: at least 7 days @ 25 °C; 32 days refrigerated [1]

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 0.35 to 29 mg/m^3 [1,2] (3-L samples)

BIAS: 2.0%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.08 [1]

ACCURACY: ± 17.7%

MEASUREMENT

TECHNIQUE: ION CHROMATOGRAPHY, CONDUCTIVITY DETECTION

ANALYTE: chloroacetate ion

DESORPTION: 2 mL deionized water

INJECTION LOOP VOLUME: 500 µL

ELUENT: 1.5 mM $NaHCO_3$; 1.0 mL/min

COLUMNS: US Pharmacopeia (USP) L12 separator column and manufacturer's compatible anion guard column

CALIBRATION: standard solutions of chloroacetic acid in deionized water

RANGE: 1 to 80 µg per sample [1]

ESTIMATED LOD: 0.04 µg per sample [2]

PRECISION ($\bar{S}_r$): 0.016 [1]

APPLICABILITY: The working range is 0.09 to >85 ppm (0.3 to 30 mg/m^3) for a 3-L air sample.

INTERFERENCES: Chloroacetyl chloride is a positive interferent since it is hydrolyzed to monochloroacetic acid by the measurement procedure and is efficiently collected by silica gel [3]. Particulate salts of the acid are positive interferents. The chromatographic conditions given will separate acetate, chloride, dichloroacetate, fluoride, glycolate, and trichloroacetate ions from chloroacetate ion.

OTHER METHODS: This revises P&CAM 332 [2]. The columns used in P&CAM 332 are no longer available. The newer columns indicated here show improvements in the analytical range and sensitivity.

REAGENTS:

1. Water, filtered, deionized. Specific conductance ≤10 µS/cm.
2. Sodium bicarbonate ($NaHCO_3$), reagent grade.
3. Chloroacetic acid, ≥99%.*
4. Eluent: 1.5 mM $NaHCO_3$. Dissolve 0.504 g $NaHCO_3$ in 4 L filtered, deionized water.
5. Calibration stock solution, 1000 µg/mL. Dissolve 100 mg chloroacetic acid in 100 mL filtered, deionized water.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: silica gel sorbent tube; glass tube, 7 cm long, 6-mm OD, 4-mm ID, with plastic caps, containing two sections of 20/40 mesh silica gel (front = 100 mg; back =50 mg) contained and separated by three silanized glass wool plugs. Pressure drop across the tube at 0.2 L/min is ca. 0.6 kPa (2.6 in. H_2O). Tubes are commercially available.
   NOTE: Chloroacetic acid is irreversibly adsorbed on urethane plugs. Use sorbent tubes with glass wool plugs.
2. Personal sampling pump, 0.05 to 0.2 L/min, with flexible connecting tubing.
3. Ion chromatograph (IC), anion separator (USP L12) and compatible guard column, anion suppressor (page 2008-1), conductivity detector and integrator.
4. Ultrasonic bath.
5. Vials, 20-mL, glass, with aluminum-lined plastic screw caps.
6. Syringes, 3-mL, polyethylene with luer tip.
7. Filter holder, luer tip, 13-mm, with polytetrafluoroethylene (PTFE) filter, 5-µm pore size, or PTFE syringe filter.
8. Pipets, 10-µL to 2-mL.
9. Flasks, volumetric, 10- and 100-mL.

SPECIAL PRECAUTIONS: Chloroacetic acid is irritating to skin and mucous membranes [4]. Work with concentrated material only in a hood.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Break ends of sampler immediately before sampling. Attach sampler to personal sampling pump with flexible tubing.
3. Sample at an accurately known flow rate between 0.05 to 0.2 L/min for a total sample size of 1 to 100 L.
4. Cap the samplers. Pack securely for shipment.
   NOTE: Store samples in the dark. Refrigerate samples if stored longer than 7 days.

SAMPLE PREPARATION:

5. Allow refrigerated samples to equilibrate to room temperature.
6. Transfer front sorbent section with front glass wool plug to vial. Place back sorbent section and other two glass wool plugs in separate vial.
7. Add 2.0 mL deionized water to each vial. Cap immediately.
8. Agitate vials in ultrasonic bath for 30 min at room temperature.
9. Draw sample extract through 13-mm PTFE filter with 3-mL syringe.

CALIBRATION AND QUALITY CONTROL:

10. Calibrate daily with at least six working standards.
    a. Add known aliquots of calibration stock solution to deionized water in 10-mL volumetric flasks and dilute to the mark. Use serial dilutions as needed to obtain chloroacetic acid concentrations in the range 0.02 to 40 µg/mL.
    b. Analyze together with samples and blanks (steps 13 through 15).
    c. Prepare calibration graph [peak height (mm or µS) vs. µg chloroacetic acid per sample].
11. Determine desorption efficiency (DE) for each batch of silica gel used for sampling in the calibration range. Prepare at least three tubes at each of five levels.
    a. Place silica gel from unused front section in vial.
    b. Inject a known amount (2 to 20 µL) of calibration stock solution, or a serial dilution thereof, onto front sorbent section with a microliter syringe.
    c. Cap the vial. Allow to stand overnight.
    d. Desorb (steps 7 through 9) and analyze together with working standards (steps 13 through 15).
    e. Prepare graph of DE vs. µg chloroacetic acid recovered.
12. Analyze three quality control spikes and three analyst spikes to ensure that the calibration graph and DE graph are in control.

MEASUREMENT:

13. Set ion chromatograph according to manufacturer's recommendations and to conditions given on page 2008-1.
14. Inject sample aliquot manually or use autosampler.
    a. Flush sample loop with 0.5 mL sample extract, then inject 0.5 mL sample.
    b. Rinse sample loop with 1 to 2 mL deionized water between determinations of separate samples.
    NOTE: All samples, eluents, and water flowing through the IC must be filtered to avoid plugging the system valves or columns.
15. Measure peak height.
    NOTE: If sample peak height exceeds linear calibration range, dilute with deionized water, reanalyze, and apply appropriate dilution factor.

CALCULATIONS:

16. Determine mass, µg (corrected for DE), of analyte found in the sample front (W_f) and back (W_b) sorbent sections, and in the average media blank front (B_f) and back (B_b) sorbent sections.
17. Calculate concentration, C, of chloroacetic acid in the air volume sampled, V (L):

$$C = \frac{W_f + W_b - B_f - B_b}{V} \; mg/m^3$$

EVALUATION OF METHOD:

This method was developed and evaluated by Southern Research Institute [1] using dynamically-generated atmospheres of chloroacetic acid over the concentration range of 0.35 to 29 mg/m^3 at 25 to 27 °C and at relative humidity (RH) ≥80%. Average recovery based on 18 samples, six at each of three levels, was 98% representing a negligible bias. Precision at 0.35 mg/m^3 was inhomogeneous with those of higher levels; therefore, precisions were not pooled. Using this poorest precision ($\bar{S}_r$ = 0.064), the overall precision ($\hat{S}_{rT}$) was estimated to be ≤0.081.

The breakthrough volume of the 100-mg sorbent section was found to be >100 L at 0.2 L/min when sampling chloroacetic acid concentrations of 60 mg/m^3 at 42 °C and RH of 10 and 80% and 35 mg/m^3 at 27 °C and 10 and 90% RH. Samples stored at ambient temperature for 7 days had a mean recovery of 91%

and a precision, $\bar{S}_r$, of 0.047. Samples refrigerated after day 7, and stored for 32 days exhibited a mean recovery of 100% with a precision, $\bar{S}_r$, of 0.085 based on samples analyzed on day 1.

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p-CHLOROPHENOL 2014

C_6H_4ClO MW: 128.56 CAS: 106-48-9 RTECS: SK2800000

METHOD: 2014, Issue 2 **EVALUATION:** FULL **Issue 1:** 19 September 1980
Issue 2: 25 February 2016

OSHA: None
NIOSH: None

PROPERTIES: crystals; d 1.224 g/mL @ 20 °C; MP 43.2-43.7 °C; BP 220 °C; VP 0.013 kPa (0.1 mm Hg) @ 20 °C; flash point 121 °C (closed cup)

SYNONYMS: 4-chlorophenol; 4-chloro-1-hydroxybenzene

SAMPLING

SAMPLER: SORBENT TUBE (silica gel, 150 mg/75 mg)

FLOW RATE: 0.05 - 0.2 L/min

VOL-MIN: 1.5 L @ 1 ppm
-MAX: 40 L

SHIPMENT: routine

SAMPLE STABILITY: 7 days @ 25 °C at least 29 days @ 0 °C [1]

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 0.910 to 23.4 mg/m^3 [1] (3-L samples)

BIAS: none identified

OVERALL PRECISION ($\hat{S}_{rT}$): 0.061 for range studied [1]

ACCURACY: ± 15% (12-28%)

MEASUREMENT

TECHNIQUE: HPLC/UV

ANALYTE: *p*-chlorophenol

EXTRACTION: 1 mL acetonitrile

MOBILE PHASE: 30% acetonitrile, 70% water to 80% acetonitrile/20% water in 20 minutes, 1 mL/min

COLUMN: C18 (5 µm particle size, 4-mm ID by 30-cm long, stainless steel)

DETECTOR: UV @ 280 nm

CALIBRATION: *p*-chlorophenol in 30% (v/v) acetonitrile in water

RANGE: 8 to 64 µg/sample [1]

ESTIMATED LOD: 2.5 µg/sample [1]

PRECISION ($\bar{S}_r$): 0.024 [1]

APPLICABILITY: The working range is 0.15 to 53 ppm (0.8 to 280 mg/m^3) for a 10-L air sample.

INTERFERENCES: None identified. The chromatographic conditions described will separate phenol; *o*-chlorophenol; 2,3-, 2,4-, 2,5-, 2,6-, 3,4-, and 3,5- dichlorophenol; *o*- and *p*-nitrophenol; 2,4-dimethylphenol; 2,4,5-trichlorophenol; 4-chloro-*o*-methylphenol; 2,4-dinitrophenol; 4,6-dinitro-2-methylphenol; and pentachlorophenol.

OTHER METHODS: This method replaces P&CAM 337 [2]. The other columns for the analysis of *p*-chlorophenol have been reported in the literature [3-5].

REAGENTS:

1. *p*-Chlorophenol 99%.*
2. Acetonitrile, distilled in glass.
3. Hexane, distilled in glass.
4. Water, HPLC quality distilled, deionized.
5. *p*-Chlorophenol stock solution, 20 mg/mL. Dissolve 500 mg *p*-chlorophenol in 30% (v/v) acetonitrile in water to make 25 mL solution. Stable at least 3 months in airtight container.
6. Desorption efficiency (DE) stock solution, 5 mg/mL. Dissolve 125 mg *p*-chlorophenol in hexane to make 25 mL solution.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: borosilicate glass tubes, 7 cm long with a 6-mm OD and a 4-mm ID, flame sealed at both ends. Each tube contains two sections of 20/40 mesh silica gel (a 150-mg sorbent section and a 75-mg backup section separated and held in place with glass wool plugs). Tubes are commercially available.
2. Personal sampling pump, calibrated, capable of operating 8 hours at 0.05 to 0.2 L/min with flexible connecting tubing.
3. HPLC with UV detector (280 nm), C18 column, injector, and electronic integrator.
4. Microliter syringes, various sizes.
5. Volumetric flasks, various sizes.
6. Centrifuge tubes, 12-mL, glass with screw caps.
7. Pipette, 1- and 2-mL, and convenient sizes for making dilutions.
8. Vials, 1-mL, with caps containing PTFE-lined silicone septa.
9. Ultrasonic bath.

SPECIAL PRECAUTIONS: *p*-Chlorophenol is toxic by skin absorption, inhalation, or ingestion. It also is a strong irritant to tissue and is combustible with a flash point of 121 °C.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Immediately before sampling, break open the ends of the tube to provide openings that are at least 2-mm in diameter. Attach sampler to personal sampling pump with flexible tubing.
3. Sample at an accurately known flowrate between 0.05 and 0.2 L/min for a total sample size of 1 to 40 liters.
4. Cap the tubes, record sample identity and all relevant sample data (duration, ambient temperature and pressure). Pack securely for shipment.
   NOTE: Refrigerate all samples at 0 °C when stored longer than 7 days.

SAMPLE PREPARATION:

5. If refrigerated, allow tube to equilibrate to room temperature.
6. Transfer each section of silica gel in a sorbent tube to a separate 12-mL centrifuge tube. Combine the glass wool plug near the inlet with the front sorbent section. Combine the two urethane foam plugs with the back section.
7. Add 1 mL of acetonitrile, cap, and desorb in an ultrasonic bath for 30 minutes.
8. Add 2 mL of distilled, deionized water to each tube, cap, and mix the solutions.
9. Centrifuge the samples and transfer about 1 mL of the supernatant in each tube to a separate vial and seal with a PTFE-lined septum.

CALIBRATION AND QUALITY CONTROL:

10. Calibrate daily with at least six working standards in the range 2.5 to 64 µg per sample.
    a. Dilute aliquots of *p*-chlorophenol stock solution with 30% (v/v) acetonitrile in water in volumetric flasks to encompass the range of interest. Prepare fresh daily.
    b. Analyze working standards with samples and blanks steps.
    c. Prepare calibration graph (peak area or peak height vs. µg of *p*-chlorophenol per sample.
11. Determine desorption efficiency (DE) for each lot of silica gel used for sampling in the calibration range. Prepare three tubes at each of five levels.
    a. Remove backup section. Inject known amounts of DE stock solution (2 to 10 µL) onto the silica gel with a microliter syringe.
    b. Cap the tubes and allow to stand overnight.
    c. Desorb (steps 7 through 9) and analyze together with standards and blanks (steps 13 and 14).
    d. Prepare a graph DE vs. µg *p*-chlorophenol recovered.
12. Analyze three quality control spikes and three analyst spikes to ensure that the calibration graph and DE graph are in control.

MEASUREMENT:

13. Set HPLC according to manufacturer's recommendations and to conditions on page 2014-1. Inject sample aliquot manually or with autosampler.
    NOTE: If peak is above the linear range of the working standards, dilute with 30% (v/v) acetonitrile in water, reanalyze, and apply the appropriate dilution factor.
14. Measure peak area or peak height.

CALCULATIONS:

15. Determine the mass, µg (corrected for DE), of analyte found on the sample front (W_f) and back (W_b) sorbent sections, and in the average media blank front (B_f) and back (B_b) sorbent sections.
16. Calculate concentration of *p*-chlorophenol in the air volume sampled, V (L):

$$C = \frac{W_f + W_b - B_f - B_b}{V}, mg/m^3$$

EVALUATION OF METHOD:

The overall method was evaluated by collecting 3-L samples of test atmospheres containing *p*-chlorophenol in the range of 0.91 - 23.4 mg/m^3 at 29 °C and a relative humidity of greater than 80%. The amounts collected ranged from 2.6 - 64 µg per 150-mg bed of silica gel. The breakthrough volume of the sorbent tube was found to be approximately 60 L with a sampling rate of 0.2 L/min at a *p*-chlorophenol concentration of about 70 mg/m^3, a sampling temperature of 43 °C, and a relative humidity of greater than 80%. Samples of *p*-chlorophenol on silica gel were found to be stable at 25 °C for 7 days and for 29 days if stored at 0 °C after the seventh day. Silica gel gave an average desorption efficiency of 96% with a $\bar{S}_r$ 2.4% for loadings of 2.54 - 48.0 µg of *p*-chlorophenol on 150-mg beds of sorbent material.

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FORMALDEHYDE 2016

$H_2C=O$ MW: 30.03 CAS: 50-00-0 RTECS: LP8925000

METHOD: 2016, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 January 1998
Issue 3: 25 February 2016

OSHA: 0.75 ppm; 2 ppm STEL
NIOSH: 0.016 ppm; C 0.1 ppm; carcinogen
(1 ppm = 1.23 mg/m^3 @ NTP)

PROPERTIES: Gas; BP -19.5 °C; specific gravity 1.067 (air = 1); explosive range 7 to 73% (v/v) in air

SYNONYMS: methanal; formalin (aqueous 30 to 60% w/v formaldehyde); methylene oxide

SAMPLING

SAMPLER: CARTRIDGE (Cartridge containing silica gel coated with 2,4-dinitrophenylhydrazine)

FLOW RATE: 0.03 to 1.5 L/min

VOL-MIN: 1 L @ 0.25 mg/m^3
-MAX: 15 L @ 2.5 mg/m^3

SHIPMENT: Place caps onto cartridge. Ship on ice.

SAMPLE STABILITY: 34 days @ 5 °C [1]

BLANKS: 2 to 10 field blanks per set; 6 to 10 media blanks per set

ACCURACY

RANGE STUDIED: 0.025 to 2.45 mg/m^3 (22-L samples) [2]

BIAS: +4.4%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.057 [1, 2]

ACCURACY: ±19.0%

MEASUREMENT

TECHNIQUE: HPLC, UV DETECTION

ANALYTE: 2,4-dinitrophenylhydrazone of formaldehyde

EXTRACTION: Elution with 10 mL of carbonyl-free acetonitrile

INJECTION VOLUME: 20 µL

MOBILE PHASE: 45% acetonitrile/55% water (v/v), 1.3 mL/min

COLUMN: 3.9 x 150-mm, stainless steel, packed with 5-µm C18

DETECTOR: UV @ 360 nm

CALIBRATION: Samplers fortified with standard solutions of formaldehyde in water

RANGE: 0.23 to 37 µg per sample [1, 2]

ESTIMATED LOD: 0.07 µg/sample [1]

PRECISION ($\bar{S}_r$): 0.032 @ 1.0 to 20.0 µg/sample [1]

APPLICABILITY: The working range is 0.015 to 2.5 mg/m^3 (0.012 to 2.0 ppm) for a 15-L sample. This method can be used for the determination of formaldehyde for both STEL and TWA exposures [1, 2].

INTERFERENCES: Ozone has been observed to consume the 2,4-dinitrophenylhydrazine (2,4-DNPH) reagent and to degrade the formaldehyde derivative [3]. Ketones and other aldehydes can react with 2,4-DNPH; the derivatives produced, however, are separated chromatographically from the formaldehyde derivative.

OTHER METHODS: NIOSH methods 2541 [4] and 3500 [5] and OSHA method 52 [6] are other methods for determination of formaldehyde in air. NIOSH method 5700 employs 2,4-DNPH and HPLC for determination of formaldehyde on textile or wood dust [7]. A journal method employs the same procedure for formaldehyde in automobile exhaust [8].

REAGENTS:

1. Formaldehyde stock solution,* aqueous, standardized, 1 mg/mL (see APPENDIX A). Alternatively, standardized formaldehyde solution, aqueous, 4 m g/mL (commercially available).
2. Acetonitrile,* distilled in glass, low carbonyl content.**
3. Water, deionized and distilled.
4. Sulfuric acid, 0.02 N (pH standardization procedure) or 0.1 N (colorimetric procedure).
5. Sodium hydroxide, 0.01 N.
6. Sodium sulfite (Na_2SO_3), 1.13 M (pH procedure) or 0.1 M (colorimetric procedure). Prepare fresh immediately before use.
7. Thymophthalein indicator solution, 0.04% (w/v) in 50:50 ethanol:water.

*See SPECIAL PRECAUTIONS.

**Carbonyl content of acetonitrile can be determined by passing 10 mL of the solvent through a cartridge of DNPH-coated silica gel and analyzing by HPLC. Formaldehyde content should be below the LOD.

EQUIPMENT:

1. Sampler: Plastic holder containing 0.35 g of 150-250 µm (60-100 mesh) silica gel coated with 1.0 mg of acidified 2,4-dinitrophenylhydrazine. Pressure drop across sampler should be less than 28 inches of water (7 kPa) at 1.5 L/min. Samplers are commercially available. (See APPENDIX B for additional information.)
2. Personal sampling pump, 0 .03 to 1 .5 L/min with flexible connecting tubing.
3. Vials, 4-mL, glass with PTFE-lined rubber septa caps.
4. Vials, 20-mL, glass.
   NOTE: Do not use vials with "polycone" liners (sources of high formaldehyde blanks) [5, 9].
5. Liquid chromatograph with UV detector, recorder, integrator, and column (page 2016-1).
6. Syringes, 100-µL, 500-µL and 10-mL.
7. Volumetric flasks, 10-mL, 25-mL, and 1-L.
8. Burets, 50-mL.
9. pH meter.
10. Magnetic stirrer.
11. Beaker, 50-mL.
12. Flask, Erlenmeyer, 250-mL.
13. Ozone scrubber (optional).
14. Aluminum foil or black electrical tape (optional).

SPECIAL PRECAUTIONS: Formaldehyde is a suspect carcinogen and a proven human sensitizer; it should be handled in a fume hood [10-12]. Acetonitrile is toxic and is a fire hazard (flash point = 12.8 °C).

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler (and ozone scrubber, if used) in line.
2. Open sampler packet and remove end caps.
3. Attach sampler to the sampling pump with flexible tubing. Bi-directional samplers can be connected at either end.
   NOTE: The sampler does not have a backup section for determination of breakthrough. If high concentrations of aldehydes and ketones are anticipated, connect two samplers in series. The back pressure of the sampling train will be higher and a lower flow rate may be required.
4. Sample 1 to 15 L of air at 0.03 to 1.5 L/min.
   NOTE: To protect from intense light, such as bright sunlight, the sampler can be wrapped with aluminum foil or electrical tape.
5. Place end caps onto the sampler and seal sampler in an envelope. Protect samples from heat.
6. Ship samples on ice (0 °C).

SAMPLE PREPARATION:

NOTE: Check acetonitrile for formaldehyde content by elution and analysis of a blank cartridge; the formaldehyde level should be below the detection limit. Since background levels of formaldehyde on the samplers may change during storage, compare samples with sampler blanks from the same lot. Samples and blanks should be stored under the same conditions.

7. Elute the formaldehyde derivative from the cartridge samplers with 10-mL quantities of acetonitrile.
   a. Collect effluent from each sampler in a 10-mL volumetric flask.
   b. Add acetonitrile to the mark for each sampler.
      NOTE: The silica gel bed of the sampler will retain approximately 0.5 mL of the original 10 mL.

CALIBRATION AND QUALITY CONTROL:

8. Calibrate daily with at least six media working standards over the range of interest.
   a. Prepare a series of aqueous formaldehyde solutions for the fortification of samplers. Suggested concentrations include 1, 4, and 20 µg/mL. See APPENDIX A for standardization of formaldehyde in water.
   b. Connect the outlet of a cartridge sampler to a personal sampling pump with flexible tubing. Turn on the pump and make sure there is a flow of air through the sampler.
   c. Load a 100-µL syringe with a selected volume of aqueous formaldehyde solution in the range of 30 to 90 µL. Suggested quantities of formaldehyde for spiking include 0.04, 0.10, 0.20, 0.30, 0.40, 0.80, 1.0 and 2.0 µg/sample.
   d. Place the tip of the syringe needle against the frit in the inlet of the sampler and eject the formaldehyde solution.
   e. Prepare the media working standard (steps 7a and 7b).
   f. Prepare additional working standards (steps 8b through 8e).
   g. Transfer 3-mL aliquots of working standards to 4-mL vials, and analyze (steps 10, 12 and 13).
   h. Prepare calibration graph, peak area or peak height vs. µg formaldehyde per sample.
9. Fortify and analyze three quality control spikes and three analyst spikes to ensure that calibration graph is in control.

MEASUREMENT:

10. Set liquid chromatograph according to manufacturer's recommendations and to conditions given on page 2016-1.
11. Transfer a 3-mL aliquot of the sample solution from step 7 to a 4-mL vial. Cap the vial.
12. Inject a 20-µL sample aliquot.
13. Measure peak area or peak height.
    NOTE 1: If sample peak is larger than the largest standard peak, dilute an aliquot of the remaining sample solution, reanalyze, and apply appropriate dilution factor in the calculations.
    NOTE 2: To ensure validity of the samples, identify those samples which contain more than 37 µg of formaldehyde. The capacity of the samplers before breakthrough may have been exceeded for these samples, and collection of smaller samples would be warranted.
    NOTE 3: The size of the 2,4-DNPH peak should be about 2.7 times the size of the formaldehyde-DNPH peak or larger. Otherwise, breakthrough from the sampler may have occurred.

CALCULATIONS:

14. Determine mass, µg, of formaldehyde, W, found in the sample and the average media blank, B, from the calibration graph.

15. Calculate concentration, C, of formaldehyde in the air volume sampled, V (L).

$$C = \frac{W - B}{V}, mg/m^3$$

NOTE: µg/L ≙ mg/m^3

EVALUATION OF METHOD:

Issue 1

This method was originally evaluated with Waters Sep-Pak XPoSure Aldehyde samplers using data produced at NIOSH and at Waters Corporation [2]. Test atmospheres of formaldehyde were generated at Waters Corp. [2]. Overall measurement precision, $\hat{S}_{rT}$, was 0.057 based on NIOSH guidelines [13] including a 5% pump error factor and estimated bias of +4.4%. Sample storage stability was evaluated over the range of 0.5 to 55 µg formaldehyde/sample. Losses for Waters samplers were 4 to 8% when stored up to 14 days at 4 °C. An additional study with Waters samplers found that losses were 5% or less after 4 days of storage at ambient temperature. All calibration standards used at Waters Corporation were liquid standard solutions of formaldehyde-DNPH derivative in acetonitrile [2, 14].

The capacity of DNPH-coated silica gel samplers was found to vary with relative humidity (RH) in addition to concentration of formaldehyde. At a formaldehyde concentration of 1.2 m g/m^3 and at 5% breakthrough, the Waters sampler had a capacity at <10% RH of 55 µg, and at >85% RH a capacity of 77 µg. At 2.4 mg/m^3 and <10% RH, the 5% breakthrough capacity of the Waters sampler was 59 µg of formaldehyde. At 2.6 mg/m^3 and >85% RH, the 5% breakthrough capacity was 106 µg. Thus, the smallest capacity at 5% breakthrough was 55 µg of formaldehyde; the upper limit of the range of the method is two thirds of 55 µg, or 37 µg. Capacity information for the Waters sampler is applicable to the Supelco sampler because (a) the Waters and Supelco samplers contain 0.9 and 1 mg of DNPH, respectively, and (b) each sampler contains 350 mg of silica gel.

Issue 2

In subsequent work on this method, additional formaldehyde samplers were evaluated, Supelco S10 LpDNPH cartridges and SKC, Inc. Aldehyde samplers (DNPH-coated silica gel tubes No.226-119) [1]. The sorbent beds of Supelco and Waters cartridges and front sections of SKC samplers were treated with acetonitrile. Formaldehyde was not detected on any blank sampler (LOD = 0.01 µg/mL). The SKC sampler for aldehydes may be used for formaldehyde with modifications of this method (See APPENDIX B). However, evaluation of the SKC sampler at NIOSH has been limited.

Supelco samplers were fortified with known quantities of free formaldehyde in water, and calibration was performed with media standards prepared from Supelco samplers fortified with known quantities of free formaldehyde in water; average recoveries ranged from 96.3% to 99.3% for five levels at 1.00 to 20 µg of formaldehyde per sampler (pooled $\overline{S_r}$ = 0.0316; n = 6 at each level).

In a storage study, six Supelco samplers were fortified with 4-µg quantities of free formaldehyde in water. Samplers were stored 34 days at 5 °C in the dark; the average recovery based on media standards was 99% ($\overline{S_r}$ = 0.014).

Eight media standards were prepared by fortification of Supelco samplers with solutions of free formaldehyde in water. The solutions were drawn through the DNPH-coated silica gel beds with an air pump. The resulting LOD and LOQ were 0.07 and 0.23 µg/sample, respectively, according to a least squares calibration graph.

Standard solutions of formaldehyde-DNPH at 0.10 and 1.0 µg/mL (formaldehyde equivalent concentrations) were stored in airtight vials at 5 °C in the dark and were analyzed periodically. The standard solutions were found to be stable (with no detectable loss) for at least 10 weeks and at least 12 weeks, respectively.

It is suggested that the reader see the Backup Data Report for a comparison of media standards with liquid standards for calibration [1]. Air sampling for a 24-hour period can be performed with a single Supelco sampler. Thus, background levels at <1 ppb can be determined.

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APPENDIX A -PREPARATION AND STANDARDIZATION OF FORMALDEHYDE STOCK SOLUTION (ca. 1 mg/mL)

Preparation. Dilute 2.7 mL 37% aqueous formalin solution to 1 L with distilled, deionized water. This solution is stable for at least three months when stored at room temperature.

Standardization by pH Titration. Place 5.0 mL of freshly prepared 1.13 M sodium sulfite solution in a 50-mL beaker and stir magnetically. Adjust pH to between 8.5 and 10 with base or acid. Record the pH. Add 3.0 to 12.0 mL formaldehyde stock solution. The pH should now be greater than 11. Titrate the solution back to its original pH with 0.02 N sulfuric acid (1 mL acid = 0.600 mg formaldehyde; about 17 mL acid needed). If the endpoint pH is overrun, back-titrate to the endpoint with 0.01 N sodium hydroxide. Calculate the concentration, C_s (mg/mL), of the form aldehyde stock solution:

$$C_s = \frac{30.0(N_a V_a - N_b V_b)}{V_s}, mg/mL$$

Where:

30.0 = 30.0 g/equivalent of formaldehyde
N_a = normality of sulfuric acid (0.02 N)
V_a = volume of sulfuric acid (mL) used for titration
N_b = normality of NaOH (0.01 N)
V_b = volume of NaOH (mL) used for back-titration
V_s = volume of formaldehyde stock solution (mL)

Standardization by Colorimetric Titration. Place 50 mL of freshly prepared 0.1 M sodium sulfite and 3 drops of 0.04% thymophthalein indicator (w/v) in 50:50 ethanol:water into a 250-mL Erlenmeyer flask. Titrate the contents of the flask to a colorless endpoint with 0.1 N sulfuric acid (usually 1 or 2 drops is sufficient). The indicator is blue at pH values above the endpoint and is colorless at pH values below the endpoint. Transfer 3.0 to 12.0 mL of the formaldehyde solution to the same flask and titrate the mixture with 0.1 N sulfuric acid to a colorless endpoint. Calculate the concentration, C (mg/mL), of formaldehyde in solution.

$$C = \frac{30.0(N_a V_a)}{V_s}, mg/mL$$

Where:

30.0 = g/equivalent of formaldehyde
N_a = normality of sulfuric acid (0.1 N)
V_a = volume of sulfuric acid used for titration (mL)
V_s = volume of formaldehyde stock solution (mL)

NOTE: Sulfuric acid (0.1 N) is substituted for 0.1 N hydrochloric acid, which is specified in OSHA Method 52, in order to prevent possible formation of bis(chloromethyl)ether, a potent carcinogen, by reaction of formaldehyde with hydrochloric acid [12].

This colorimetric titration was adapted from OSHA Method 52 [5], which was based on the procedure of Walker [15].

APPENDIX B - USE OF SKC SAMPLER FOR FORMALDEHYDE

DNPH-coated silica gel tubes may be used for sampling formaldehyde with modifications of this method. These modifications include the following:

(a) The maximum recommended air volume should be less than 15 L at an air concentration of 2.5 mg/m^3 (indicated on page 2016-1), because the upper limit of the method for the SKC sampler is probably less than 37 µg.

(b) The procedure for recovery of analyte from the sorbent would be modified, i.e., placement of the sorbent sections in vials, addition of solvent, and possible use of an ultrasonic bath.

(c) A volume of solvent much less than 10 mL can be used for recovery. However, the minimum volume should be tested for adequate recovery.

(d) Consequences of using a much smaller volume of solvent for recovery include a lower LOD and LOQ, the need for a different range of calibration standards, and the need for a different range of fortification levels (step 8).

(e) The maximum volume of solution for fortification of the front sorbent bed must be less than 90 µL and should be determined (step 8).

Disclaimer: Mention of any company or product does not constitute endorsement by NIOSH. In addition, citations to websites external to NIOSH do not constitute NIOSH endorsement of the sponsoring organizations or their programs or products. Furthermore, NIOSH is not responsible for the content of these websites. All web addresses referenced in this document were accessible as of the publication date.

KETONES 2027

Formula: Table 1 MW: Table 1 CAS: Table 1 RTECS: Table 1

METHOD: 2027, Issue 1 **EVALUATION:** FULL **Issue 1:** 19 July 2016

OSHA: Table 2
NIOSH: Table 2
Other OELs: Refs [1,2}

PROPERTIES: Table 1

SYNONYMS: See individual compounds in Table 1

SAMPLING

SAMPLER: SOLID SORBENT TUBE (silica gel, 500 mg/1000 mg); min. of 2 field blanks per set

FLOW RATE: 0.05 – 0.1 l/min

VOL-MIN: 2 L
-MAX: 10 L

SHIPMENT: routine

SAMPLE STABILITY: Stable at least 28 days @ 20 °C [3,4]

ACCURACY

RANGE STUDIED: Table 3

BIAS: Negligible

OVERALL PRECISION ($\widehat{S}_{rT}$): Table 3

UNCERTAINTY: Table 3

MEASUREMENT

TECHNIQUE: gas chromatography, FID

ANALYTE: see Table 1

DESORPTION: ternary mixture of CH_2Cl_2/methanol/water (65:33:2)

INJECTION VOLUME: 1 µL

COLUMNS (IN PARALLEL): 60 m low-polarity fused silica, ID 0.25 mm and film thickness 0.25 µm; and 60 m high-polarity polyethylene glycol, ID 0.25 mm and film thickness 0.25 µm.

TEMPERATURE:
INJECTION: 250 °C
DETECTOR: 250 °C
COLUMN: 50 °C (11 min) to 150 °C (4 °C/min)

CALIBRATION: solution of analytes in desorption solvent

RANGE: Table 3

ESTIMATED LOD: Table 3

PRECISION ($\bar{S}_r$): Table 3

APPLICABILITY: 2-2400 mg/m^3 for air sample vol. up to 10 L.

INTERFERENCES: Organic compounds with similar retention times as the analytes of interest may interfere.

OTHER METHODS: NIOSH 2553 and 2555 [5] are partially validated methods for the determination of ketones using CS_2 for desorption. OSHA methods based on sorbent tube sampling, solvent desorption and GC/FID analysis have been promulgated for several ketones [6].

REAGENTS:

1. Acetone, >99.8%, analytical grade.
2. 2-Butanone, >99.8%, analytical grade.
3. Cyclohexanone, >99.5%, analytical grade.
4. Cyclopentanone, >99.0% purity.
5. 2-Hexanone, >98 % purity.
6. 4-Methyl -2-pentanone, >99.0%, analytical grade.
7. 2,6-Dimethyl-4-heptanone, ≥99%, analytical grade.*
8. Methanol, >99.9 %, analytical grade.
9. Dichloromethane, analytical grade.
10. Water, ultrapure, ≥18.2 MΩ-cm resistivity.
11. 2-Methylheptane, chromatographic quality.
12. n-Undecane, chromatographic quality.
13. Air, prepurified and filtered.
14. Hydrogen, prepurified and filtered.
15. Helium, prepurified and filtered.
16. Nitrogen, prepurified and filtered.
17. Internal standard solution: Mix 500 µL of n-undecane and 500 µL 2-methylheptane.
18. Ternary mixture: Mix 650 mL dichloromethane, 330 mL methanol and 20 mL water in a 1000-mL- volumetric flask.

    *NOTE: Each new bottle must be analyzed immediately after opening to accurately measure the concentration.

EQUIPMENT

1. Sampler: glass tube, length 125 mm, 7-mm OD, 5-mm ID, flame sealed ends, containing two sections of silica gel (front 500 mg, back 1000 mg) separated by a 2-mm ceramic plug. The ceramic plug is in front and a silylated glass wool plug follows the back section. Tubes are commercially available.
2. Personal sampling pump capable of producing flow rates between 0.05 to 0.1 L/min, with flexible connecting tubing.
3. Gas chromatograph, equipped with split injector (capillary flow split), two separation columns with separate FIDs, and data processing unit.
4. Fused silica capillary columns (for parallel separation): 60 m low-polarity fused silica, 0.25 mm ID and film thickness 0.25 µm. 60 m high-polarity polyethylene glycol, 0.25 mm ID and film thickness 0.25 µm.
5. Vessels, 15-mL, glass, with screw caps and PTFE septum.
6. Volumetric flasks, 5, 50 and 1000 mL.
7. Syringes, glass, 10 to 500 µL.
8. Pipettes, glass, 5 and 10 mL.
9. Bottles, polyethylene, 100 mL.
10. Syringes, polypropylene, 2 mL.
11. Syringe filter cartridges, with 0.45-µm pore size polytetrafluoroethylene (PTFE) membrane filters.
12. Micro-syringes, 50 µL, with 60 mm x 0.6 mm needles.
13. Auto-sampler vials, with PTFE septum, 1.5 mL capacity.

SPECIAL PRECAUTIONS: Analytes should be handled in a fume hood. Wear protective clothing and eyewear. Dichloromethane is a potential occupational carcinogen [12].

SAMPLING, SAMPLE TRANSPORT AND STORAGE

1. Calibrate each personal sampling pump with a representative sampler in the line.
2. Break the ends of the sampler immediately before sampling. Attach sampler to the personal sampling pump with flexible tubing.
3. Sample at an accurate known flow rate between 0.05 and 0.1 L/min for a total sample size of not more than 10 L.
4. Cap the samplers with plastic (not rubber) caps and pack securely for shipment.
5. Analyze samples within 28 days of receipt.

SAMPLE PREPARATION

6. Place the entire contents of the sorbent tube in a 15-mL screw-cap-vessel.
7. Add 5 mL ternary mixture and securely cap the vessel immediately.
8. Allow to stand at least 18 hours with occasional agitation.
9. Add 2.5 µl of internal standard solution.
10. Take sample solution with a 2-ml-polypropylene syringe and filter through a PTFE filter into an auto sampler vial.

CALIBRATION AND QUALITY CONTROL

11. Calibrate with at least six standards for each substance in the range given in Table 3.
    a. Place the contents of a sorbent tube in a 15-mL screw-cap-vessel and add 5 mL ternary mixture solvent.
    b. Add known amount of analyte.
    c. Store at room temperature for 18 hours and then add 2.5 µL of internal standard solution. Note: Internal standards are used to aid in identification of retention times of unknowns.
    d. Analyze and prepare a calibration graph for the two columns separately (peak areas of analyte and internal standard (nonpolar column:2-methylheptane; polar column: n-undecane) vs concentration).
12. Prepare each day at least three quality control solutions in the same manner and range and analyze together with samples and blanks.
13. Determine desorption efficiency (DE) at least once for each batch of sorbent used for sampling in the calibration range.
    a. Prepare three tubes at each of five levels plus three media blanks.
    b. Inject a known amount of analyte solution directly onto the front sorbent section while drawing purified air through the tube.
    c. Draw approximately 10 L air through the sorbent tube, then cap the ends of each tube and allow to stand overnight.
    d. Desorb (steps 6 to 9) and analyze together with quality control samples and blanks (steps 14 to 15).
14. Analyze a minimum of three quality control spikes and three analyst spikes to insure that the calibration graph and the DE graph are in control.

MEASUREMENT

15. Set gas chromatograph parameters to manufacturer's recommendations and to conditions give on Page 1. Inject a 1-µL sample aliquot into the gas chromatograph.
    NOTE: If the peak area exceeds the linear calibration range, dilute with desorption solvent, reanalyze and apply the appropriate dilution factor in calculations.
16. Measure analyte peak areas at applicable retention times (Table 4).

CALCULATIONS:

17. Calculate the mass concentration of each analyte, C (mg/m^3), in the air volume sampled, V (L):

$$C = \frac{(C_1 \cdot V_1 \cdot F_d) - (C_0 \cdot V_0)}{V \cdot \eta}$$

where:

C_0 = mean concentration, in mg/L, of analyte in the field blank test solutions;

C_1 = concentration, in mg/L, of analyte in the sample test solution;

V = volume, in liters, of the air sample;

V_0 = volume, in mL, of the field blank test solutions;

V_1 = volume, in mL, of the sample test solutions;

F_d = dilution factor for each sample test solution;

η = desorption efficiency.

EVALUATION OF METHOD:

The method recovery, at levels from the LOQ to at least 2 times the REL, was determined for each analyte by carrying out sampling and analytical experiments at a dynamic test gas facility [3,4]. Experiments were conducted at four concentration levels of each analyte and for relative humidities of 20%, 50% and 80% at 20 °C. All analytes exhibited method recovery >95 % at the levels evaluated (see Table 3). At low relative humidity (<30%) the recoveries of cyclohexanone, cyclopentanone and 2-hexanone were reduced without water in the extraction solution. Use of a small content of water (2%) during extraction avoids losses based on low humidity during sampling. Each analyte, at levels below and above the REL, was evaluated for its storage stability [3,4]. The samples were prepared by sampling at a dynamic test gas device at a relative humidity of 50% (20 °C). The samples were then stored at room temperature for four weeks. All analytes demonstrated acceptable recoveries (>90%) after 28 days of storage [3]. The performance of the method was separately verified in independent laboratories [4,13].

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METHOD WRITTEN BY:

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Table 1. Synonyms, Formulae, Molecular weights, Properties, CAS#, RTECS

Compound/ synonyms CAS# RTECS	Empirical formula	Molecular weight	Boiling point[a] (°C)	Melting point[a] (°C)	Vapor pressure @ 20°C (kPa)[a]	Vapor pressure @ 20°C (mm Hg)[a]	Density @ 20 °C[a] (g/mL)
Acetone / 2-Propanone 67-64-1 AL3150000	C_3H_6O	58.08	56.2	-95	24.6	184	0.79
2-Butanone Methylethyl ketone 78-93-3 EL6475000	C_4H_8O	72.11	79.6	-86	10.5	78.8	0.81
Cyclohexanone / Cyclohexyl ketone 108-94-1 GW1050000	$C_6H_{10}O$	98.14	155.6	-26	0.455	3.41	0.95
Cyclopentanone / Ketocyclopentane 120-92-3 GY4725000	C_5H_8O	84.12	130.6	-58.2	1.14	8.55	0.95
2-Hexanone / Butyl methyl ketone 591-78-6 MP1400000	$C_6H_{12}O$	100.16	127.2	-56	1.28	9.60	0.81
4-Methyl-2-pentanone / MIBK/Methyl isobutyl ketone 108-10-1 SA9275000	$C_6H_{12}O$	100.16	116.8	-80.3	1.88	14.1	0.80
2,6-Dimethyl-4-heptanone/ Diisobutyl ketone 108-83-8 MJ5775000	$C_9H_{18}O$	142.24	168	-46	0.23[b]	1.7[b]	0.81

[a] Physical and chemical property data from GESTIS substance database, except where noted otherwise [7]

[b] Vapor pressure for 2,6-dimethyl-4-heptanone [8]

Table 2. Occupational exposure limits, ppm [9]

Substance	OSHA PELs	NIOSH RELs		
	TWA	TWA	STEL	mg/m³ per ppm
Acetone	1000	250		2.41
2-Butanone	200	200	300	2.95
Cyclohexanone	50	25		4.08
Cyclopentanone				3.50
2-Hexanone	100	1		4.16
4-Methyl-2-pentanone	100	50	75	4.16
2,6-Dimethyl4-heptanone	50	25		5.91

Table 3. Measurement range, precision, uncertainty and recovery (N=6)

Substance	LOD (mg/sample)	LOQ (mg/sample)	Measurement Range (mg/sample)	Precision (S_r)	U^a (%)	Mean Recovery (DE)
Acetone	0.006	0.02	0.02 – 26	0.0083-0.024	11 – 12	0.97
2-Butanone	0.006	0.02	0.02 – 14	0.0078-0.024	11 – 12	0.98
Cyclohexanone	0.006	0.02	0.02 – 12	0.010-0.022	12 – 13	0.97
Cyclopentanone	0.006	0.02	0.02 – 2	0.008-0.023	11 – 12	0.95
2-Hexanone	0.006	0.02	0.02 – 0.47	0.018-0.022	11 – 12	0.98
4-Methyl2-pentanone	0.006	0.02	0.02 – 2	0.011-0.023	11 – 12	0.99
2,6-Dimethyl-4-heptanone	0.005	0.02	0.02 – 5	0.006-0.023	11 – 12	1.01

[a] Expanded uncertainty calculated in accordance with EN 482 [10] and EN 1076 [11]

Table 4. Approximate retention times on polar and nonpolar separation columns

Substance	Approximate retention time non-polar column (min)	Approximate retention time polar column (min)
Acetone	6.5	7.1
2-Butanone	9.2	[a)]
Cyclohexanone	25.5	25.9
Cyclopentanone	20.3	21.2
2-Hexanone	20.0	17.3
4-Methyl-2-pentanone	17.2	13.8
2,6-Dimethyl4-heptanone	28.4	22.0

[a)] The retention time of butanone is equal to that of the solvent on the polar column.

ANISIDINE

CH_3OC_6H MW: 123.16 CAS: (*o*-) 90-04-0 (*p*-) 104-94-9 RTECS: (*o*-) BZ5410000 (*p*-) BZ5450000

METHOD: 2514, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 May 1985 **Issue 3:** 26 February 2016

OSHA: 0.5 mg/m³ (skin)
NIOSH: 0.5 mg/m³ (skin); *o*-isomer suspect carcinogen

PROPERTIES: *o*-isomer: liquid; d 1.092 g/mL @ 15 °C; BP 225 °C; MP 5 °C; VP 0.1 mm Hg @ 27 °C. *p*-isomer: solid; MP 57 °C; BP 246 °C

SYNONYMS: *o*-isomer: 2-aminoanisole; 2-methoxybenzenamine; *o*-methoxyaniline; *p*-isomer: 4-aminoanisole; 4-methoxybenzenamine; *p*-methoxyaniline

SAMPLING

SAMPLER: SOLID SORBENT TUBE (XAD-2, 150 mg/75 mg)

FLOW RATE: 0.05 – 1.0 L/min

VOL-MIN: 24 L
MAX: 320 L

SHIPMENT: routine

SAMPLE STABILITY: at least 1 week @ 25 °C [1]

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 0.13 to 0.58 mg/m³ [1] (225-L samples)

BIAS: 0.12%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.068 [1]

ACCURACY: ± 13.3%

MEASUREMENT

TECHNIQUE: HPLC, UV DETECTION

ANALYTE: *o*-anisidine and *p*-anisidine

DESORPTION: 5 mL methanol; stand 15 min

INJECTION VOLUME: 10 µL

MOBILE PHASE: 5% acetonitrile/65% water @ 1.2 mL/min; ambient temperature

COLUMN: 50 cm x 2-mm ID stainless steel packed with C18

DETECTOR: UV absorption @ 254 nm

CALIBRATION: analytes dissolved in methanol

RANGE: 12 to 360 µg per sample (each isomer) [2]

ESTIMATED LOD: 0.35 µg per sample [2]

PRECISION ($\bar{S}_r$): 0.029 @ 30 to 240 µg per sample [1] HPLC/UV

APPLICABILITY: The working range is 0.06 to 0.8 mg/m³ (0.012 to 0.16 ppm) for a 200-L air sample

INTERFERENCES: None identified

OTHER METHODS: This revises Method S163 [2]. This method replaces P&CAM 168 [3] because XAD-2 has a much greater capacity than silica gel for *o*-anisidine at high humidity [1].

REAGENTS:

1. *p*-Anisidine, reagent grade.*
2. *o*-Anisidine, reagent grade.*
3. Methanol, HPLC grade.*
4. Acetonitrile, HPLC grade.*
5. Water, distilled, deionized.
6. Methylene chloride.
7. Calibration stock solution, 15.0 mg/mL *p*-anisidine and 15.3 mg/mL *o*-anisidine. Dissolve 750 mg *p*-anisidine and 700 µL *o*-anisidine in methanol to make 50 mL solution.
8. HPLC mobile phase: 35% acetonitrile/65% water. Filter (5-µm PTFE) and degas prior to use.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: glass tube, 7-cm long, 8-mm OD, 6-mm ID, with plastic caps, containing two sections of 20/50 mesh XAD-2 (150 mg front and 75 mg back) separated and held in place by plugs of silylated glass wool. Pressure drop across the tube must be <3.4 kPa (2.5 cm Hg) at 1 L/min airflow.
2. Personal sampling pump, 0.5 to 1 L/min, with flexible connecting tubing.
3. HPLC with UV absorption detector at 254 nm, integrator and column (page 2514-1).
4. Vials, 20-mL, scintillation.
5. Pipet, 5-mL.
6. Syringes, 10-µL, readable to 0.1 µL.
7. Volumetric flasks, 5- and 50-mL.

SPECIAL PRECAUTIONS: Anisidine can irritate the skin. Methanol and anisidine can be absorbed through the skin. Avoid inhalation of vapors of these compounds and of acetonitrile [4].

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Uncap the sampler immediately before sampling. Attach sampler to personal sampling pump with flexible tubing.
3. Sample at an accurately known flow rate between 0.5 and 1.0 L/min for a total sample size of 24 to 320 L. Do not sample at less than 0.5 L/min.
4. Cap the samplers. Pack securely for shipment.

SAMPLE PREPARATION:

5. Place the front and back sections of the sampler in separate vials. Discard the glass wool plugs.
6. Add 5.0 mL methanol to each vial. Cap each vial and swirl vigorously.
7. Allow to stand for 15 min. Analyze within one day.

CALIBRATION AND QUALITY CONTROL:

8. Calibrate daily with at least six working standards over the range 0.4 to 360 µg anisidine per sample for each isomer.
   a. Add a known volume of calibration stock solution, or a dilution thereof in methanol, to a 5-mL volumetric flask and dilute to the mark with methanol.
   b. Analyze together with samples and blanks (steps 11 and 12).
   c. Prepare calibration graph (peak area vs. µg analyte) for each isomer.
9. Determine desorption efficiency (DE) at least once for each lot of XAD-2 used for sampling in the concentration range of interest. Prepare four tubes at each of five levels.
   a. Remove and discard the back sorbent section of a media blank sampler.
   b. Inject a known amount (e.g., 1 to 20 µL) of calibration stock solution, or a dilution thereof in methanol, directly onto the front section with a microliter syringe.
   c. Cap the tube. Allow to stand overnight.

d. Desorb (steps 5 through 7) and analyze with working standards (steps 11 and 12).
e. Prepare graphs of DE vs. µg isomer recovered.

10. Analyze three quality control blind spikes and three analyst spikes with each subsequent set from the same lot to ensure that the calibration graph and DE graph are in control.

MEASUREMENT:

11. Set HPLC to conditions given on page 2514-1. Inject sample aliquot.
NOTE: Sensitivity is ca. 0.083 absorbance unit/mg of either isomer in a 10-mL injection volume with a 1-cm flow cell. Approximate retention times are 7.5 min for *p*-anisidine and 12 min for *o*-anisidine.
12. Measure peak area.

CALCULATIONS:

13. Determine the quantities (sum of quantities of the *o*-and the *p*-isomers corrected for DE), mg of analytes found in the sample front (W_f) and back (W_b) sorbent sections, and in the average media blank front (B_f) and back (B_b) sorbent sections.
NOTE: If $W_b > W_f/10$, report breakthrough and possible sample loss.
14. Calculate the sum of the concentrations, C, of the isomers in the air volume sampled, V (L):

$$C = \frac{W_f + W_b - B_f - B_b}{V}, mg/m^3$$

EVALUATION OF METHOD:

Method S163 was issued on February 16, 1979 [2], and was validated over the range 0.13 to 0.58 mg/m^3 for the *o*-isomer and 0.12 to 0.58 mg/m^3 for the *p*-isomer using 225-L air samples [1, 5]. The generation system was constructed so that samples were generated for both isomers at the same time. Concentrations were verified by an independent method using bubblers containing methanol and HPLC analysis [1]. The overall precision, $\hat{S}_{rT}$, for the combined sampling and measurement of both isomers was 0.068 with an average recovery of 100.7% for the *o*-isomer and 99.7% for the *p*-isomer [1], which represent non-significant biases for the isomers. A separate breakthrough test was conducted for each isomer with XAD-2. Samples were taken at ca. 1.0 L/min. *o*-Anisidine was generated at 1.03 mg/m^3 with a relative humidity of 81% at 21 °C. Breakthrough (3%) from 150 mg XAD-2 occurred after 236 min, but did not increase above this amount up to 479 min. *p*-Anisidine was generated at 1.04 mg/m^3 with a relative humidity of 82% at 20 °C. Breakthrough did not occur during the 361-min test. Samples containing both isomers were stored for one week at room temperature and found to be stable. Desorption efficiencies averaged 0.95 and 0.91 for *o*- and *p*-anisidine, respectively, in the range 30 to 240 µg per sample.

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METHOD REVISED BY:

Edward Slick, NIOSH; S163 originally validated under NIOSH Contract 210-76-0123.

METHYL BROMIDE 2520

CH_3Br MW: 94.94 CAS: 74-83-9 RTECS: PA4900000

METHOD: 2520, Issue 3 **EVALUATION: FULL** **Issue 1: 15 May 1985**
Issue 3: 20 January 2016

OSHA: C 20 ppm (skin)
NIOSH: Lowest feasible; carcinogen (1 ppm = 3.95 mg/m³ @ NTP)

PROPERTIES: Gas; d 1.73 g/mL @ 0 °C; BP 4 °C; VP 189.34 kPa (1420 mmHg) @ 20 °C

SYNONYMS: Monobromomethane; bromomethane

SAMPLING

SAMPLER: SOLID SORBENT TUBES (two petroleum charcoal tubes, 400 mg and 200 mg; drying tube, 9 g sodium sulfate, necessary at humidity >50%)

FLOW RATE: 0.01 L/min to 0.1 L/min

VOL-MIN: 1 L @ 5 ppm
-MAX: 5 L with drying tube, 1 L without drying tube [1]

SHIPMENT: Ship on dry ice at −10 °C [1]

SAMPLE STABILITY: Six d at −10 °C [1]

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 0.84 ppm to 32.0 ppm (5 L samples)

BIAS: −5.2%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.089

ACCURACY: ±19.4%

MEASUREMENT

TECHNIQUE: GAS CHROMATOGRAPHY, ATOMIC EMISSION DETECTION (GC-AED) monitoring bromine, carbon, and hydrogen channels

ANALYTE: Methyl bromide

DESORPTION: 400 mg tube: 3 mL methylene chloride; 200 mg tube: 2 mL methylene chloride

INJECTION: 1 µL

TEMPERATURE-INJECTOR: 250 °C
-TRANSFER LINE/ CAVITY BLOCK: 250 °C
-COLUMN: 30 °C, 3.5 min; 12 °C /min to 130 °C; hold 1 min

CARRIER GAS: Helium

COLUMN: US Pharmacopeia (USP) G2 capillary, 30 m × 0.32 mm ID, 1.0 µm film thickness; 1 m × 0.53 mm deactivated fused silica pre-column

CALIBRATION: Brominated compounds in methylene chloride

RANGE: 33.0 µg to 2687 µg bromine per sample

ESTIMATED LOD: 16.6 µg per sample [1]

PRECISION ($\bar{S}_r$): 0.066 [1]

APPLICABILITY: The working range is 0.84 ppm to 32.0 ppm (3.3 mg/m³ to 126 mg/m³) for a 5 L sample. Ceiling measurement samples may require dilution when analyzed.

INTERFERENCES: Water vapor interferes with collection at relative humidities (RH) >50%. To eliminate the interference, precede the sampling train with a drying tube, and limit the sample volume to 5 L. If drying tubes are not available, limit the sample volume to 1 L under humid conditions.

OTHER METHODS: This is NIOSH method 2520 [2] revised to account for humidity effects, as well as instability of standards and samples. Other researchers [3] have prepared methyl bromide standards gravimetrically and used GC-ECD for analysis. The gravimetric calibration procedure did not give consistent results when compared with the procedure used in this revision of NIOSH method 2520. GC-ECD with a US Pharmacopeia (USP) S3 capillary column may be an alternative technique to GC-AED if other bromine standards are used to confirm the concentration of methyl bromide standards.

REAGENTS:

1. Eluant: methylene chloride,* chromatographic grade.
2. Methyl bromide,* 99.5%.
3. Calibration stock solution: To 4 mL of methylene chloride, add 12 µL dibromomethane.
   NOTE: Other brominated compounds may be used if liquid at room temperature.
4. Desorption stock solution: Bubble methyl bromide gas slowly into chilled eluant. Determine the methyl bromide concentration by comparison with calibration standards.
5. Helium,* prepurified, 99.995%.
6. Oxygen,* ultra purified, as reagent gas for plasma, 207 kPa (30 psi).
7. Air, filtered.
8. Dry ice, flaked, for chilling solvent.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: petroleum charcoal sampling tubes; two glass tubes, each tube, 10 cm long, 8 mm OD, 6 mm ID, containing 20/40 mesh activated (600 °C) petroleum charcoal, first tube 400 mg, second tube 200 mg, held in place with silylated glass wool plugs; drying tube, glass, 9 g sodium sulfate. Tubes are connected in series with short pieces of plastic tubing. Pressure drop across sampler <3.4 kPa (25 mmHg) at 1.0 L/min airflow. Tubes are commercially available.
   NOTE: If RH ≥50%, precede sampling train with drying tube.
2. Personal sampling pump, 0.01 to 0.1 L/min, with flexible connecting tubing.
3. Gas chromatograph, atomic emission detector (helium plasma), integrator or computer, and column (page 2520-1).
4. Vials, 4 mL and 10 mL, glass, with PTFE-lined caps.
5. Syringe, gas-tight, 10 mL.
6. Microliter syringes, 10 µL, 50 µL, 100 µL, 250 µL, 500 µL for preparing standard solutions.
7. Pipettes, 2 mL, graduated in 0.1 mL increments.

SPECIAL PRECAUTIONS: Methylene chloride is a suspect carcinogen. Methyl bromide is a suspect carcinogen and is toxic by ingestion, inhalation, and skin absorption [4]. Users must be familiar with the proper use of flammable and nonflammable gases, cylinders, and regulators.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Break the ends of the sampling tubes immediately before sampling. Attach sampler to personal sampling pump with flexible tubing.
   NOTE: Place drying tube in front of the sorbent train.
3. Sample at an accurately known flow rate between 0.01 L/min and 0.1 L/min for a total sample size of 1.0 L to 5.0 L.
   NOTE: Limit sample volume to 1.0 L if RH ≥ 50% and no drying tube is used.
4. Separate the front and back tubes immediately after sampling. Cap the tubes. Pack securely in dry ice for shipment. Store at –10 °C until analysis.

SAMPLE PREPARATION:

5. Place the sorbent sections from each sampling tube in separate vials. Discard the glass wool plugs.
6. Add 3.0 mL chilled eluant (methylene chloride) to each 400 mg section, and 2.0 mL chilled eluant to each 200 mg section. Immediately cap each vial.
7. Allow to stand at least 30 min at room temperature with occasional agitation. Rechill before transferring to autosampler vials or diluting.
   NOTE: Because of the volatility of the analyte, it is suggested that any dilutions be prepared at the

time of transfer to autosampler vials. Dilutions can be stored in the freezer until determined that they are needed.

CALIBRATION AND QUALITY CONTROL:

8. Calibrate daily with at least six working standards over the range 0.14 µg to 272 µg methyl bromide per sample from calibration stock solution.
   NOTE: 0.085 µmol/µL bromine is equivalent to a methyl bromide concentration of 8.07 µg/µL.
   a. Add known aliquots (2.0 µL, 20 µL, 45 µL, and 120 µL) of calibration stock solution to methylene chloride in 10 mL vials with PTFE-lined caps. Take 1 mL of lowest standard and dilute to 10 mL with methylene chloride. Transfer standards to autosampler vials and immediately cap each vial.
   b. Analyze together with samples and blanks (steps 11 and 12).
   c. Prepare calibration graph (peak area vs. concentration).
9. Determine desorption efficiency (DE) at least once for each lot of charcoal used for sampling in the calibration range (step 8). Prepare three tubes at each of five levels plus three media blanks.
   a. Inject a known amount (1 µL to 10 µL) of methyl bromide desorption stock solution (concentration determined against other brominated compounds), or a serial dilution thereof, directly onto media blank samplers with a microliter syringe.
   b. Cap the tubes. Allow to stand overnight at 0 °C.
   c. Desorb (steps 5, 6, and 7) and analyze together with working standards (steps 11 and 12).
   d. Prepare a graph of DE vs. µg bromine recovered.
10. Analyze three quality control blind spikes and three analyst spikes to ensure that the calibration graph and DE graph are in control.

MEASUREMENT:

11. Set gas chromatograph-atomic emission detector to manufacturer's recommendations and to conditions given on page 2520-1. Inject sample aliquot manually using solvent flush technique or with autosampler.
    NOTE 1: Methyl bromide elutes before the methylene chloride solvent peak. Vent the solvent peak to avoid extinguishing the helium plasma. Vent time ranges from 3.2 min to 5.9 min; this may need to be adjusted for each system.
    NOTE 2: If peak area is above the linear range of the working standards, dilute with eluant, reanalyze, and apply the appropriate dilution factor in calculations.
12. Measure peak area.

CALCULATIONS:

13. Determine the mass, µg (corrected for DE) of methyl bromide found in the 400 mg sample tube (W_f) and 200 mg sample tube (W_b), and in the average media blanks for the 400 mg (B_f) and 200 mg (B_b) sorbent tubes.
    NOTE: If $W_b > W_f / 10$, report breakthrough and possible sample loss.
14. Calculate concentration, C, of methyl bromide in the air volume sampled, V (L):

$$C = \frac{W_f + W_b - B_f - B_b}{V}, \text{ µg/L or mg/m}^3.$$

EVALUATION OF METHOD:

NIOSH method 2520 for methyl bromide, issued in May 1985 [2], was based on NIOSH method S372 [5]. Issue 2 (dated 5/15/96) of NIOSH method 2520 was further revised to account for the effect of humidity and to address the instability of standards and samples [1]. The addition of a drying tube to the sampling train helped reduce the effects of >50% RH. The analytical technique was changed to GC

with atomic emission detection (GC-AED). The atomic emission detector monitors individual elements, in this case bromine, independent of the source compound. Calibration can be done with brominated compounds that are liquid at room temperature, thereby eliminating the need for methyl bromide standards. Methylene chloride replaced carbon disulfide as desorption solvent.

The revised NIOSH method 2520 (issued 5/15/96) for methyl bromide was evaluated at 7.8 mg/m^3, 20.0 mg/m^3, and 125.0 mg/m^3 (2 ppm, 5 ppm, and 32 ppm, respectively) [1]. Test atmospheres were generated by delivering methyl bromide gas from two diffusion tubes kept at −12 °C into an airstream flowing at 12 L/min. Humidity was added downstream when needed, and airflow passed through two mixing chambers before reaching a sampling manifold. The concentration was monitored with a total hydrocarbon analyzer and confirmed by calibrating against other brominated standards by GC-AED. Three compounds used as calibration standards (dibromomethane, 1-bromopropane, and 1-bromobutane) were chosen as closest in chemical structure to methyl bromide, although a compound-independent response was assumed [6]. A three-compound calibration was used during the development of the GC-AED analytical procedure. Since there was good agreement between the three compounds, the method was written with only one brominated standard, dibromomethane.

When challenged with methyl bromide at a calculated concentration of 27 ppm, the capacity of the sampler (a 400 mg petroleum charcoal tube plus a 200 mg petroleum charcoal tube) at 40% RH and 20 °C was 1386.5 µg regardless of flow rate (10.5 mL/min, 40 mL/min, or 100 mL/min). However, at 100% RH and 39 °C, the average capacity fell to 298.6 µg. With a 9 g sodium sulfate drying tube in line, the capacity was increased to 651.8 µg; concentration averaged 130 mg/m^3 (33 ppm). Even with a drying tube in line, severe breakthrough occurred at the 10 L sample volume (50% was found on the back tube). Without the use of a drying tube, a 1 L sample volume is recommended, based on a 170.6 µg capacity (1.6 L) found at the 40 mL/min rate multiplied by a 0.67 caution factor.

Recovery fell below 70% for sample loadings less than 58 µg when carbon disulfide was used for desorption (Figure 1). This would not allow accurate sampling at 7.8 mg/m^3 (2 ppm), the exposure level most frequently encountered. Therefore, alternate desorption solvents were tested. Desorption with methylene chloride improved recovery at the 15 µg level to 76.7%. However, sample stability still fell below 70% after storage for six days at −10 °C regardless of sample level. This stability limitation remains a concern and rapid sample analysis is required.

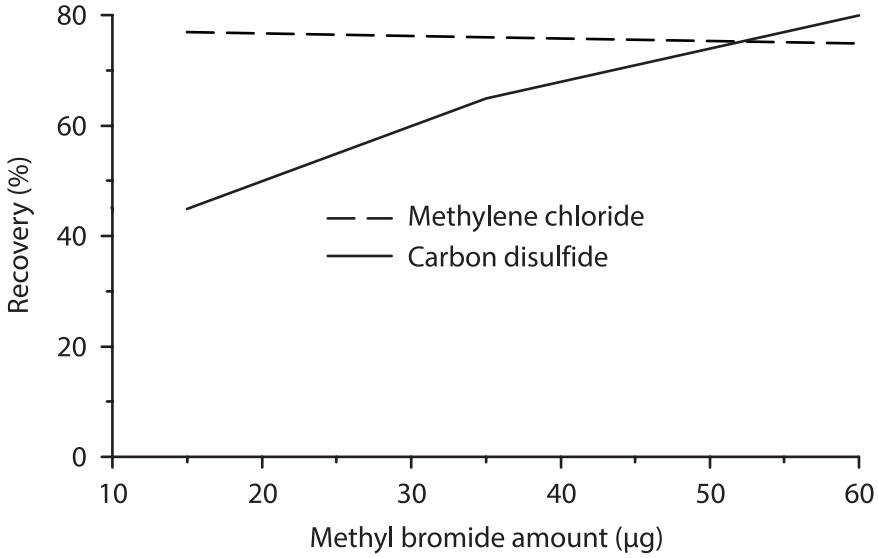

Figure 1. Comparison of desorption solvents.

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METHOD REVISED BY:

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GLUTARALDEHYDE 2531

$O=CH(CH_2)_3CH=O$ MW: 100.12 CAS: 111-30-8 RTECS: MA2450000

METHOD: 2531, Issue 3 **EVALUATION: FULL** **Issue 1: 15 May 1989**
Issue 3: 20 January 2016

OSHA: No PEL
NIOSH: C 0.2 ppm
(1 ppm = 4.09 mg/m³ @ NTP)

PROPERTIES: Oil; d 0.72 g/mL @ 20 °C; BP 188 °C; MP −14 °C; VP 2.2 kPa (17 mmHg) @ 20 °C

SYNONYMS: Glutaric dialdehyde; 1,5-pentanedial

SAMPLING

SAMPLER: SOLID SORBENT TUBE (10% 2-(hydroxymethyl)piperidine on XAD-2, 120 mg/60 mg)

FLOW RATE: 0.01 L/min to 0.08 L/min, or 0.2 L/min for 20 min

VOL-MIN: 4 L @ 0.2 ppm
-MAX: 39 L

SHIPMENT: Routine

SAMPLE STABILITY: At least 5 weeks @ 25 °C [1]

FIELD BLANKS: 2 to 10 field blanks per set

MEDIA BLANKS: 10 per set

ACCURACY

RANGE STUDIED: 0.8 mg/m³ to 9 mg/m³ [1] (22 L samples)

BIAS: 0.3%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.087 [1]

ACCURACY: ±17.4%

MEASUREMENT

TECHNIQUE: GAS CHROMATOGRAPHY, FID

ANALYTE: Oxazolidine derivative of glutaraldehyde

DESORPTION: 2 mL toluene; 60 min ultrasonic

INJECTION: 1 µL splitless; split vent time 30 s

TEMPERATURE-INJECTOR: 250 °C
-DETECTOR: 280 °C
-COLUMN: 1 min @ 70 °C; 20 °C/min; hold 2 min @ 290 °C

CARRIER GAS: Helium, 0.5 mL/min; makeup 2.9 mL/min

COLUMN: Capillary, 10 m × 0.25 mm, 5% phenyl, 95% methyl polysiloxane (US Pharmacopeia (USP) phase G27)

CALIBRATION: Standard glutaraldehyde solutions spiked on sorbent

RANGE: 3 µg to 180 µg per sample [1]

ESTIMATED LOD: 1 µg per sample [2]

PRECISION ($\bar{S}_r$): 0.093 [2] @ 5 µg to 50 µg per sample [1]

APPLICABILITY: The working range is 0.03 ppm to 2 ppm (0.14 mg/m³ to 8 mg/m³) for a 22 L air sample; the method is sensitive enough for ceiling determinations. The method is suitable for the simultaneous determination of furfural and glutaraldehyde.

INTERFERENCES: None have been observed.

OTHER METHODS: This is a new method. A wide-bore 10 m capillary column is an alternate chromatographic column.

REAGENTS:

1. Toluene,* chromatographic quality.
2. 2-(Hydroxymethyl)piperidine. Recrystallize several times from isooctane until there is one major peak (>95% of area) by GC analysis. Store in desiccator.
3. XAD-2 resin.
4. Glutaraldehyde,* 250 g/L solution in water.
5. Glutaraldehyde stock solution, 10 µg/µL (see Appendix A).
6. Glutaraldehyde oxazolidine (see Appendix B) stock solution, 2 mg/mL. Add 20 mg to toluene and dilute to 10 mL.
7. Sulfuric acid,* 0.01 mol/L.
8. Sodium hydroxide,* 0.01 mol/L.
9. Sodium sulfite, 1.13 mol/L. Dissolve 14.2 g reagent grade sodium sulfite in deionized, distilled water and dilute to 100 mL. Prepare fresh immediately before use.
10. Water, deionized, then distilled.
11. Hydrogen,* prepurified.
12. Air, filtered.
13. Helium,* prepurified.
14. Magnesium sulfate.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

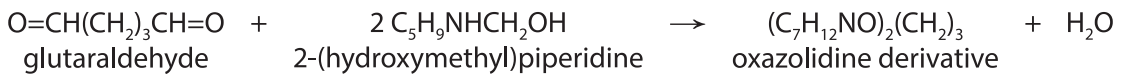
1. Sampler: resin-filled sampling tube; glass tube, 10 cm long, 6-mm OD, 4-mm ID, flame-sealed ends and plastic caps, containing two sections of 40/60 mesh 2-(hydroxymethyl)piperidine-coated XAD-2 (see Appendix C). Sorbent sections are retained and separated by small plugs of silanized glass wool. Pressure drop across the tube at 0.10 L/min airflow must be less than 0.76 kPa (5.7 mmHg). Tubes are commercially available.
2. Personal sampling pump, 0.01 L/min to 0.08 L/min, with flexible connecting tubing.
3. Gas chromatograph, flame ionization detector, integrator, and column (page 2531-1).
4. Ultrasonic bath.
5. Vials, glass, 4 mL, with septum and plastic screw caps.
6. Flasks, volumetric, 10 mL, 25 mL, and 50 mL.
7. Pipets, TD, 1 mL, 2 mL, and 10 mL with pipet bulb.
8. Pipets, disposable, 2 mL.
9. Syringes, 10 µL (readable to 0.1 µL), 25 µL, and 50 µL.
10. File.
11. Beakers, 50 mL.
12. pH meter.
13. Magnetic stirrer.
14. Burets, 50 mL.
15. Flasks, round-bottomed, 100 mL.
16. Soxhlet extraction apparatus.
17. Vacuum oven.
18. Distillation apparatus.

SPECIAL PRECAUTIONS: Glutaraldehyde can irritate the mucous membranes and act on the central nervous system [3]. Toluene is flammable. Sulfuric acid is highly corrosive and sodium hydroxide is caustic. All work with these compounds should be performed in a well-ventilated hood. Use proper protective clothing including gloves, safety glasses, and laboratory coat. Users must be familiar with the proper use of flammable and nonflammable gases, cylinders, and regulators.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Break ends of the sampler immediately before sampling. Attach sampler to personal sampling pump with flexible tubing.
3. Sample at an accurately know flow rate between 0.01 and 0.08 L/min for a total sample size of 4 L to 39 L. For ceiling determination, sample at 0.2 L/min for 20 min.

   NOTE: The aldehyde reacts with the 2-(hydroxymethyl)piperidine to form an oxazolidine derivative in the sorbent bed during sampling (see equation below). Sampling rate is limited by the speed of this reaction. Sampling rates above 0.1 L/min for extended periods may cause breakthrough owing to incomplete reaction, possibly invalidating the sample.



SAMPLE PREPARATION:

4. Score each sampler with a file in back of the back sorbent section.
5. Break sampler at score line. Remove and place back glass wool plug and back sorbent section in a vial.
6. Transfer front section with remaining glass wool plugs to a second vial.
7. Add 2.0 mL toluene to each vial. Screw cap tightly onto each vial.
8. Agitate vials in an ultrasonic bath for 60 min.
   NOTE: Desorption efficiency is affected by the amount of time that the vials are allowed to spend in the ultrasonic bath. A minimum of 60 min residence time in the ultrasonic bath is required to ensure adequate desorption.

CALIBRATION AND QUALITY CONTROL:

9. Prepare glutaraldehyde oxazolidine standard solutions.
   a. Add known amounts of glutaraldehyde oxazolidine stock solution (equivalent to the range of the samples) to toluene in 10 mL volumetric flasks and dilute to the mark.
   b. Analyze (steps 12 and 13) with samples and blanks for qualitative identification of derivative peaks.
10. Calibrate daily with at least five working standards covering the range of the samples.
    a. Weigh 120 mg portions of unused sorbent from media blanks into vials.
    b. Add aliquiots of glutaraldehyde stock solution or dilutions thereof. Cap vials and allow them to stand overnight at room temperature.
    c. Desorb (steps 7 and 8) and analyze (steps 12 and 13) with samples and blanks.
    d. Prepare calibration graph (combined peak area vs. µg glutaraldehyde).
       NOTE: Because the working standards are prepared on media blanks, no additional blank correction or desorption efficiency correction is necessary. Check desorption efficiency occasionally in the range of interest (see Appendix D).
11. Analyze three quality control blind spikes to ensure that the calibration graph is in control.

MEASUREMENT:

12. Set gas chromatograph to manufacturer's recommendations and to conditions given on page 2531-1. Inject 1 µL sample aliquot.
    NOTE: If the amount of oxazolidine in the aliquot exceeds the capacity of the column, dilute the sample with toluene and apply the appropriate dilution factor in calculations.
13. Measure total peak area of the two analyte peaks.
    NOTE: On the recommended column, the oxazolidine derivative gives two peaks, since the diastereoisomers are resolved; t_r for the glutaraldehyde derivative = 9.4 min and 9.7 min; t_r for 2-(hydroxymethyl)piperidine = 2.6 min for these conditions.

CALCULATIONS:

14. Determine the mass, µg, of glutaraldehyde found in the sample front (W_f) and back (W_b) sorbent sections.
    NOTE: If $W_b > W_f / 10$, report breakthrough and possible sample loss.
15. Calculate concentration, C, of glutaraldehyde in the air volume sampled, V (L):

$$C = \frac{W_f + W_b}{V}, \text{ µg/L or mg/m}^3.$$

EVALUATION OF METHOD:

Atmospheres were generated by injection of an aqueous solution of glutaraldehyde by syringe pump into a heated block injector and flash vaporization into a stream of air flowing at a fixed rate [1]. Relative humidity during generation was controlled at 80% ±5%. The generator and sampling manifold systems have been described previously [4]. Concentration of glutaraldehyde vapor was independently verified by the 2,4-dinitrophenylhydrazine procedure of Lipari and Swarin [5]. No bias with dynamically-generated atmospheres was observed with the method over the range 0.8 mg/m^3 to 8 mg/m^3 using 22 L air samples. Desorption efficiencies on statically-spiked samples averaged 87% in the ranges 5 µg to 50 µg per sample. Recovery averaged 1.10 with S_r = 0.043 for twelve tubes spiked with 67 µg glutaraldehyde [6].

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METHOD WRITTEN BY:

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APPENDIX

A. Preparation and Standardization of Glutaraldehyde Stock Solution (about 10 µg/µL)

Dilute 1 mL of 250 g/L aqueous glutaraldehyde to 25 mL with distilled, deionized water to make the glutaraldehyde stock solution. Put 10.0 mL of 1.13 mol/L sodium sulfite solution in a beaker and stir magnetically. Adjust pH to between 8.5 and 10 with base or acid. Record the pH. Add 1.0 mL glutaraldehyde stock solution. The pH should be about 12. Titrate the solution back to its original pH with 0.01 mol/L sulfuric acid. If the endpoint pH is overrun, back-titrate to the endpoint with 0.01 mol/L sodium hydroxide. Calculate the concentration, C_s, of the glutaraldehyde stock solution:

$$C_s = \frac{(C_a V_a - C_b V_b) \times 50.06}{V_s}, \text{ µg/µL},$$

where: 50.06 = MW of glutaraldehyde divided by 2,
C_a = concentration (mol/L) of sulfuric acid,
V_a = volume of sulfuric acid (mL) used for titration,
C_b = concentration (mol/L) of sodium hydroxide,
V_b = volume of sulfuric acid (mL) used for titration, and
V_s = volume of glutaraldehyde stock solution (1.0 mL).

B. Synthesis of Glutaraldehyde Oxazolidine

Place a solution of purified 2-(hydroxymethyl)piperidine (0.57 g, 5 mmol) in 10 mL of toluene in a 50 mL round-bottomed flask. Several 2 mL portions of toluene can be used to rinse residual 2-(hydroxymethyl) piperidine from the container used for weighing. Add magnesium sulfate (2.5 g) to the round-bottomed flask to dry the glutaraldehyde solution as it is added and to remove the water which forms during the reaction. Add a solution of 1 mL of 250 g/L aqueous glutaraldehyde (0.25 g, 2.5 mmol) in 10 mL of toluene to the 2-(hydroxymethyl)piperidine solution dropwise with stirring over 1 h. Stir the solution overnight, then filter to remove the magnesium sulfate. Remove the toluene from the solution at reduced pressure by rotary evaporation. The product is a yellow viscous oil, about 90% to 95% pure.
NOTE: Exact amounts of reagent are required for this synthesis since excess glutaraldehyde can cause appreciable formation of the mono-oxazolidine derivative of glutaraldehyde.

C. Sorbent Preparation (optional if commercially prepared tubes are used)

Extract XAD-2 sorbent 4 h in a Soxhlet extractor with a mixture of equal volumes of acetone and methylene chloride. Replace with fresh solvent and repeat. Vacuum dry overnight. Add 1 g purified 2-(hydroxymethyl)piperidine in 50 mL toluene for each 9 g extracted XAD-2 sorbent. Allow this mixture to stand 1 h with occasional swirling. Remove the solvent by rotary evaporation at 37 °C and dry at 0.13 kPa (1 mmHg) at ambient temperature for approximately 1 h. To determine the amount of background for each batch, extract several 120 mg portions of the coated sorbent with toluene and analyze (steps 7, 8, 9, 10, 11, 12, and 13). No blank peak is expected for glutaraldehyde.

D. Desorption Efficiency

The determination of desorption efficiency (DE) is not necessary when using the calibration procedure in step 10. If desired, the following procedure can be used to determine DE:

1. Prepare and analyze a set of glutaraldehyde oxazolidine standard solutions (step 9.a) and a set of working standards (step 10), including media blanks.
2. Treating the working standards as unknowns, read the mass (µg) of oxazolidine found in each working standard (W), and in the average media blank (B).
3. Using the mass of glutaraldehyde, µg, spiked onto the working standard (W_o) and the stoichiometric conversion factor between glutaraldehyde and glutaraldehyde oxazolidine (2.94), calculate the desorption efficiency $(W - B) / (W_o \times 2.94)$.
4. Prepare a graph of DE vs. µg glutaraldehyde recovered per sample $(W - B) / 2.94$.

VALERALDEHYDE 2536

$CH_3(CH_2)_3CH=O$ MW: 86.13 CAS: 110-62-3 RTECS: YV3600000

METHOD: 2536, Issue 4 **EVALUATION:** FULL **Issue 1:** 15 May 1989
Issue 4: 3 March 2016

OSHA: none
NIOSH: 50 ppm

PROPERTIES: liquid; d 0.810 g/mL @ 20 °C; BP 103 °C; VP 6.7 kPa (50 mm Hg) @ 25 °C; vapor density (air = 1) 3.0; flash point = 12.2 °C

SYNONYMS: pentanal; amyl aldehyde.

SAMPLING

SAMPLER: SOLID SORBENT TUBE (10% 2-(hydroxymethyl)piperidine on XAD-2, (120 mg/60 mg)

FLOW RATE: 0.01 - 0.04 L/min

VOL-MIN: 0.5 L @ 50 ppm
-MAX: 10 L

SHIPMENT: routine

SAMPLE STABILITY: at least 4 weeds @ 25 °C [1]

FIELD BLANKS: 2 to 10 field blanks per set

MEDIA BLANKS: 18 per set

ACCURACY

RANGE STUDIED: 9 to 374 mg/m^3 [1] (12-L samples)

BIAS: 0.12%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.073 [1]

ACCURACY: ± 14.4%

MEASUREMENT

TECHNIQUE: GAS CHROMATOGRAPHY, FID

ANALYTE: valeraldehyde oxazolidine (9-butyl-1-aza-8-oxabicyclo[4.3.0]nonane)

DESORPTION: 2 mL toluene, 60 min ultrasonic

INJECTION VOLUME: 1 µL splitless

TEMPERATURE
INJECTION: 250 °C
- DETCTOR: 280 °C
-COLUMN: 0.5 min @ 70°C; 50 °C/min to 120°C, hold 4 min; 20°C/min to 170°C, hold 7 min

CARRIER GAS: He, 27 cm/sec linear velocity
makeup flow 29 mL/min

COLUMN: capillary, 15 m x 0.32-mm, 5% phenyl, 95% methyl polysiloxane, 1-µm film (US Pharmacopeia (USP) G-27)

CALIBRATION: standard solutions of valeraldehyde on sorbent

RANGE: 4 to 3900 µg/sample [1]

ESTIMATED LOD: 2 µg/sample [1]

PRECISION ($\bar{S}_r$): 0.066 @ 2 to 508 µg per sample [1]

APPLICABILITY: The working range is 0.11 to 110 ppm (0.4 to 390 mg/m^3) for a 10-L air sample. The method is also suitable for determination of furfural and glutaraldehyde in a mixture [2].

INTERFERENCES: None have been observed; an alternate capillary column, 15 m x 0.32-mm cyanopropylphenyl dimethylpolysiloxane 1-µm film (USP G43) can be used.

OTHER METHODS: The method of Lipari and Swarin [3] uses 2,4-dinitrophenylhydrazine for the collection of valeraldehyde.

REAGENTS:

1. Toluene, chromatographic quality.
2. 2-(Hydroxymethyl) piperidine. Recrystallize several times from isooctane until there is one major peak (>95% of area) by GC analysis. Store in desiccator.
3. XAD-2. Extract 4 h in Soxhlet with 50/50 (v/v) acetone/methylene chloride. Replace with fresh solvent and repeat. Vacuum dry overnight. (Optional if commercial tubes are used.)
4. Valeraldehyde, * 99% purity.
5. Valeraldehyde stock solution, 40 µg/µL (see APPENDIX). Add 400 mg valeraldehyde to toluene and dilute to 10 mL.
6. Valeraldehyde oxazolidine stock solution, 10 mg/mL (see APPENDIX A). Add 0.10 g 9-butyl-1-aza-8-oxabicyclo-[4.3.0] nonane to toluene and dilute to 10 mL.
7. Hydrogen, prepurified.
8. Air, filtered, compressed.
9. Helium, purified.
10. Magnesium sulfate, anhydrous.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: resin-filled sampling tube; glass tube, 10 cm long, 6-mm OD, 4-mm ID, flame-sealed ends with plastic caps, containing two sections of 2-(hydroxymethyl) piperidine-coated XAD-2 (front = 120 mg, back = 60 mg) (see APPENDIX B). Sorbent sections are retained and separated by small plugs of silanized glass wool. Pressure drop across the tube at 0.1 L/min must be less than 760 Pa (5.7 mm Hg). Tubes are commercially available.
2. Personal sampling pump, 0.01 to 0.04 L/min, with flexible connecting tubing.
3. Gas chromatograph, flame ionization detector, integrator and column (page 2536-1).
4. Ultrasonic bath.
5. Vials, glass, 4-mL, with septum and plastic screw caps.
6. Flasks, volumetric, 10-, 25-, and 50-mL.
7. Pipets, volumetric, 1-, 2-, and 10-mL with pipet bulb.
8. Pipets, disposable, 2-mL.
9. Syringes, 10-µL (readable to 0.1 µL), 25-, and 50-µL.
10. File or tube scorer.
11. Beakers, 50-mL.
12. Magnetic stirrer.
13. Flasks, round-bottomed, 100-mL.
14. Soxhlet extraction apparatus.
15. Vacuum oxen.
16. Distillation apparatus.

SPECIAL PRECAUTIONS: Valeraldehyde can irritate the mucous membranes [4]. It is flammable, a dangerous fire risk. Toluene is extremely flammable. All work should be performed in a well-ventilated fume hood.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Break ends of the sampler immediately before sampling. Attach sampler to personal sampling pump with flexible tubing.
3. Sample at an accurately known flow rate between 0.01 and 0.04 L/min for a total sample size of 0.5 to 10 L.
   NOTE: Sampling rate is limited by the speed of the following reaction. Rates above 0.04 L/min may cause appreciable breakthrough owing to incomplete reaction, possibly invalidating the sample.

$CH_3(CH_2)_3CH=0$ valeraldehyde	+	$C_5H_9NHCH_2OH$ 2-(hydroxymethyl)- piperidine	→ toluene/ ultrasonic energy	$C_5H_9NHC_2H_2O(CH_2)_3CH_3$ valeraldehyde oxazolidine	+	H_20

SAMPLE PREPARATION:

4. Score each sampler with a file or tube scorer in back of the back sorbent section.
5. Break sampler at score line. Remove and place back glass wool plug and back sorbent section in a vial.
6. Transfer front section with remaining glass wool plugs to a second vial.
7. Add 2.0 mL toluene to each vial. Screw cap tightly onto each vial.
8. Agitate in an ultrasonic bath for 60 min.

CALIBRATION AND QUALITY CONTROL:

9. Identification of analytical peaks.
   a. Add known amounts of valeraldehyde oxazolidine stock solution to toluene in 10-mL volumetric flasks and dilute to the mark.
   b. Analyze (steps 12 and 13) with samples and blanks for qualitative identification of derivative peaks.
10. Calibrate daily with a least six working standards prepared in triplicate covering the range 2 to 3900 µg valeraldehyde per sample.
    a. Weigh 120-mg portions of unused sorbent from media blanks into vials.
    b. Add aliquots (1 to 10 µL) of valeraldehyde stock solution, or dilutions thereof, to the sorbent. Cap vials and allow to stand overnight at room temperature.
    c. Desorb (steps 7 and 8) and analyze (steps 12 and 13) with samples and blanks.
    d. Prepare calibration graph (combined peak area vs. µg valeraldehyde).
    NOTE: Because the standard samples are prepared on media blanks, no additional blank correction or desorption efficiency correction is necessary. Check desorption efficiency in the range of interest and at least once over the entire range of the method with each lot of sorbent used. (see APPENDIX C).
11. Analyze three quality control blind spikes and three analyst spikes to ensure that the calibration graph is in control.

MEASUREMENT:

12. Set gas chromatograph to manufacturer's recommendations and to conditions given on page 2536-1. Inject 1-µL sample aliquot.
    NOTE: If the amount of valeraldehyde oxazolidine in the aliquot exceeds the capacity of the column, dilute with toluene, reanalyze and apply the appropriate dilution factor in calculations. The upper limit for the column on (page 2536-1) is equivalent to ca. 260 µg valeraldehyde per sample.
13. Measure total peak area of the two analyte peaks.
    NOTE: Valeraldehyde oxazolidine gives two peaks, since the diastereoisomers are resolved with retention times 5.4 and 6.3 min. Retention time for 2-(hydroxymethyl) piperidine is 2.2 min for these conditions.

CALCULATIONS:

14. Determine the mass, µg, of valeraldehyde found in the sample front (W_f) and back (W_b) sorbent sections.
    NOTE: If $W_b > W_f/10$, report breakthrough and possible sample loss.
15. Calculate concentration, C, of valeraldehyde in the air volume sampled, V (L):

$$C = \frac{W_f + W_b}{V}, mg/m^3$$

EVALUATION OF METHOD:

Atmospheres were generated by injection of valeraldehyde with a syringe pump into a heated block injector and flash vaporizer into a stream of air at 80% ± 5% RH flowing at a fixed rate. The generator and sampling manifold system have been described previously [5]. Concentration of valeraldehyde vapor was independently verified by the 2,4-dinitrophenylhydrazine procedure of Lipari and Swarin [3] or by monitoring with an AID Model 590 organic vapor monitor. Breakthrough studies of valeraldehyde at 100 ppm, conducted at 75 and 50 mL/min flow rates, gave 5% breakthrough at 170 min and 280 min, respectively.

The method was evaluated over the range of 9 to 374 mg/m^3 using 12-L samples. Desorption efficiencies from statically-spiked samples average 102.5% (89.2-126.6%) for the range 2 to 508 µg/sample. No bias with dynamically-generated samples was observed with the method when samples were collected at 40 mL/min and below. When samples were collected at ca. 60 mL/min, a negative bias of approximately 20-30% was observed. Samples were found to be stable for at least 4 weeks when stored at room temperature.

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METHOD REVISED BY:

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APPENDIX A: Synthesis of 9-Butyl-1-Aza-8-Oxabicyclo[4.3.0]nonane:

Place a solution of purified 2-(hydroxymethyl)piperidine (1.15 g; 10 mmol) in 20 mL of toluene in a 100- mL round-bottomed flask. Use several 2-mL portions of toluene to rinse residual 2- (hydroxymethyl)piperidine from the container used for weighing. Add anhydrous magnesium sulfate (2.0 g) to the flask to dry the valeraldehyde solution as it is added and to remove the water which forms during the reaction. Add a solution of 0.947 g valeraldehyde (11 mmole) in 20 mL of toluene to the 2- (hydroxymethyl)piperidine solution dropwise with stirring over 1 h. (NOTE: Excess aldehyde was added to ensure complete conversion of 2-(hydroxymethyl)piperidine to oxazolidine.) Stir the solution overnight, then filter to remove the magnesium sulfate. Remove the toluene from the solution at reduced pressure (1 mm Hg) by rotary evaporation. The product is a pale yellow viscous oil, ca. 90 to 95% pure by gas chromatography. Store the oxazolidine at 0 °C to prevent decomposition.

Mass spectral data for 9-butyl-1-aza-8-oxabicyclo[4.3.0]nonane: m/e with relative intensities in parenthesis, 182 (7.0%), 152 (4.6%), 126 (100%), 110 (11.3%), 98 (37%). IR data (Vapor phase @ 280 °C) for this compound in cm-1 with relative intensity in parenthesis are: 2945 (s), 2874 (m), 2781 (m), 1455 (w), 1383 (w), 1339 (w), 1265 (w), 1203 (w), 1133 (m), 1075 (w), 1028 (m).

APPENDIX B: Sorbent Preparation (optional if commercially-prepared tubes are used):

Add 1 g purified 2-(hydroxymethyl)piperidine in 50 mL toluene for each 9 g extracted XAD-2 sorbent. Allow this mixture to stand 1 h with occasional swirling. Remove the solvent by rotary evaporation at 37°C. Dry at 130 Pa (1 mm Hg) at ambient temperature for approximately 1 h. To determine the amount of background for each batch, desorb several 120-mg portions of the coated sorbent with toluene and analyze (steps 7 through 13). No blank peak is expected for valeraldehyde.

APPENDIX C: Desorption Efficiency:

The determination of desorption efficiency (DE) is not necessary when using the calibration procedure in step 10, although the DE should be determined once for each lot of sorbent used, using the following procedure:

a. Prepare and analyze a set of valeraldehyde oxazolidine standard solutions (step 9.a) and a set of working standards (step 10), including media blanks.
b. Treating the working standards as unknowns, read the mass (µg) of valeraldehyde oxazolidine found in each working standard (W), and in the average media blank (B).
c. Using the mass of valeraldehyde, µg, spiked onto the working standard (W_o) and the stoichiometric conversion factor of 2.13 between valeraldehyde and valeraldehyde oxazolidine, calculate the desorption efficiency:

$$DE = \frac{W - B}{W_o \cdot 2.13}$$

d. Prepare a graph of DE vs. µg valeraldehyde recovered per sample, (W - B)/2.13.

ORGANIC AND INORGANIC GASES by Extractive FTIR Spectrometry

3800

FORMULA: Table 1 MW: Table 1 CAS: Table 1 RTECS: Table 1

METHOD: 3800, Issue 2 **EVALUATION: FULL** **Issue 1: 15 March 2003**
Issue 2: 13 January 2016

OSHA: Table 1
NIOSH: Table 1

PROPERTIES: Table 1

SYNONYMS: See example compounds in Table 1

SAMPLING

SAMPLER: PORTABLE DIRECT-READING INSTRUMENT (with filter, if required)

FLOW RATE: ~0.1 L/min to ~20 L/min (system-dependent)

VOL-MIN: Instrument dependent
-MAX: None

PRESSURE: Extracted gases between 96.6 kPa and 103 kPa (725 mmHg and 795 mmHg) absolute

TEMPERATURE: Extracted gases between 10 °C and 30 °C

BLANKS: Nitrogen gas, or zero air

ACCURACY

RANGE STUDIED: See APPENDIX E

BIAS: See APPENDIX E

OVERALL PRECISION ($\hat{S}_{rT}$): See APPENDIX E

ACCURACY: See APPENDIX E

MEASUREMENT

TECHNIQUE: EXTRACTIVE FOURIER TRANSFORM INFRARED (FTIR) SPECTROMETRY

ANALYTE: See Table 1 (additional compounds may be identified/quantified according to data quality objectives and QA/QC requirements)

ANALYTICAL FREQUENCIES: See Table 2 for example compounds

CALIBRATION: Calibration gas standards

IDENTIFICATION: Infrared spectra interpretation and computerized reference library searches

RANGE: See Table 2 (dependent on compound and absorption path length)

ESTIMATED LOD: See Table 2 for example values at 10 m absorption path length

PRECISION ($\bar{S}_r$): See APPENDIX E

APPLICABILITY: The usefulness of FTIR techniques has been demonstrated in ambient air and combustion gas mixtures [1,2]. With the participation of an experienced analyst (see APPENDIX A), the method can be used for the characterization of workspace air containing mixtures of volatile organic and inorganic compounds. See Table 1 for examples.

INTERFERENCES: Overlap of infrared absorption features may affect the quantification of each compound. By appropriate use of multivariable least squares analyses, the analyst may be able to obtain accurate compound concentrations for overlapping compounds.

OTHER METHODS: This method is based on portions of EPA method 320 and its addendum [3], which describe the determination of gaseous compound concentrations by extractive FTIR spectrometry. Several compatible ASTM standards describing infrared techniques and terminology are also available [4,5,6,7].

REAGENTS:

1. Nitrogen gas or zero air, high purity or better.
2. Calibration transfer standard (CTS) gas, 2% accuracy or better. The proper concentration depends on both the compound used and the system absorption path length. For ethylene in nitrogen, a standard concentration leading to a concentration-path length product (CPP) of 100 ppm · m to 400 ppm · m is recommended. (For example, a standard of 10 ppm to 40 ppm ethylene in nitrogen is recommended for a 10 m absorption cell).
3. Liquid nitrogen* for cooling the infrared detector, if required.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. FTIR spectrometer system (source, interferometer, sample absorption cell, and detector) configured for absorption. A minimum instrumental linewidth (MIL) of 2 cm^{-1} or lower is recommended.
   NOTE: A lower or higher MIL may be required or suitable for specific gas matrices. Choose internal absorption cell materials to minimize surface/analyte interactions.
2. Computer system with hardware, software, and required reference spectra for acquisition, storage, and analysis of sample spectra. (A data backup system is recommended.)
3. Sampling pump, 0.1 to 10 L/min, with appropriate particulate filters.
4. Non-reactive gas regulators and sample tubing.
5. Rotameters or other devices, 5% precision or better, for measuring flow rates of sample and calibration gases.
6. Temperature measurement and/or control equipment for all sampling system elements and IR absorption cell.
   NOTE: Temperature control equipment required if ambient temperature <10 °C or >30 °C.
7. Pressure gauge for measuring absolute gas pressure in absorption cell, 5% accuracy at 101.3 kPa (1 atm, 760 mmHg) absolute pressure.
8. For system tests (but not for normal operation): Vacuum pump and gauge capable of 13.3 kPa (100 mmHg) absolute pressure; mid-infrared attenuating filters (50% and 25%); impinger.

SPECIAL PRECAUTIONS: This method requires the use of compressed gases and/or cryogenic liquids and/or toxic chemicals. These materials are dangerous and should be handled only by experienced personnel and according to relevant safety standards. This method does not address all of the safety concerns associated with its use. It is the responsibility of the user to establish appropriate safety and health practices and to determine the applicability of regulatory limitations.

NOTE: Please refer to the appendices for explanations of the terminology used in this document (APPENDIX A) and several FTIR system tests, which must be completed before any testing is performed (APPENDIX B). Appendices C, D, and E provide (respectively) a general description of FTIR spectrometry, considerations for preparing reference libraries, and examples of calculations required for performance of this method.

PRETEST PROCEDURES:

The following procedures (steps 1 and 2) may be performed only by an experienced "analyst" (see APPENDIX A).

1. Verify that the FTIR system has been tested for wavenumber reproducibility, MIL, absorption path length, system response time, residual squared area (RSA), and detector linearity as described in APPENDIX B. If the system is new and/or has been recently assembled and/or has been recently serviced, perform and document results of the tests described in APPENDIX B before proceeding.
2. Prepare a test plan. The plan must include the following:
   a. The proposed system configuration, including the absorption path length and integration time for sample spectra.
   b. The data quality objectives, analytical regions, and expected LOD values for each analyte. See Table 2 and APPENDIX E for example values and calculations.
   c. The names of all "operators" and "analysts" to be involved in the test. Analysts must be experienced in all aspects of the test procedures listed below and may perform any or all of the test procedures. Operators must be experienced in the performance of steps 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13 listed below and may perform *only* those portions of the test procedures.
   d. Verification that the system configuration, existing RSA values, and related LOD values are consistent with the test's data quality objectives. (See APPENDIX E.)

The following procedures (steps 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and 13) may be performed by an experienced operator or analyst.

3. Activate the FTIR system according to the manufacturer's instructions. Allow sufficient time for the infrared source, the infrared detector, and (if required) the temperature control systems to stabilize.
4. Verify that the computer system is programmed to store interferograms; if the available data storage capacity is insufficient for storage of all interferograms, store single-beam spectra instead. Verify adequacy and performance of the (recommended) data backup system.
5. Bypassing the sampling system, flow nitrogen or zero air directly into the infrared absorption cell until a stable infrared response and moisture levels are reached. Record a background spectrum using an integration time equal to or greater than that planned for subsequent sample spectra.
6. Use the entire FTIR system (including all sampling components) to record an absorbance spectrum of a sample stream of nitrogen or zero air. Use the integration time planned for subsequent sample spectra. Verify that the sample flow rate meets or exceeds that specified in the system response time documentation. Examine the resulting "system zero" (SZ) spectrum and verify the absence of contaminants in the sampling system and infrared absorption cell. If contaminants are detected, clean or replace the appropriate sampling system components and/or infrared absorption cell and record a new SZ spectrum. If contaminants cannot be eliminated, the test results and LOD values may require revision/correction during the quality control procedures (see steps 14, 15, 16, and 17).

CALIBRATION:

7. Using the entire sampling system, acquire two or more pretest CTS spectra and use them to calculate the system absorption path length L_S (see APPENDIX B, section B1). Use the integration time planned for subsequent sample spectra. Verify that L_S is within 5% of the value quoted in the test plan. Verify that the sample temperature and pressure are within 10 °C to 30 °C and 96.6 kPa to 103 kPa (725 mmHg to 795 mmHg), respectively.
8. When possible, perform the following system checks before sampling. If necessary, they may be delayed until performance of the (post-testing) quality control procedures (see steps 14, 15, 16, and 17). If performed after sampling, the results of these procedures may require revision of the test results and LODs.

a. LOD check. Using one of the SZ spectra, calculate the RSA values (see APPENDIX B, section B2) and LOD values (see Appendix E, section E1) in the analytical regions pertaining to the test analytes. Verify that the system path length (see APPENDIX B, section B1), current RSA values, and current LODs are consistent with the test's data quality objectives (see Appendix E, section E1).
b. Wavenumber reproducibility check. Record a preliminary workspace air sample spectrum and perform the calculations described in Appendix B, section B4.

SAMPLING:

9. Using the integration time specified in the test plan, obtain samples and record infrared spectra of the desired workplace gases using the entire sampling system. The sampling location may be changed as desired. For tests of duration greater than 2 h, or if the FTIR system is moved during sampling, monitor the system's single-beam response level. If changes greater than 5% in non-absorbing regions of the single-beam spectrum occur, suspend sampling and record a new background spectrum (see step 5). Sample spectra must be acquired at each sampling location for a time period no less than the system response time (see the system test documentation).
10. Repeat step 6; acquire at least one posttest SZ spectrum of nitrogen or zero air; confirm the absence of sampling system contaminates.
11. Record at least one posttest CTS spectrum (see step 7); confirm that the system configuration and the system absorption path length (to within 5%) match those of the test plan.
12. (Optional.) Acquire a posttest background spectrum (see step 5).

SAMPLE ANALYSIS:

13. Using the analytical regions specified in the test plan, employ an appropriate mathematical analysis (see APPENDIX E) to determine preliminary analyte concentrations and their 3σ uncertainties from the sample spectra, reference spectra, absorption path length, and gas pressure.
    NOTE: Reference spectra for all analytes must meet or exceed the QA/QC requirements of APPENDIX D. The reference library must include at least one wavenumber standard spectrum and at least one CTS spectrum. The sample absorption due to any analyte may not exceed the maximum CPP represented in the reference library for that compound.

QUALITY CONTROL:

The following procedures (steps 14, 15, 16, 17, and 18) may be performed only by an experienced analyst.

14. Using one of the SZ spectra, calculate the RSA and LOD values (see APPENDIX E) in the analytical regions pertaining to the test analytes. Verify that the system path length, current RSA values, and current LODs are consistent with the test's data quality objectives. Using a suitable workspace air spectrum, perform the wavenumber reproducibility and resolution tests described in APPENDIX B, sections B3 and B4. If either the wavenumber reproducibility or resolution results fail to meet the specifications, corrective actions are necessary (see step 17).
15. Perform qualitative and/or quantitative analyses of the pretest and posttest SZ spectra and confirm the absence of sampling system contaminants. If contaminants are found that possess significant absorbance in any analytical region, corrective actions may be necessary (see step 17). Perform qualitative and/or quantitative analyses of the pretest and posttest CTS spectra and confirm that the system absorption path length is within 5% of the value quoted in the test plan.
16. Verify that the reference spectra and results meet the data quality objectives of the test plan (see APPENDIX D). If they do not, corrective actions may be necessary (see step 17). Examine the results of the quantitative sample analysis (step 13) and verify some subset of them (including those with relatively high and relatively low concentrations) manually to ensure proper operation of analytical

program. (Techniques for generating spectra representing the analytes at the concentration indicated by the analysis — "scaled spectra," as defined in APPENDIX A — are described in APPENDIX E. The analyst should generate such spectra and compare them, either visually or mathematically, to the indicated sample spectra.)

17. Corrective actions: If the results of steps 14, 15, and 16 indicate that the data quality objectives of the test plan have not been achieved, the analyst may perform one or more of the following actions:
    - Averaging of sequential sample spectra to reduce the RSA.
    - Inclusion of contaminant reference spectra in the mathematical analysis.
    - Development of more accurate analyte or interferant reference spectra.
    - Inclusion of reference spectra for additional compounds in the mathematical analysis.
    - Exclusion from the mathematical analysis of analyte and/or interferant compounds that are clearly absent in the samples.
    - Deresolution or wavenumber adjustment of the reference spectral library to match that of the sample spectra (or vice versa).
    - Revision of the original data quality objectives (those included in the test plan) to levels supported by the test data.

    NOTE: After performing any such corrective actions, the analyst must repeat steps 13, 14, 15, and 16 and reevaluate the LOD value for each analyte compound.

REPORTING:

18. Reporting requirements include the analyte and interferant concentrations, the concentration uncertainties, the FTIR spectrometer configuration, the sampling locations and conditions, the source(s) of the reference spectra, the CTS spectral analysis results, the results of QA/QC procedures, and certificates of analysis for all standard gases. Any variations of the test procedures and original data quality objectives from those included in the test plan should also be documented and reported. (Several of the terms used here are defined in APPENDIX A and described in the following appendices. In particular, see Table D1 for a description of the FTIR spectrometer configuration parameters.)

EVALUATION OF METHOD:

Field evaluations of extractive FTIR methods have been performed for many compounds (see, for example, references 1 and 2) according to EPA method 301 [8].

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METHOD WRITTEN BY:

Grant M. Plummer, Ph.D. (Rho Squared), William K. Reagen, Ph.D. (3M), and Perry W. Logan (3M).

Table 1. Representative volatile compounds and chemical data

Name	Synonyms*	Formula	MW†	CAS No.	RTECS No.	BP (°C)†	VP at 20 °C (kPa)†	Exposure Limits (OELs)*	
								NIOSH	OSHA
Acetone	Dimethyl ketone, Ketone propane, 2-Propanone	$(CH_3)_2CO$	58.1	67-64-1	AL3150000	56	24	TWA 250 ppm (590 mg/m^3)	TWA 1000 ppm (2400 mg/m^3)
Ammonia	Anhydrous ammonia, Aqua ammonia, Aqueous ammonia	NH_3	17.0	7664-41-7	BO0875000	–33	1.01 × 10^3 (26 °C)	TWA 25 ppm (18 mg/m^3) ST 35 ppm (27 mg/m^3)	TWA 50 ppm (35 mg/m^3)
Benzene	Benzol, Phenyl hydride	C_6H_6	78.1	71-43-2	CY1400000	80	10	Ca TWA 0.1 ppm ST 1 ppm	[1910.1028] TWA 1 ppm ST 5 ppm
2-Butanone	Ethyl methyl ketone, MEK, Methyl acetone, Methyl ethyl ketone	$CH_3COCH_2CH_3$	72.1	78-93-3	EL6475000	80	10.5	TWA 200 ppm (590 mg/m^3) ST 300 ppm (885 mg/m^3)	TWA 200 ppm (590 mg/m^3)
Carbon disulfide	Carbon bisulfide	CS_2	76.1	75-15-0	FF6650000	46	48 (25 °C)	TWA 1 ppm (3 mg/m^3) ST 10 ppm (30 mg/m^3) [skin]	TWA 20 ppm C 30 ppm 100 ppm (30 min maximum peak)
Ethylene oxide	Dimethylene oxide; 1,2-Epoxyethane; Oxirane	C_2H_4O	44.1	75-21-8	KX2450000	11	146	Ca TWA <0.1 ppm (0.18 mg/m^3) C 5 ppm (9 mg/m^3) [10 min per day]	[1910.1047] TWA 1 ppm 5 ppm [15 min excursion]
Formaldehyde	Methanal, Methyl aldehyde, Methylene oxide	H_2CO	30.0	50-00-0	LP8925000	–19.5§	519‡ (3890 mmHg, 25 °C)	Ca TWA 0.016 ppm C 0.1 ppm [15 min]	[1910.1048] TWA 0.75 ppm ST 2 ppm
n-Hexane	Hexane, Hexyl hydride, normal-Hexane	$CH_3(CH_2)_4CH_3$	86.2	110-54-3	MN9275000	69	17	TWA 50 ppm (180 mg/m^3)	TWA 500 ppm (1800 mg/m^3)
Hydrogen fluoride	Anhydrous hydrogen fluoride; Aqueous hydrogen fluoride (i.e., Hydrofluoric acid); HF-A	HF	20.0	7664-39-3	MW7875000	20	122 (25 °C)	TWA 3 ppm (2.5 mg/m^3) C 6 ppm (5 mg/m^3) [15 min]	TWA 3 ppm

See footnotes at end of table.

(Continued)

Table 1 (Continued). Representative volatile compounds and chemical data

Name	Synonyms*	Formula	MW†	CAS No.	RTECS No.	BP (°C)†	VP at 20 °C (kPa)†	Exposure Limits (OELs)*	
								NIOSH	OSHA
Methanol	Carbinol, Columbian spirits, Methanol, Pyroligneous spirit, Wood alcohol, Wood naphtha, Wood spirit	CH_3OH	32.0	67-56-1	PC1400000	65	12.3	TWA 200 ppm (260 mg/m^3) ST 250 ppm (325 mg/m^3) [skin]	TWA 200 ppm (260 mg/m^3)
Methylene chloride	Dichloromethane, Methylene dichloride	CH_2Cl_2	84.9	75-09-2	PA8050000	40	47.4	Ca	TWA 25 ppm ST 125 ppm
Nitrous oxide	Dinitrogen monoxide, Hyponitrous acid anhydride, Laughing gas	N_2O	44.0	10024-97-2	QX1350000	–88.5	5.06 × 10^3	TWA 25 ppm (46 mg/m^3) (TWA over the time exposed) [Note: REL for exposure to waste anesthetic gas.]	
Styrene	Ethenyl benzene, Phenylethylene, Styrene monomer, Styrol, Vinyl benzene	$C_6H_5CH=CH_2$	104.1‡	100-42-5	WL3675000	145	0.67	TWA 50 ppm (215 mg/m^3) ST 100 ppm (425 mg/m^3)	TWA 100 ppm C 200 ppm 600 ppm (5 min maximum peak in any 3 h)
Sulfur dioxide	Sulfurous acid anhydride, Sulfurous oxide, Sulfur oxide	SO_2	64.1	7446-09-5	WS4550000	–10	330	TWA 2 ppm (5 mg/m^3) ST 5 ppm (13 mg/m^3)	TWA 5 ppm (13 mg/m^3)
Tetrafluoroethylene	Tetrafluoroethene; Perfluoroethylene; Perfluoroethene; TFE‡	$F_2C=CF_2$	100.0‡	116-14-3	KX4000000	–75.9§	3.27 ×10^3‡ (24500 mmHg, 25 °C)		
Tetrahydrofuran	Diethylene oxide; 1,4-Epoxybutane; Tetramethylene oxide; THF	C_4H_8O	72.1	109-99-9	LU5950000	66	19.3	TWA 200 ppm (590 mg/m^3) ST 250 ppm (735 mg/m^3)	TWA 200 ppm (590 mg/m^3)

See footnotes at end of table.

(Continued)

Table 1 (Continued). Representative volatile compounds and chemical data

Name	Synonyms*	Formula	MW†	CAS No.	RTECS No.	BP (°C)†	VP at 20 °C (kPa)†	Exposure Limits (OELs)*	
								NIOSH	OSHA
Toluene	Methyl benzene, Methyl benzol, Phenyl methane, Toluol	$C_6H_5CH_3$	92.1	108-88-3	XS5250000	111	3.8 (25 °C)	TWA 100 ppm (375 mg/m^3) ST 150 ppm (560 mg/m^3)	TWA 200 ppm C 300 ppm 500 ppm (10 min maximum peak)
Trichloroethylene	Ethylene trichloride, TCE, Trichloroethene, Trilene	$ClCH=CCl_2$	131.4	79-01-6	KX4550000	87	7.8	Ca	TWA 100 ppm C 200 ppm 300 ppm (5 min maximum peak in any 2 h)
Vinylidene fluoride	Difluoro-1,1-ethylene; 1,1-Difluoroethene; 1,1-Difluoroethylene; Halocarbon 1132A; VDF; Vinylidene difluoride	$F_2C=CH_2$	64.0	75-38-7	KW0560000	–83	3.57 $\times 10^3$* (35.2 atm)	TWA 1 ppm C 5 ppm [use 1910.1017]	
m-Xylene	1,3-Dimethylbenzene; meta-Xylene; *m*-Xylol	$C_6H_4(CH_3)_2$	106.2	108-38-3	ZE2275000	139	0.8	TWA 100 ppm (435 mg/m^3) ST 150 ppm (655 mg/m^3)	TWA 100 ppm (435 mg/m^3)
o-Xylene	1,2-Dimethylbenzene; ortho-Xylene; *o*-Xylol	$C_6H_4(CH_3)_2$	106.2	95-47-6	ZE2450000	144	0.7	TWA 100 ppm (435 mg/m^3) ST 150 ppm (655 mg/m^3)	TWA 100 ppm (435 mg/m^3
p-Xylene	1,4-Dimethylbenzene; para-Xylene; *p*-Xylol	$C_6H_4(CH_3)_2$	106.2	106-42-3	ZE2625000	138.4	0.9	TWA 100 ppm (435 mg/m^3) ST 150 ppm (655 mg/m^3)	TWA 100 ppm (435 mg/m^3)

*Source: NIOSH Pocket Guide to Chemical Hazards [www.cdc.gov/niosh/npg/]. Date accessed: February 2016.
†Source: International Chemical Safety Cards (ICSC) [www.cdc.gov/niosh/ipcs/]. Date accessed: February 2016.
‡Source: PubChem [pubchem.ncbi.nlm.nih.gov/]. Date accessed: February 2016.
§Source: Haynes WM, Lide DR, Bruno TJ [2013]. CRC handbook of chemistry and physics: a ready-reference book of chemical and physical data. 94th ed. Boca Raton, FL: CRC Press.

Table 2. Representative infrared data for the compounds of Table 1

Compound	Analytical Region (cm^{-1})	Reference Spectrum Filename*	LOD at 10 m† (ppm)	Maximum concentration at 10 m‡ (ppm)	Maximum RSA§ (cm^{-1})	Reference Spectrum Source
Acetone	1163 to 1265	192mav01.spc	0.95	148	0.0211	EPA**
Ammonia	998 to 1131	nh3mav01.spc	0.77	470	0.0363	3M††
Benzene	3000 to 3150	015mav01.spc	0.32	149	0.036	EPA**
2-Butanone	1127 to 1235	mekmav01.spc	0.27	463	0.0233	3M††
Carbon disulfide	2109 to 2200	028mav01.spc	0.13	151	0.0123	EPA**
Ethylene oxide	3059 to 3070	084mav01.spc	0.11	138	0.0025	EPA**
Formaldehyde	2727 to 2844	087bb.spt	0.4	1125	0.0267	EPA**‡‡
n-Hexane	2778 to 3051	095mav01.spc	0.1	150	0.0639	EPA**
Hydrogen fluoride	4034 to 4206	21hfrav	0.93	15.8	0.15	3M††
Methanol	941 to 1100	104mav01.spc	0.28	151	0.0447	EPA**
Methylene chloride	701 to 789	117mav01.spc	0.31	150	0.062	EPA**
Nitrous oxide	1226 to 1333	n2omav01.spc	0.36	904	0.0301	3M††
Styrene	738 to 944	147mav01.spc	1.84	150	0.0363	EPA**
Sulfur dioxide	1290 to 1410	so2.spc	0.35	~200§§	0.1394	NIST§§
Tetrafluoroethylene	1080 to 1215	tfemav05.spc	0.17	25.7	0.093	3M††
Tetrahydrofuran	2750 to 3085	thf405.spc	0.18	41	0.0782	3M††
Toluene	701 to 768	tolmav01.spc	1.16	463	0.0499	EPA**
Trichloroethylene	762 to 966	tcemav01.spc	0.43	464	0.1071	3M††
Vinylidene fluoride	1080 to 1215	dfemav05.spc	0.21	25.7	0.093	3M††
m-Xylene	782 to 805	172mav01.spc	1.36	146	0.0377	EPA**
o-Xylene	709 to 781	171mav01.spc	0.65	150	0.0444	EPA**
p-Xylene	749 to 840	173mav01.spc	1.17	151	0.0561	EPA**

*Used in LOD calculations; averaged spectra from the quoted libraries; data available from the authors.

†Approximate LOD for a 10 m absorption path length. Typical values of the RSA, quoted analytical regions, and quoted reference spectral data were used to calculate the LOD as described in Equation E1. Note: The LOD may vary from laboratory to laboratory, analyst to analyst, instrument to instrument, and day to day. Therefore, any determination of this value should be performed under the same conditions used for sample analysis and reported only with those analyses. It is stressed that the values below are only conservative estimates of the expected performance of this method.

‡The maximum ppm · m value available for the compound in the quoted reference spectrum source.

§Maximum RSA in the specified analytical regions consistent with the quoted LOD values. See APPENDIX E, section E1.

**See reference 9. Average absorbance and accepted standard concentration values for the low-concentration pairs of spectra were used. Interferograms were truncated to 0.5 cm^{-1} resolution and triangular apodization was employed.

††Data available from the authors.

‡‡From EPA reference spectra recorded at 100 °C [9].

§§NIST quantitative infrared database [10]. The quoted maximum concentration for sulfur dioxide is based on linearity studies of 0.5 cm^{-1} resolution spectra with triangular apodization. Nonlinear absorbance leads to errors of less than 10% at 1000 ppm · m.

APPENDIX A. TERMINOLOGY

absorbance — in terms of the incident intensity I_0 and transmitted intensity I, the absorbance A is given by $A = -\log(I / I_0)$. From a pair of FTIR single-beam spectra B (the background spectrum) and S (the sample spectrum), the sample absorbance for each wavenumber value (with index i) in the spectra is approximated by $A_i = -\log(I_{Si} / I_{Bi})$.

absorbance linearity — a characteristic of (ideal) absorbance spectrum; for such a spectrum, the measured absorbance is described by Beer's law (Equation C1).

absorption band — a contiguous wavenumber region of a spectrum (equivalently, a contiguous set of absorbance spectrum data points) in which the absorbance passes through a maximum or a series of maxima.

absorption cell — a structure that contains a fluid sample, but allows light to pass through a sample at known temperature, pressure, and absorption path length.

absorption path length — the distance, measured in the direction of propagation of the beam of radiant energy, between the surface of the specimen on which the radiant energy is incident and the surface of the specimen from which it is emergent.

absorptivity — a measure of the fraction of the incident infrared radiation that is absorbed by a particular compound per molecule and per absorption path length; see Equation C1.

analyst — a person familiar with and experienced in performance of all aspects of this FTIR-based method. Analysts may perform any portion(s) of the method and must perform certain portions of the method (see also "operator").

analyte — a compound whose concentrations in a sample is of interest and is to be accurately quantified (see also "interferant").

analytical region — a contiguous wavenumber region (equivalently, a contiguous set of absorbance spectrum data points) used in the quantitative analysis for one or more analytes.
NOTE: The quantitative result for a single analyte may be based on data from more than one analytical region.

aperture — an optical device that physically restricts the diameter of the optical beam.

apodization — modification of the interferogram through its multiplication by a weighing function whose magnitude varies with the position of the interferometer's moving element.

background spectrum — the single-beam spectrum obtained with all system components and without sample present (or in the presence of a non-absorbing gas replacing the sample).

baseline — any line (or smooth function of wavenumber) drawn on an absorption spectrum to establish a reference point that represents a function of the radiant power incident on a sample at a given wavelength.

Beer's law — the direct proportionality of the absorbance of a compound in a homogeneous sample to its concentration. See Equation C1, which also describes the more general case of gas mixtures.

calibration transfer standard (CTS) gas — a gas standard of a compound used to measure the sample absorption path length; see step 7, step 11, APPENDIX B (section B1), and APPENDIX D (section D5).

cm^{-1} — see "wavenumber."

compound — a substance possessing a distinct, unique molecular structure.

concentration — the quantity of a compound contained in a unit quantity of sample. The unit "ppm" (number, or mole, basis) is recommended and is equivalent to the volume basis for ideal gases.

concentration-path length product (CPP) — the mathematical product of concentration of the species and the absorption path length. For reference spectra, this is a known quantity; for sample spectra, it is the quantity directly determined from Beer's law. The unit "parts per million · meters" (ppm · m) is recommended.

data quality objectives — parameters pertaining to a certain application of this method, including the estimated LOD values for each compound.

deresolve — to form spectra of lower resolution (higher full-width-at-half-maximum) from spectra of higher resolution (lower full-width-at-half-maximum); see reference 11 for a deresolution program.

detector linearity — a characteristic of an (ideal) IR detector; for such a detector, the measured detector output voltage, when plotted against the total IR in a broadband IR signal incident on the detector, would form a straight line.

double-beam spectrum — a transmittance or absorbance spectrum derived by dividing the sample single-beam spectrum by the background spectrum.

NOTE: The term "double-beam" is used elsewhere to denote a spectrum in which the sample and background interferograms are collected simultaneously along physically distinct absorption paths. Here, the term denotes a spectrum in which the sample and background interferograms are collected at different times along the same absorption path.

extractive — the type of spectroscopy that includes extracting and transporting a sample stream from gases at a certain location to an absorption cell and isolating the sample in the absorption cell for analysis. Other types of spectroscopy in which the sample is not isolated in an absorption cell include "remote", "open path", and "local open path" techniques.

FFT (fast Fourier transform) — a discrete (digital) approximation to an FT (Fourier transform; see below) involving the factoring of the original data into sparse matrices containing mostly zeros.

filter — (1) A device, made of inert materials, that physically removes solid and liquid phase particles from a gas stream. (2) An optical device that transmits some fraction of the radiation incident on it; "neutral density" and "mesh" filters transmit an approximately constant fraction of the incident radiation at all wavelengths over a specified wavelength range.

frequency, ν — the number of cycles per unit time; for light, $\nu = c / \lambda$, where c is the speed of light and λ is the light's wavelength. Unlike the speed and wavelength, which are medium-dependent, the frequency of light is independent of the medium through which the light travels. The term "frequency" is often used to denote the wavenumber (w, cm^{-1}) in FTIR spectroscopy because (in a given medium) the wavenumber is proportional to the frequency. (See APPENDIX C, section C4, and "wavenumber" in this appendix.)

FT (Fourier transform) — the mathematical process for converting an analytical (non-discrete) amplitude-time function to an amplitude-frequency function, or vice versa.

FTIR (Fourier transform infrared) spectrometer — an analytical system that employs a source of mid-infrared radiation, an interferometer, an enclosed sample cell of known absorption path length, an infrared detector, optical elements that transfer infrared radiation between components, and a computer system. The time-domain detector response (interferogram) is processed by a Fourier transform to yield a representation of the infrared power vs. infrared frequency. See Figures C1 and C2.

FTIR spectrometry — use of an FTIR system to perform quantitative measurements.

FTIR system — the combination of an FTIR spectrometer and a sample interface.

FTIR system configuration — the set of parameters required to reproduce, as closely as possible, results from a particular FTIR system at a later time. This set includes (at least) the nominal MIL, the absorption path length, the apodization function, the gas temperature, the gas pressure, the zero filling factor, the measured wavenumbers of specific water absorption bands, the sources of the reference library spectra, the integration time, the detector type and serial number, the detector gain (including hardware and software settings).

FTIR system response time — the minimum time required for the output of an FTIR system to accurately reflect a sudden change in the sample gas composition; see APPENDIX B, section B5.

full-width-at-half-maximum (FWHM) — for a single, symmetric absorption band, the full width of the band in wavenumbers (cm^{-1}) between its 50% relative maximum absorption levels.

impinger — a sample collection device, constructed of inert materials, that passes a gas stream through a liquid phase.

infrared detector — a device that (ideally) produces a voltage proportional to the total infrared power incident on it. Examples are 1) the mercury-cadmium-telluride (MCT) detector, which requires cooling (and is often cooled to liquid nitrogen temperature) and 2) the deuterated triglycine sulfate (DTGS) detector, often operated at ambient temperature.

infrared source — a device that emits a pattern, stable in intensity and wavelength profile, of infrared radiation over a wide range of infrared wavelengths. High temperature filaments or ceramic elements, in conjunction with appropriate focusing optics, are often employed.

integration time — the total time over which the interferometric results of single scans are averaged to produce an interferogram (and its subsequent single- and double-beam spectra). Most software packages allow selection of the number of scans rather than the integration time. The integration time is approximately equal to (but is always less than) the time interval over which the selected number of scans is actually executed.

interferant — a compound whose presence in a sample spectrum must be taken into account to accurately determine one or more analyte concentrations, but whose concentration need not be accurately determined.

interferogram — record of the IR detector's response to the modulated component of the interference signal measured as a function of retardation.

interferometer — device that divides a beam of radiant energy into two or more paths, generates an optical path difference between the beams, and recombines them in order to produce repetitive interference maxima and minima as the optical retardation is varied.

least squares fitting (LSF) algorithm — a calculation whereby one or more compound concentrations are estimated from a sample spectrum by minimizing the squared error in Beer's law within a defined analytical region (see Equations C1, C2, C3, C4, C5, and C6).

limit of detection (LOD, ppm) — for a defined FTIR system configuration and sample matrix, an estimate of the lowest detectable concentration of a specific analyte based on the FTIR system's RSA and the analyte's integrated absorbance for a selected analytical region.

line — see "absorption band."

linewidth — see "full-width-at-half-maximum" and "minimum instrumental linewidth."

metering valve — a gas valve allowing reproducible adjustments of a gas stream flow rate on the order of 2% of the valves full flow rate.

mid-infrared — the region of the electromagnetic spectrum from approximately 400 cm^{-1} to 5000 cm^{-1}.

minimum instrumental linewidth (MIL) — for a given FTIR spectrometer and FTIR system configuration, the minimum measured FWHM for any absorption band. In wavenumbers, the MIL is often estimated as the reciprocal of the retardation expressed in cm. The MIL depends on the choice of apodization function and is often larger than the MIL estimated from the retardation.

multi-pass cell — an absorption cell that uses mirrors to pass the infrared radiation through the gas sample more than once; this leads to an absorption path length larger than the physical length of the cell (see also "White cell").

operator — a person familiar with and experienced in performance of only some aspects of this FTIR-based method. Operators may perform many portions of this method, but specific portions of the method must be performed by an "analyst."

peak — see "absorption band."

qualitative analysis — examination of sample spectra to determine the presence or absence of particular compounds in a sample.

quantitative analysis — estimation of the actual concentrations of a specific set of compounds using a specific set of analytical regions.

reference spectra — absorption spectra of gases with known chemical compositions, recorded at a known absorption path length, which are used in the quantitative analysis of gas samples.

residual squared area (RSA) — a measure of the noise (random and systematic) and/or spectral artifacts for an absorbance spectrum in some analytical region; see APPENDIX B, section B2 for a mathematical definition. The RSA can be used to estimate the LOD for a given compound measured with a given FTIR system configuration.

retardation — optical path difference between two beams in an interferometer; also known as "optical path difference" or "optical retardation." In the case of a standard Michelson interferometer, the retardation is simply twice the distance moved by a mirror in the interferometer during a scan.

rotameter — a device indicating the volumetric flow rate of a gas by the vertical displacement of an object suspended by the gas stream.

sample interface — that part of the FTIR system that comes in contact with the sample and/or calibration gases. It includes the sample probe, sample filter, sample line, sample pump, gas valves, internal surfaces of the absorption cell, pressure gauge, sample rotameter, the vent lines, and the calibration components (gas cylinders, regulators, and rotameters).

sampling location — the point in space at which sample gases enter the sample interface.

scaling — application of a multiplicative factor to the absorbance values in a spectrum.

scan — digital representation of the detector output obtained during one complete motion of the interferometer's moving assembly or assemblies.

single-beam spectrum — Fourier-transformed interferogram, representing the relative detector response vs. wavenumber.

NOTE: The term "single-beam" is used elsewhere to denote any spectrum in which the sample and background interferograms are recorded on the same physical absorption path; such usage differentiates such spectra from those generated using interferograms recorded along two physically distinct absorption paths (see "double-beam spectrum" above). Here, the term applies (for example) to the two spectra used directly in the calculation of transmittance and absorbance spectra of a sample.

system zero (SZ) spectrum — the absorbance spectrum of a non-absorbing gas (nitrogen or zero air) acquired using those portions of the sampling interface used to acquire actual sample gases.

transmittance, T — the ratio of radiant power transmitted by the sample to the radiant power incident on the sample. Estimated in FTIR spectroscopy by forming the ratio of the single-beam sample and background spectra; often presented as $\%T$ ($100 \times T$) in spectral representations.

uncertainty — a mathematical quantity determined in an LSF procedure, used to estimate the likely error in the determination of the sample concentration in a procedure; see Equations C1, C2, C3, C4, C5, and C6.

wavelength λ, — the physical distance between successive maxima in the electromagnetic waves that comprise light. The wavelength and speed of light depend on the medium through which the light travels.

wavenumber, w — the reciprocal of the wavelength, also the number of wavelengths of light per unit length, usually expressed in the units cm^{-1}. As is true of both the speed and wavelength of light, the wavenumber is dependent on the medium through which the light travels. (See APPENDIX C, section C4 and "frequency" in this appendix.)

wavenumber adjustment — reassignment of the cm^{-1} values associated with single- and/or double-beam spectra. Adjustments may be made locally by shifting or stretching the wavenumber scale, or globally stretched by changing the laser wavenumber during the FFT.

White cell — alternate name for a multi-pass absorption cell (see "multi-pass" above) indicating its inventor.

zero filling — the addition of zero-valued points to the end of a measured interferogram. In most computer programs, specification of a zero filling "factor" of N results in an interferogram with N times as many points as the original interferogram.

APPENDIX B. SYSTEM TESTS

These procedures must be conducted at least once on new or significantly altered (by replacement of components, dis- and reassembly, etc.) systems. The tests described in sections B2 and B4 must also be repeated during either the pretest preparations or quality assurance procedures. In all cases, activate the FTIR system and allow sufficient time for the infrared source, the infrared detector, and (if required) the temperature control systems to stabilize before proceeding.

B1. Absorption Path Length

Obtain one or more absorbance spectra of a CTS gas (ethylene at 200 ppm · m to 300 ppm · m is recommended) at the gas temperature and pressure of a reference CTS spectrum of the same compound. For each spectrum, calculate the indicated absorption path length as

$$L_S = \frac{L_R P_R A_S}{P_S A_R}, \qquad \text{(Equation B1)}$$

where: L_S = path length indicated by the sample CTS spectrum (m),
L_R = path length of the reference CTS spectrum (m),
A_S = area of the sample CTS spectrum (cm^{-1}),
A_R= area of the reference CTS spectrum (cm^{-1}),
P_S = pressure of the sample CTS spectrum (kPa), and
P_R = pressure of the reference CTS spectrum (kPa).

When multiple CTS spectra are available, assign to L_S the mean of the single-spectrum L_S results. The reference CTS spectrum path length and concentration used must be based on multiple, high-quality gas standards and physical length measurements (see APPENDIX D, section D5). The analyst must document criteria for the selection of the analytical region and any baseline correction procedures employed.

B2. Residual Squared Area

NOTE: If the following calculations are performed during testing or as part of the QC procedures (steps 14, 15, 16, and 17), perform them using a workspace air spectrum instead of the "water vapor (absorbance) spectrum" described in the two paragraphs below.

Use the integration time selected for field testing in recording the spectra described below. Record a background spectrum of dry nitrogen gas or zero air. Using a suitable impinger, humidify the nitrogen or zero air stream and record a single-beam spectrum at an absolute pressure between 96.6 kPa and 103 kPa (725 mmHg and 795 mmHg). Form the absorbance spectrum of this water vapor sample from the single-beam spectra. Assign the spectrum a unique filename and save it for the calculations described below.

From this water vapor spectrum, subtract a scaled spectrum (see APPENDIX A) formed from the water vapor reference spectrum to be used in subsequent quantitative analyses. The scaling factor may be varied to minimize the absorbance in the resulting difference spectrum in the various analytical regions to be used in the analyses. Subtract a constant offset, a linear function, or a quadratic function from the difference spectrum in each analytical region to form a residual spectrum R for each region. For each residual spectrum R with discrete absorbance value R_i for wavenumber $i = p$ to q, in the wavenumber range w_p to w_q, the RSA, A_{RS}, is defined as:

$$A_{RS} = \frac{w_p - w_q}{q - p + 1}\sqrt{\sum_{i=p}^{i=q}\frac{R_i^2}{q-p}}. \qquad \text{(Equation B2)}$$

The RSA has the dimensions (cm^{-1}) and serves as a measure of the integrated absorbance of spectral noise and water subtraction artifacts over the analytical region. The RSA is compared to the total absorbance of a compound in the same region to estimate the LOD for the compound in that region (see APPENDIX D, section D9 and APPENDIX E, section E1).

The calculation described above assumes that water is the only significant infrared absorber in the samples besides the analytes and that only one analyte absorbs in any analytical region. If other analytes or interferants are present, a more conservative RSA may be estimated by adding the absorbance of the additional compounds to the difference spectrum using a set of suitable reference spectra, then subtracting their absorbance using a *different* set of reference spectra.

B3. Minimum Instrumental Linewidth

Evacuate the absorption cell to a pressure below 13.3 kPa (100 mmHg) and record a background spectrum. Obtain a workspace air sample at an absolute pressure of approximately 40 kPa (300 mmHg). Record the absorbance spectrum of this low-pressure sample. Measure at the FWHM linewidth, in cm^{-1}, of at least two isolated water vapor lines (for example, the lines near 1918 cm^{-1} and 2779 cm^{-1}). The MIL is the mean of these FWHM measurements.

B4. Wavenumber Reproducibility

NOTE: If this calculation is performed during testing or as part of the QC procedures (see steps 6 and 10), perform these determinations using a workspace air spectrum instead of the water vapor absorbance spectrum described in section B2.

Using a water vapor spectrum recorded as described in section B2, determine the center wavenumber values w_{S1} and w_{S2} of two isolated water vapor absorption features; the peaks near 1918 cm^{-1} and 2779 cm^{-1} are suggested, though any other pair of isolated lines separated by 500 cm^{-1} or more is suitable. Compare these results to those center wavenumber values w_{R1} and w_{R2} and for the same absorbance features in the water vapor wavenumber standard associated with the reference library to be used in quantitative analyses as follows: Calculate the wavenumber reproducibility, R_W, in cm^{-1} for each of the two absorption bands as

$$R_{Wi} = \left| w_{Ri} - w_{Si} \right|, \qquad \text{(Equation B3)}$$

for $i = 1, 2$.

Compare the maximum of these two values to the MIL for the FTIR system (see section B3). If the wavenumber reproducibility to MIL ratio exceeds 2%, adjustment of the wavenumber scale for the sample spectra may be required.

Mathematical wavenumber adjustments may be made locally by shifting or stretching the wavenumber scale, or globally stretched by changing the laser wavenumber during the FFT. However, large shifts (on the order of 5% or more of the MIL) indicate that the system requires physical adjustments, such as realignment of the laser system responsible for control of the interferometer's moving element. In addition, mathematical wavenumber adjustments require some sort of interpolation procedure in conjunction with the quantitative spectral analysis, and those procedures may result in spectral mismatches whose effects on the accuracy of the analysis are not easily quantified.

The necessity of such wavenumber adjustments depends, in part, on the widths of the absorption peaks of the compounds involved in the spectral analysis. Because many of the absorption bands of water — a nearly ubiquitous interferant in workspace air IR analysis — are very narrow, an accurate analysis usually requires the relatively stringent limits placed above on the wavenumber reproducibility to MIL ratio. However, it is possible to obtain accurate results when this ratio exceeds the recommended limit, especially when only broad absorbance features are actually employed. The analyst may choose to approve analytical results obtained when this ratio exceeds the recommended limit.

B5. System Response Time

Direct nitrogen or zero air through the entire sample interface and record spectra at approximately 30 s intervals. Abruptly replace the nitrogen or zero air gas flow with CTS gas and continue to record spectra. The system response time is the subsequent time required for the FTIR system to generate an absorbance spectrum in which the CTS compound's calculated concentration reaches 95% of the final (stable) concentration value indicated in later spectra.

B6. Detector Linearity

For the chosen optical configuration, attenuate the power incident on the detector by either 1) modifying the aperture setting or 2) placing filters (neutral density or mesh) in the infrared beam path (see Figure C1). At approximately 100%, 50%, and 25% of the system full IR power level, collect pairs of background and CTS spectra. Compare the areas of the CTS bands for the three spectra and verify that they are equal to within 5% of their mean value. If they are not, apply software linearization corrections to the interferometric data according to the manufacturer's instructions. If this option is unavailable, it is necessary to either 1) characterize the system non-linearity and/or apply appropriate concentration corrections or 2) operate the system with attenuation sufficient to ensure linear detector response.

APPENDIX C. GENERAL DESCRIPTION OF FTIR SPECTROMETRY

C1. FTIR Spectrometer Components

Figure C1 illustrates the basic FTIR spectrometer configuration required for gas phase analyses. The infrared radiation emitted by the infrared (IR) source contains energy at all wavelengths between 2.0 µm and 20 µm; this is the portion of the electromagnetic spectrum usually referred to as the "mid-infrared." In the units typically employed in FTIR spectroscopy (wavenumbers, or cm^{-1}), this is the wavenumber range 5000 cm^{-1} to 500 cm^{-1}. The IR radiation passes through an interferometer, where the motion of an optical element, usually a mirror, optically modulates the infrared beam. The modulated IR beam then enters an absorption cell through a window (typically made of potassium bromide or zinc selenide) and interacts with the gases of interest. The physical length over which this interaction takes place is the "absorption path length." In "multi-pass" (or "White") absorption cells, mirrors within the cell direct the IR beam through the sample gas many times; in such cells, the absorption path length can be from 4 to 50 (or more) times the cell's physical length. (A larger absorption path length generally leads to greater sensitivity.) The IR beam then exits the sample cell via a second window and is refocused onto an IR detector. Because this extractive technique requires the transport of gas samples through the FTIR absorption cell, the design and integrity of the sampling system is of great importance. It is also important that the sampling system allow the operator to perform all the necessary calibration and sampling procedures without compromising the speed and flexibility of the analytical system.

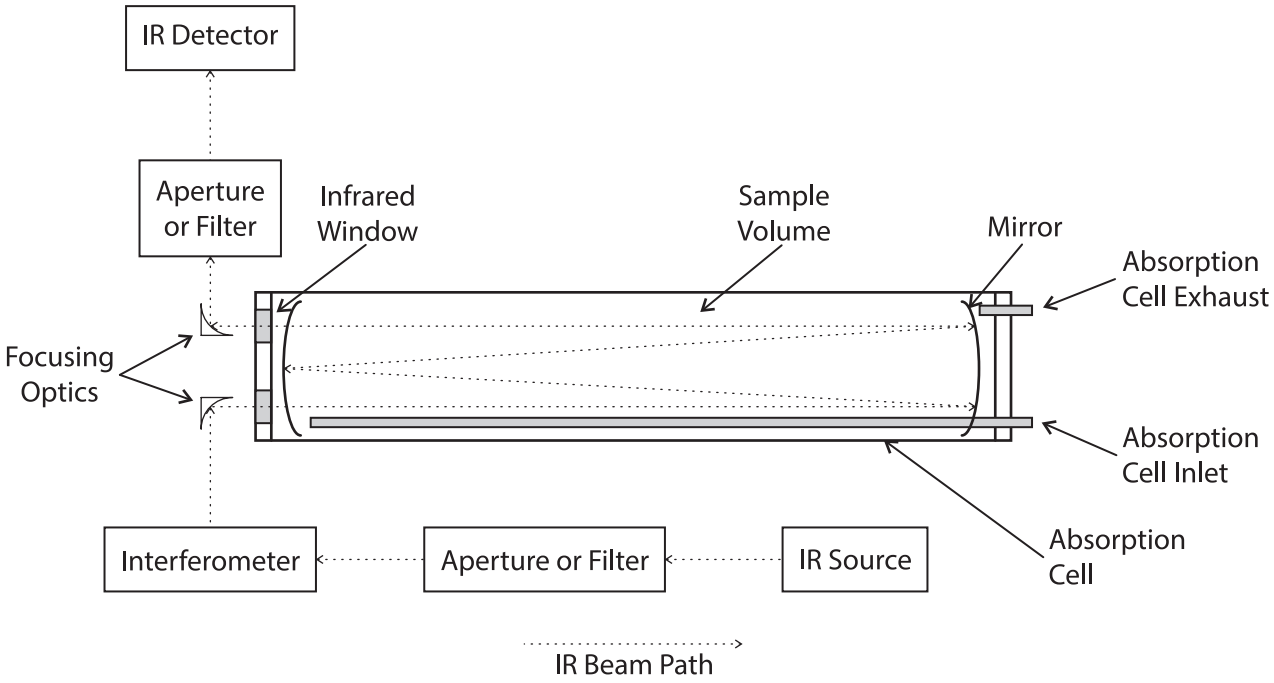

Figure C1. FTIR spectrometer components and beam path.

Figure C2 illustrates a sampling system configuration that meets these requirements, though other configurations are possible. A computer controls the actions of the interferometer and records the voltage output of the IR detector throughout the motion of the interferometer's optical element. Ideally, the detector voltage is proportional to the total power in the IR beam. The computer must accurately record the detector voltage as a function of the position of the moving element in the interferometer, so a secondary, laser-based optical system is usually used to measure the moving element's position very precisely. In most circumstances, the motion of the mirror or other optical element is repeated many times and the resulting individual "scans" are "co-added" (averaged) to reduce the system's RSA.

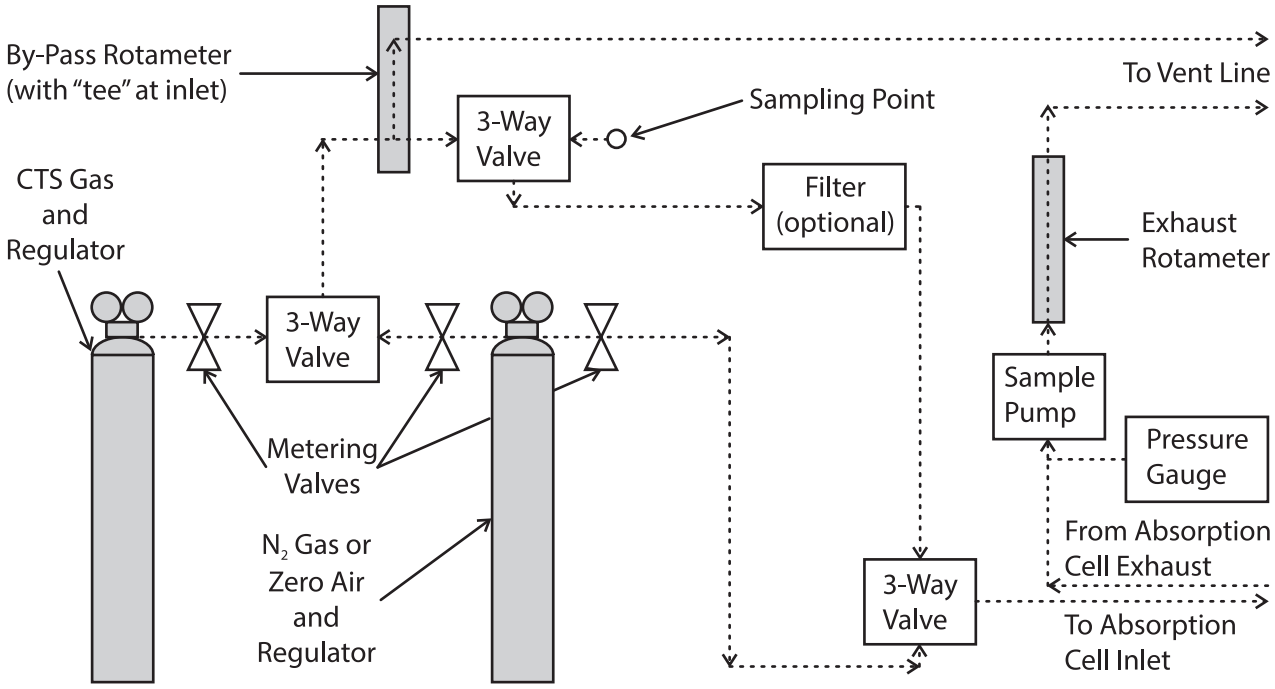

Figure C2. Sampling components and sample paths.

A plot of the resulting IR power-vs.-position signal, referred to as an interferogram, is shown in Figure C3. This interferogram is the co-added result of 64 scans with only nitrogen gas (and some low level of water vapor) present in the absorption cell. Nitrogen is one of the few compounds that does not interact with infrared radiation, so this interferogram very closely represents the fundamental FTIR system response in the absence of a sample. Note that the signal is relatively large near the beginning of the interferogram, where the "zero phase difference (ZPD) burst" is located. The ZPD is often used to rapidly obtain an estimate of the IR signal strength during alignment of the optical system.

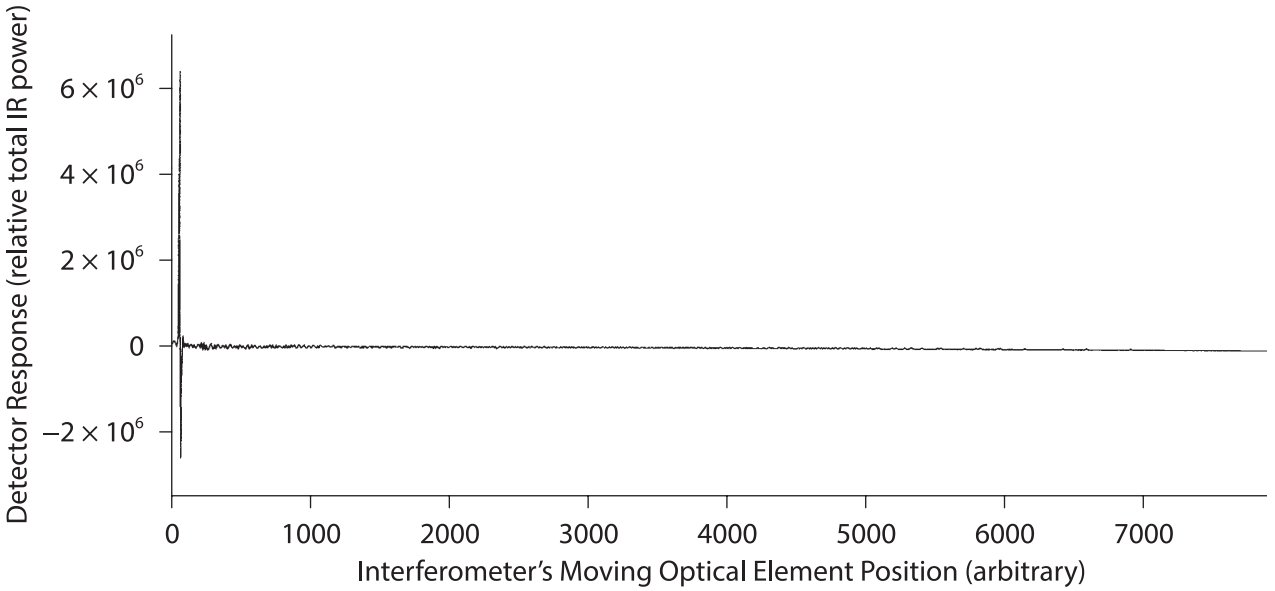

Figure C3. Mid-infrared interferogram.

C2. The FFT

Every data point in the interferogram contains intensity information about every infrared wavelength transmitted from the source to the detector. It is possible to recover the intensity information as a function of wavelength through application of an FFT, from which the FTIR technique's name is derived. This digital transformation of the interferogram can be thought of as the mathematical inverse of the optical modulation applied to the infrared beam as it passes through the interferometer. Its function is similar to that of the human brain and ear, which provide intensity information (loudness) versus wavelength (pitch) for complex signals (sound waves) incident on the eardrum. (Note that, as for an interferogram, each point in a complex sound wave contains intensity information about every pitch contained in the wave. Yet the ear and brain allow a symphony audience to immediately perceive, for instance, that the piccolo is playing very loudly while the tuba is playing very quietly.) Reference 12 (chapter 3) provides a complete mathematical description of the FFT.

C3. Instrument Resolution, Apodization Function, and MIL

Most software packages supplied with FTIR systems provide several options associated with the collection of data and application of the FFT. These typically include - at least - the nominal "instrument resolution" (specified in cm^{-1}) and the "apodization function" (e.g., "boxcar" and "triangular"). These parameters are very important in quantitative spectroscopy and are addressed in turn below.

The instrument resolution is the most fundamental and important instrument parameter. It specifies the nominal minimum FWHM, in cm^{-1}, of any spectral "peak" (or "line") in the final instrument output. Every FTIR instrument has a minimum FWHM determined by the maximum distance traversed by the interferometer's moving element during a single scan. (For the basic Michelson interferometer, the FWHM in cm^{-1} is equal to $(2d)^{-1}$, where d is the distance in cm traversed by a moving mirror during a scan.) Clearly, instruments with low FWHM provide more spectral information than instruments with higher FWHM capability. However, this additional information comes at high costs associated with the design, construction, size, mechanical stability, portability, speed, and RSA of the instruments.

It is important to recognize the two uses of the word "resolution" in the nomenclature used to describe FTIR spectrometers: Instruments of high resolving power, or "*high* resolution," provide spectral features of *low* FWHM; when the nominal resolution is specified in units of cm^{-1}, a *lower* cm^{-1} specification corresponds to *higher* resolving power, or "higher resolution". Most commercially available FTIR spectrometers suitable for field use provide FWHM values greater than or equal to 0.5 cm^{-1}, that is, they are systems whose nominal spectral resolution is specified as a number higher than 0.5 cm^{-1}. Most of the instruments capable of higher resolution (lower FWHM) are suitable for use only in very stable laboratory environments.

Standard FTIR operating software always provides options for recording spectra with FWHM values higher than the instrument's actual lower FWHM limit. These options simply move the mirror (or other optical element) through only some fraction of its maximum possible travel. Operating the instrument in this manner results in larger FWHM values ("lower" resolution, and shorter interferograms) than the instrument is mechanically capable of providing. Spectra of lower resolution (higher FWHM) provide less information, but can be generated more quickly and, in most cases, with lower RSA than spectra of higher resolution.

The instrument operator can also choose the apodization function to be used in the generation of FTIR spectra. Apodization is a mathematical alteration of the interferogram that can be performed before application of the FFT. Several standard alteration functions have been devised and each affects the final absorption spectrum of the sample gas in a different way. As with the selection of instrument resolution, each choice has its advantages and drawbacks. The simplest choice, known as the "boxcar apodization" function, results in the lowest FWHM but also in relatively low signal to noise (S/N) ratio. (Spectra generated with the boxcar function are often referred to as "unapodized" spectra.) Other choices (triangular, Norton-Beer, and several other apodization functions) provide higher S/N ratio

at the cost of higher FWHM values and other trade-offs in quantitative spectroscopy. Reference 12 provides a more thorough description of the characteristics of various apodization functions.

For a given instrument configuration — which includes the nominal spectral resolution and the choice of apodization function — every FTIR system is capable of generating absorption bands with an MIL. Unlike the actual spectral resolution (which has several accepted physical definitions — see reference 12, chapter 1, section IV) and nominal spectral resolution parameters, the MIL is a parameter that is readily measured to the accuracy required for practical applications of FTIR spectrometry. It can be measured using the water absorption bands present in low-pressure workspace air samples (see APPENDIX B, section B3).

C4. Single-Beam Spectra

The mathematical result of the FFT (applied to an apodized IR interferogram) is a called a single-beam spectrum. Single-beam spectra represent the infrared power transmitted through the FTIR spectrometer as a function of the infrared "wavenumber" w, which is usually expressed in the units of reciprocal centimeters (cm^{-1}). The wavenumber is actually a measure of the frequency, rather than the wavelength, of the infrared radiation. In a vacuum, the wavelength and frequency are related through the equation $v = c / \lambda$, where λ is the wavelength (cm), v is the frequency (s^{-1}, or Hz), and c (cm/s) is the speed of light, equal to $2.99792954 \times 10^{10}$ in a vacuum. In these units, the wavenumber in cm^{-1} is given by the equation $w = 1/\lambda = v/c$. Figure C4 presents the single-beam spectra for two samples consisting mainly of nitrogen gas (≥99%) but with different concentrations (≤1%) of water vapor. The vertical scales of the two spectra are nearly identical, but they have been offset for clarity. The detected infrared power in certain wavenumber regions is clearly lower in the high moisture sample, indicating both the qualitative nature and strength of water's absorption of infrared radiation.

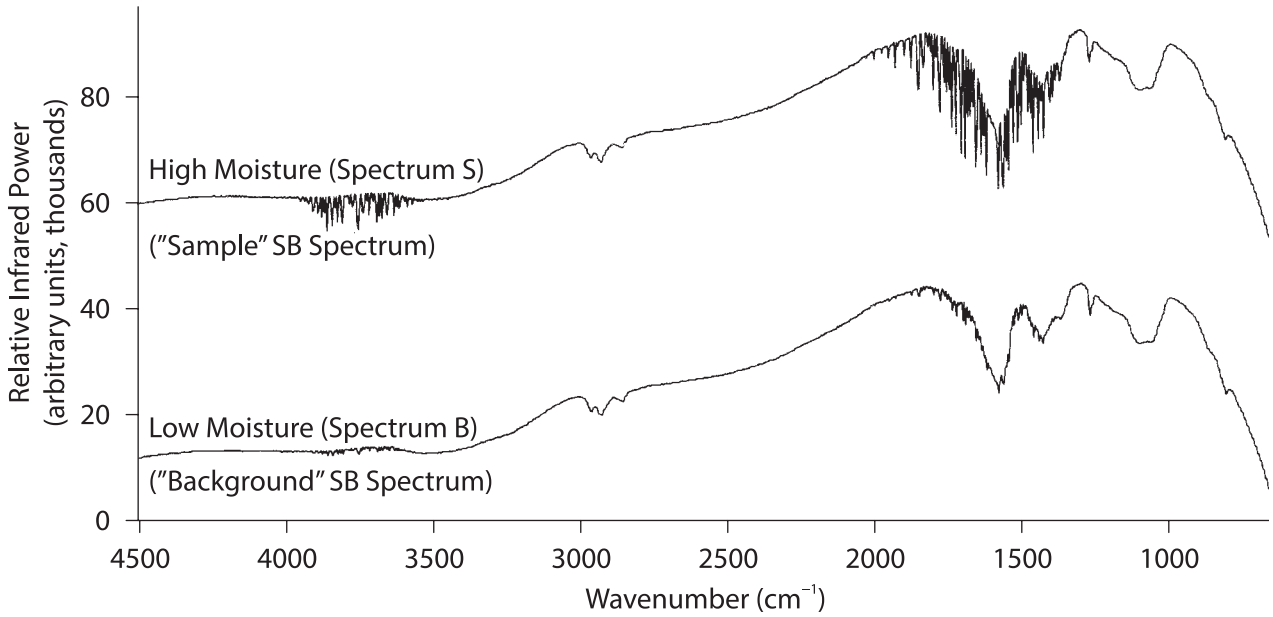

Figure C4. Single-beam spectra of nitrogen at different moisture levels.

C5. Double-Beam Spectra — Transmittance and Absorbance

Combinations of pairs of single-beam, such as the pair of spectra S and B shown in Figure C4, are referred to as double-beam spectra; they provide the quantitative basis for FTIR spectroscopy. One type of double-beam spectrum is the transmittance. The percent transmittance of a sample gas possessing the single-beam spectrum S — with respect to the background single-beam spectrum B — is defined as $T = 100 \times I_S / I_B$ (%), where I_S and I_B are the respective transmitted intensities; a transmittance value is

defined for each wavenumber value of the two spectra. If the background spectrum B closely represents the response of the FTIR system to a transparent sample, then the percent transmittance closely approximates the percentage of the infrared radiation transmitted by the sample (represented by the spectrum S). Because water is the only absorbing compound present in the single-beam spectrum B, the spectrum transmittance (shown in Figure C5) closely approximates the percent transmittance spectrum of water.

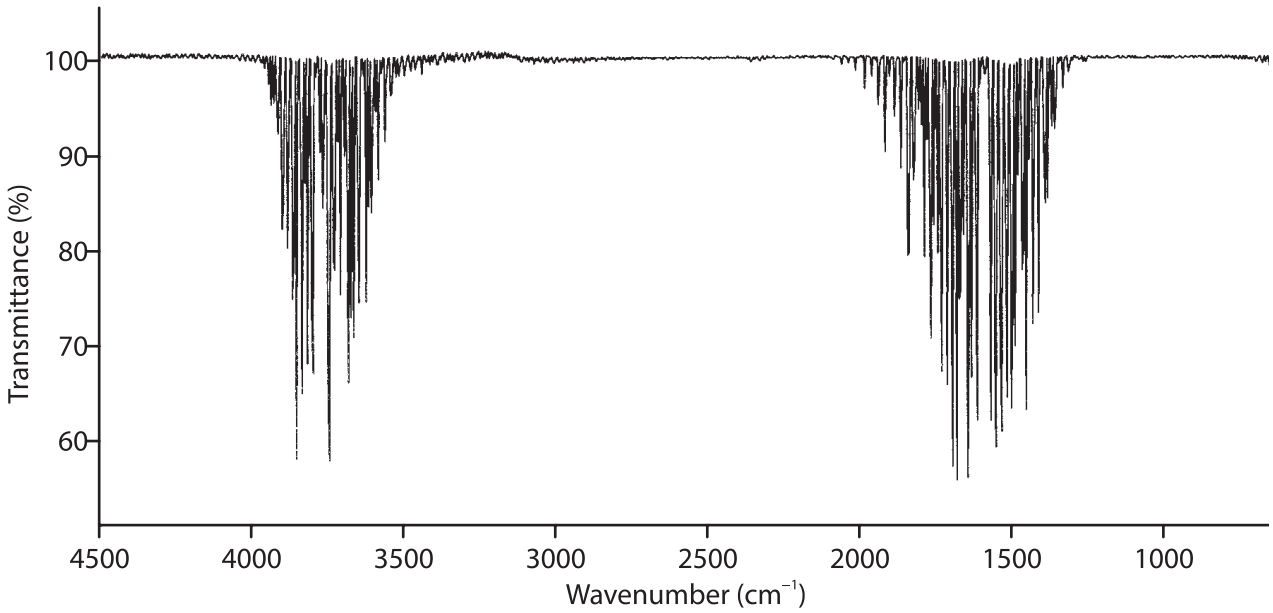

Figure C5. Double-beam transmittance spectrum of water.

The same pair of spectra define the (double-beam) absorbance *A* of the sample through the equation $A = -\log(I_S / I_B)$. The absorbance spectrum of water, as approximated by the two single-beam spectra S and B, is shown in Figure C6. The absorbance is the desired quantity because it appears in the general linear absorption model known as Beer's law (see below).

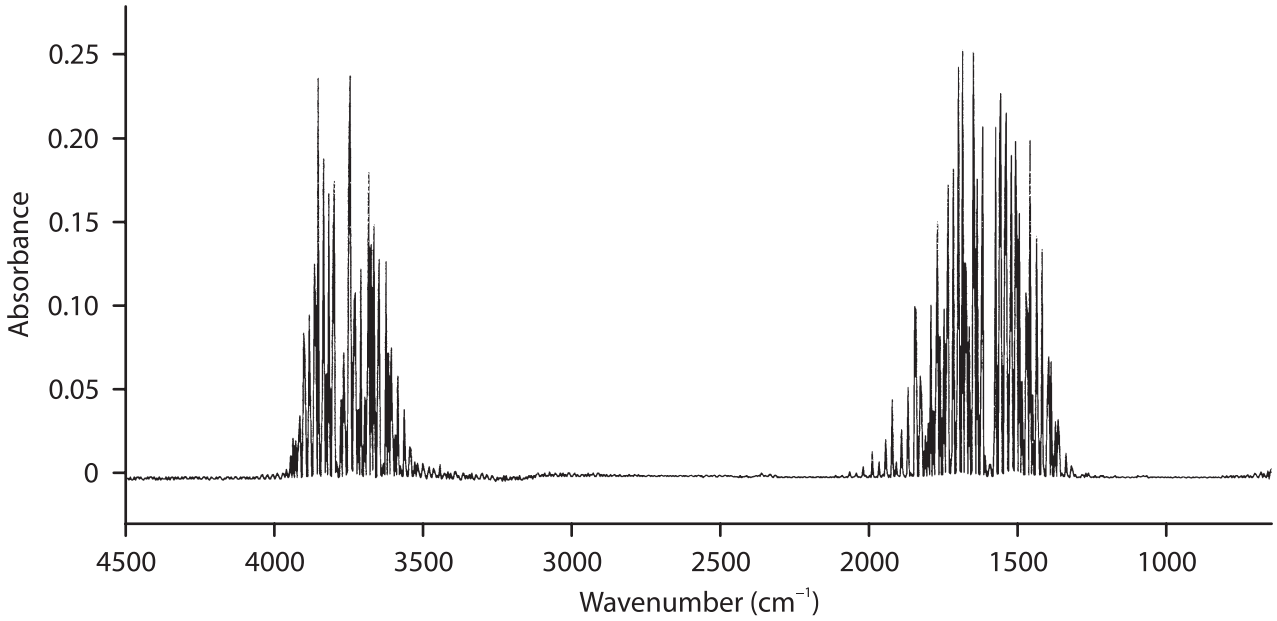

Figure C6. Double-beam absorbance spectrum of water.

C6. Beer's Law

The absorbance spectrum of a sample gas is determined from single-beam spectra of an infrared-transparent gas (the background spectrum) and the sample gas (see section C5). The fundamental relationship connecting the absorbance spectrum of a sample gas to the concentrations of the compounds comprising the sample is referred to as Beer's law. This relationship can be written as

$$A_i = \sum_{j=1}^{j=M} L_S a_{ij} C_j, \qquad \text{(Equation C1)}$$

where: i = an index labeling the frequencies of the observed absorbance values in the sample's absorbance spectrum,
A_i = the observed absorbance of a sample at the i^{th} wavenumber,
L_S = the sample absorption path length (m),
j = an index labeling the absorbing compounds comprising the sample,
a_{ij} = the absorptivity of the j^{th} compound at the i^{th} wavenumber (ppm/m),
C_j = the volumetric concentration of the j^{th} compound (ppm), and
M = the number of absorbing compounds in the sample.

The procedures described in this method are all related to the parameters that comprise Beer's law. The following list describes these procedures and relationships in a general context:

1. Record a reference absorbance spectrum for each interesting compound of a nitrogen-diluted sample of the pure compound, at a known concentration and path length, then divide the absorbance at each point in that spectrum by the CPP. This process yields the absorptivity spectrum (a_{ij}), or reference spectrum, for each compound.
2. Measure the absorbance A_i for the mixture of compounds (see steps 5 and 9 above).
3. Determine the path length L_S for the current measurement of A_i (see steps 5 and 7 above).
4. Select the analytical region — that is a set of frequencies, corresponding to the possible values of the index i — that are to be used to determine the concentration of each compound, and then mathematically invert Equation C1 to determine the desired concentrations C_j. (APPENDIX E addresses the topic of spectral analysis in detail.)

NOTE: The true absorptivity for a single gaseous compound is a characteristic only of the compound's structure. However, details of the FTIR system performance and operation affect the observed absorptivity and its accuracy. Similarly, FTIR measurements provide only an approximation of the true absorbance spectrum of a mixture of gaseous compounds, though it is, under many circumstances, a sufficiently accurate approximation. It is the responsibility of the analyst to verify and ensure that the reference and sample spectra provide a sufficiently accurate quantitative analysis according to Beer's law. The following sections of this appendix describe the mathematics of such an analysis. APPENDIX D addresses the topics of developing and using reference spectral libraries. APPENDIX E provides an illustrative example of the design and evaluation of the quantitative analytical process.

C7. Determining Concentrations with LSF Algorithms

When a sample gas contains only one absorbing compound, Equation C1 simplifies to

$$A_i = L_S a_{ij} C_j. \qquad \text{(Equation C2)}$$

This means that in any analytical region where only one gas absorbs, any one (of the usually many) absorbance spectrum values A_i can be used to yield the concentration C_j.

The absorbance area A_S for a single-component spectrum in an analytical region (from $i = p$ to $i = q$) can be written as

$$A_S = \sum_{i=p}^{i=q} A_i = \sum_{i=p}^{i=q} L_S a_{ij} C_j = L_S C_j \sum_{i=p}^{i=q} a_{ij} = L_S C_j A_R, \qquad \text{(Equation C3)}$$

where A_R is the area in the reference spectrum for that compound in the same analytical region. (This is the basis of the absorption path length L_S calculation described in step 7 and APPENDIX B, section B1.) Because calculation of the absorbance area involves many points in the sample spectrum, Equation C3 leads to much more accurate results than the single-point calculation represented by Equation C2.

However, when many absorbing compounds are present in a sample, the absorption patterns of the various compounds often overlap. In this case, there is usually not an isolated analytical region for each compound in which only that compound absorbs infrared radiation; no single absorbance point and no simple absorbance area is suitable for determining any of the component concentrations. In this case, the simplest method for determining concentrations is to use an LSF algorithm.

LSF algorithms use the fact that there is some set of estimated concentrations D_j that minimizes the "squared error" in Beer's law for any given analytical region, for any set of compounds. The only requirement on the chosen analytical region is that it must contain a sufficient number of data points; since each FTIR spectrum contains many thousands of absorbance values, this requirement is nearly always fulfilled.

If we use the estimated concentrations D_j (rather that the true concentrations C_j) in Beer's law, they will lead to some estimated error e_i at each value of i (that is, at each point in the analytical region we choose). Equation C1 becomes:

$$A_i = e_i + \sum_{j=1}^{j=M} L_S a_{ij} D_j. \qquad \text{(Equation C4)}$$

The estimated squared error E^2 (or "variance") in Beer's law using the estimated concentrations is:

$$E^2 = \sum_{i=1}^{i=N} e_i^2 = \sum_{i=1}^{i=N} \left[\sum_{j=1}^{j=M} L_S a_{ij} D_j - A_i \right]^2, \qquad \text{(Equation C5)}$$

where N represents the number of absorbance values in the analytical region. Reference 13 demonstrates that 1) for $N > M$ there is a unique set of estimated concentrations D_j that minimizes the estimated squared error; 2) this set of values is calculable from the known quantities in Equations C1, C2, C3, C4, and C5; and 3) estimates σ_j of the uncertainties in the quantities D_j are also calculable from the same quantities. The value $3\sigma_j$ is generally accepted as a conservative estimate of the statistical uncertainty in the related estimated LSF concentration (see reference 4).

The estimated LSF error at each point in the analytical region,

$$e_i = A_i - \sum_{j=1}^{j=M} L_S a_{ij} D_j, \qquad \text{(Equation C6)}$$

is usually stored following the analysis as a "residual spectrum," which can provide an estimate of the LODs for other compounds. In addition, the residual spectrum and the concentration uncertainties can allow the analyst to detect and identify compounds that are actually present in the sample gas but which were not included in the mathematical analysis. APPENDIX E provides an example illustrative of these procedures.

The above description illustrates a simple and easily interpreted LSF analysis. More sophisticated LSF analytical techniques, possibly more accurate for particular types of samples, are described in the literature (see, for example, reference 14 and references therein).

C8. Calibration Transfer and Reference Libraries

Equations C1, C2, C3, C4, C5, and C6 demonstrate the importance of quantities L_S (the absorption path length) and a_{ij} (the absorptivity) in FTIR spectrometry. Accurate determinations of these quantities allow the use of reference libraries for quantitiative analyses without the necessity of compound-specific field calibrations. The system tests described in the procedures and in APPENDIX B are intended to ensure suitability of the system configuration for such calibration transfers, as are the requirements

of obtaining CTS spectra in field. APPENDIX D describes procedures for recording and processing reference library spectra.

C9. Corrections to Deviations from Beer's Law Exhibited by FTIR Spectra

Beer's law is based on fundamental, well-established physical principles. It holds absolutely for gas samples that are at thermal equilibrium and dominated by induced (rather than spontaneous) emission and absorption processes. (See Note below.) However, *this is not to say that the absorbance, as measured by an FTIR spectrometer, follows Beer's law under all conditions*. Deviations from Beer's law in FTIR spectra are often observed; however, they indicate inaccuracies in the FTIR spectra, not "violations" of Beer's law. For example, deviation from Beer's law is commonly exhibited by sets of single-component reference spectra recorded over a range of absorbance levels. At large enough values of the absorbance, the points A_i of stronger absorption bands of such spectra no longer increase linearly with the CPP $L_R \cdot C_j$; this is why Table 2 specifies a maximum ppm · m value for the listed reference spectra. If the assumption of detector linearity does not hold (see APPENDIX B), similar effects are often present in reference and sample spectra; this is the basis for the system test described in APPENDIX B, section B6.

Mathematical correction of the concentration estimates D_j derived from Beer's law can often reduce the error in sample analyses when either type of non-linear effect occurs. Figure C7 provides an example of such a correction. The actual and calculated ppm · m values for a set of reference spectra are plotted against each other, a "piece-wise linear" approximation to the pattern is shown by the solid line, and the dashed line indicates the ideal linear behavior based on the spectrum of lowest absorbance. At any ppm · m value indicated in a Beer's law sample analysis (that is, for any y-axis value up to approximately 900 ppm · m in the example), reasonably accurate values are available from the corresponding x-axis position of the solid line. If the analyst employs such corrections, he or she should also calculate the residual (Equation C6) using the reference spectrum that minimizes the squared error (Equation C5). FTIR analysts and manufacturers have devised other correction procedures to improve the sample analysis accuracy in such circumstances, and these are included in some commercially available software packages.

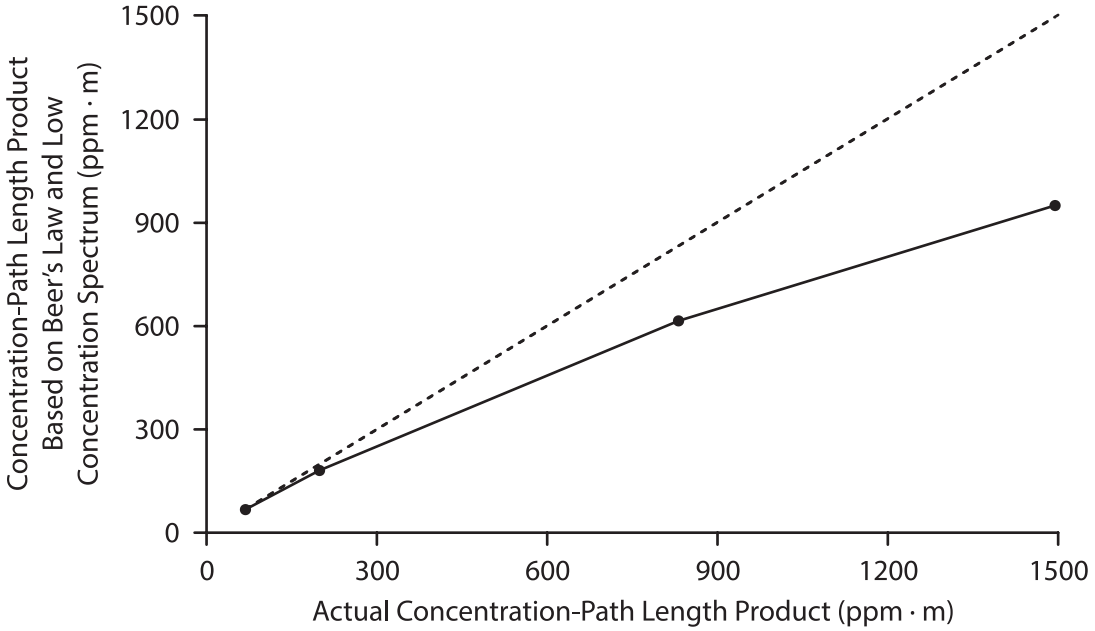

Figure C7. Example absorbance non-linearity for a set of single-component reference spectra.

NOTE: Intense infrared radiation, such as that produced by some lasers, can induce non-equilibrium populations of a molecule's rotation-vibration energy states. However, the thermal infrared sources

used in commercially available FTIR spectrometers are much weaker than such lasers. In gases at atmospheric pressure, the commercially available thermal sources induce transition rates between quantum energy states that are small, compared to those of the competing collisional relaxation processes, and cannot induce non-equilibrium energy state populations. In addition, the induced transition rates related to absorption and emission at mid-infrared frequencies are much larger than the corresponding spontaneous (natural) emission rate. As a result, all *accurate* FTIR measurements at mid-infrared frequencies obey Beer's law to within the uncertainty related *only* to the S/N ratio of the measured spectra.

APPENDIX D. PURPOSES, PREPARATION, AND USE OF REFERENCE SPECTRAL LIBRARIES

D1. Purposes of Reference Spectral Libraries

FTIR analyses rely on the availability of libraries of spectral information on the compounds of interest. For gases, the measured absorbance of a single component is often completely independent of the concentrations of other gases comprising the sample, and single-component reference spectra are usually employed. (For condensed phases, there are often strong interactions between components, and reference spectral libraries of mixtures are usually required.) Reference libraries may be used for quantitative measurements of analyte concentrations, for the mathematical removal of spectral features of interferants in a mixture, or simply for the identification of compounds in a mixture. Clearly, the required level of quantitative accuracy of the library is different for these three tasks; the highest quality is required for analyte concentration determinations, while no quantitative information is required for interferant removal and compound identification.

A useful characteristic of extractive FTIR spectrometry is that it provides accurate field measurements for many compounds, but requires field calibration procedures involving only two compounds. The water vapor available in every ambient air sample serves to calibrate the wavenumber (x) axes of FTIR absorbance spectra; a single CTS gas serves to calibrate their concentration-related (y) axes. When these two field calibrations are combined with an appropriate reference spectral library describing additional compounds, the measurement capability of the technique is practically limited only by the quality and scope of the reference library. If the reference library is carefully prepared and properly employed, this characteristic can lead to greatly lowered field test costs, since the calibration materials need be handled only once and only in the laboratory.

D2. Reference and Field FTIR System Configurations

In the ideal case, the reference library can be prepared on the field instrument, but this is often impractical; the reference library is usually prepared on specific laboratory systems and employed in measurements made with many field systems. Reference libraries recorded on a specific instrument provide accurate quantitative analyses for spectra recorded on other instruments only when the configurations of the various systems are compatible. Table D1 lists compatibility considerations for the reference system configuration parameters.

D3. Wavenumber Standard Spectra

Except in extremely dry conditions, the IR absorption by water vapor in workspace air is detectable at even very short absorption path lengths. The wavenumber positions of water vapor indicated by the reference system allow the analyst to confirm the wavenumber accuracy of sample spectra recorded on a different FTIR system in the field. Reference spectra used for this purpose are referred to here as the wavenumber standard spectra.

Every spectrum in a reference library should be associated with a wavenumber standard spectrum collected under the identical system configuration; even when the reference FTIR system is in a stable environment, it is recommended that a wavenumber standard spectrum be recorded daily with the system.

Before recording reference spectra, the analyst should check the most recent wavenumber standard spectrum against previous wavenumber standard spectra in the library; see APPENDIX B, section B4 for recommended calculations. If the wavenumber reproducibility of the system is poor, the resulting reference spectra may not be suitable for quantitative use on other field systems.

Table D1. Reference and field system configuration parameters

Parameter	Requirements for Reference and Field Systems
Minimum instrumental linewidth	Reference MIL must be less than or equal to field MIL. See APPENDIX B, section B3 for MIL measurement technique.
Gas temperature	Reference temperature within 20 °C of field temperature. Density corrections based on ideal gas law are accurate over only this narrow temperature range and their exact accuracy is compound-dependent.
Gas pressure	Reference pressure within 20% of absolute field pressure. Pressure corrections based on ideal gas law are accurate over at least this range, but their accuracy is compound-dependent. Atmospheric pressure is recommended for all measurements.
Apodization function	Reference and field apodization functions must be the same. A single set of reference interferograms (background and sample) can be used to generate a multiple sets of absorbance spectra using different apodization functions.
Zero filling factor	Reference and field zero filling factors must be the same. A single set of reference interferograms (background and sample) recorded with no zero filling can be used to generate a multiple set of absorbance spectra using different zero filling factors.
Wavenumber accuracy	Characterized by the position of water absorption bands in a wavenumber standard spectrum (see below); if additions to an existing library are being made, care must be taken to match the x-axes of all spectra as closely as possible.
Integration time	Reference integration times (for both background and sample interferograms) should be greater than or equal to expected field integration times. For reference libraries, the longest practical integration time is recommended.
Detector type and serial number	If an MCT or other potentially non-linear detector is employed in the reference system, IR attenuation may be required to ensure linearity; see APPENDIX B, section B6; because each detector may exhibit linearity to a specific degree, the serial number of the detector should be included in any specification of the system configuration.

D4. Obtaining and Preparing Standard Reference Gases

The accuracy of any FTIR quantitative analysis is limited by the accuracy of the concentrations of the gas standards used in preparing the reference library. It is therefore important to use gas standards of the highest available quality. NIST-traceable gravimetric standards are available from many commercial sources and are quoted to 2% accuracy in many circumstances; EPA has also published guidance on the preparation of "EPA Protocol Gases" (see reference 15), though these are available for only a limited number of compounds. Users should obtain documentation from the gas vendors regarding the analytical techniques applied and the stability limits (concentration and time) of the compounds in the cylinders. When possible, an alternative analytical method should be used to verify the quoted cylinder concentrations, especially for compounds that are reactive, corrosive, or have relatively high boiling points.

If cylinder standards are not available for a compound, the analyst may prepare reference gases based on gravimetric, barometric, or dynamic methods. In any case, the related mass, pressure, and flow measurements should be made with NIST-traceable equipment whenever possible. In general, methods that provide a stream of standard gas (dynamic methods) provide more reliable results than static methods, since the concentrations of static gases are more prone to change when reactions between the standards and the sampling system or absorption cell surface can occur.

D5. Determining the Reference Absorption Path Length

The accuracy of any FTIR quantitative analysis is limited by the accuracy to which the path length of the absorption cell used in preparing the reference library is known. For single-pass absorption cells through which a collimated IR beam is passed, the path length can be physically measured to high accuracy. For multi-pass cells, the nominal path length can be estimated from the base path length and the number of passes. However, because focused beams and curved mirrors are required in multi-pass cells, the path length estimated in this fashion can differ significantly from the actual path length. Because of this, combinations of physical and spectroscopic measurements with multiple CTS gas standards (see below) and single-pass absorption cells should be employed to determine the actual path length of multi-pass absorption cells.

D6. Recording CTS Spectra

The CTS gas is used to characterize the absorption path lengths of the reference and field FTIR systems. Ethylene in nitrogen, at concentrations leading to between 100 ppm · m and 300 ppm · m CPP values for the systems, is recommended; for ethylene, spectra with ppm · m values greater than 300 begin to exhibit non-linear absorbance and must be carefully analyzed (see sections D8 and D9 below). Standards of this gas with 2% accuracy are readily available and both the EPA and NIST libraries contain ethylene spectra that can be used to link those libraries to measurements performed with field instruments. However, almost any other stable compound with appropriate IR absorption characteristics can be used in developing an independent reference library and for accurate field measurements.

In the field, CTS spectra must be recorded both before and after sample spectra are acquired using the same system configuration employed in recording the sample spectra (see steps 7 and 11 above).

When developing reference spectra, the analyst must record CTS spectra at least daily; each reference spectrum should be associated with at least one CTS spectrum. The analyst must use the same system configuration employed in recording the reference spectra, with one exception: The integration time used for the CTS spectra may be less than that used for the reference spectra, if the quality of the resulting CTS spectra is still sufficient for an accurate determination of the absorption path length. It is highly recommended that the analyst store all the interferograms from which the CTS absorbance spectra are generated, including all background interferograms. The interferometric data provide the most direct method of verifying the FFT calculations and/or adding reference absorbance spectra for other apodization function choices.

D7. Recording Reference Spectra

Before recording reference spectra, verify that the requirements specified for system checks, system configuration parameters, gas standards, absorbance path length determinations, and CTS spectra described in the pertinent sections of this appendix and Appendix B have been met. Additional checks of the sample gas pressure and temperature should also be made periodically as the spectra are recorded.

It is highly recommended that the analyst store all the interferograms from which the reference absorbance spectra are generated, including all background interferograms. The interferometric data provide the most direct method of verifying the FFT calculations and/or adding reference absorbance spectra for other apodization function choices.

Beer's law (Equation C1) describes the fundamental linearity of the infrared absorbance versus concentration. However, the resolution (and other) limitations of instruments typically used to generate field FTIR spectra often lead to non-linear behavior for many compounds, even at low absorbance levels. The expected accuracy of FTIR-based measurements results for a particular compound can be

achieved only when 1) the reference absorbance is characterized at a sufficient number of CPP values, up to some maximum value and 2) the sample absorbance associated with any compound represents a value lower than that of the maximum CCP value represented in the reference library for that compound.

For each analyte, the analyst should record two reference spectra at each of two concentration values (that is, at least four spectra) at a single absorption path length; the two concentrations should be separated by no more than a factor of 10, and a maximum factor of 5 is recommended. After recording these spectra, the analyst must 1) permanently record the system parameters and the maximum measured CPP and 2) characterize the linearity of the absorbance across the measured CPP range (see section D8). It may be necessary to record additional reference spectra for the analyte if either the absorbance linearity or maximum CPP value proves unsuitable for later field measurements.

D8. Linearity Checks

The performance of linearity checks on a set of reference spectra is an important aspect of FTIR spectrometry and is best illustrated by a practical example. The following example is based on a series of reference measurements performed on the compound tetrafluoroethylene, hereafter referred to as TFE.

Five absorbance spectra for TFE are shown in Figure D1. These spectra were recorded over the entire mid-IR wavenumber range, but only that portion of the spectra showing the most intense TFE absorption bands is included in the figure. Each of the spectra was calculated by mathematically averaging a number of TFE absorbance spectra recorded with the system configuration parameters given in Table D2, and a linear baseline correction was applied to each of these spectra over the range illustrated in Figure D1.

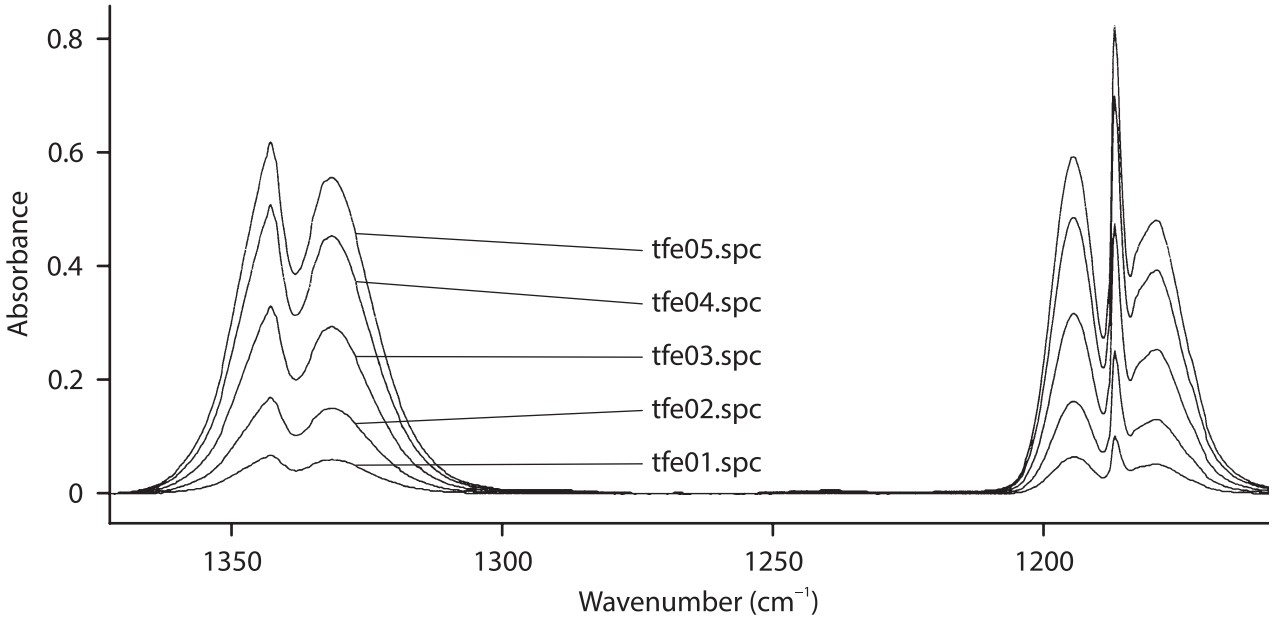

Figure D1. Reference absorbance spectra of TFE (x-axis truncated).

Table D2. System configuration parameters for TFE reference spectra (see Figure D1)

System Configuration Parameters	Values/Notes
MIL (cm^{-1})	0.5
Integration time (s)	1080 (120 s per spectrum × 9 spectra)
Absorption path length (m)	10.23
Gas temperature (°C)	15
Gas pressure (kPa)	101.3 ± 1.3 (760 mmHg ± 10 mmHg)
Apodization function	Triangular
Zero filling factor	Zero
Detector type	MCT
Detector gain (hardware)	Jumpers B, C, and D
Detector gain (software)	1
Reference CTS spectra	j2kety.spc
Wavenumber standard spectrum	j2kety.spc

The reference gas samples were generated by diluting with nitrogen the output of a single standard gas cylinder of TFE. The TFE concentration of the standard cylinder was determined (by the gas vendor) according to NIST-traceable gravimetric measurements and the flow rates of the cylinder gas were measured with a NIST-traceable volumetric device.

One technique to check for the linearity of this set is to form a normalized average of these five spectra and then use it in a linear analysis of the five original spectra. The normalization consists of dividing each spectrum by its CPP; these values, based on the CTS-derived path length of 10.23 m, are given with the actual gas concentrations and new spectral filenames in Table D3. Figure D2 illustrates the normalized spectra, all of which represent spectra of CPP values 1.00 ppm · m. These spectra are nearly equal to one another, as predicted by Beer's law. Only the spectrum tfe01n.spc, based on the original 25.53 ppm spectrum, is easily discernible from the other spectra in the figure.

Table D3. Normalization factors for TFE spectra

Original Spectrum	Concentration (ppm)	Concentration-Path Length Product (ppm · m)	Normalized Spectrum
tfe01.spc	2.50	25.5	tfe01n.spc
tfe02.spc	6.63	67.8	tfe02n.spc
tfe03.spc	13.3	133	tfe03n.spc
tfe04.spc	20.4	208	tfe04n.spc
tfe05.spc	25.1	257	tfe05n.spc

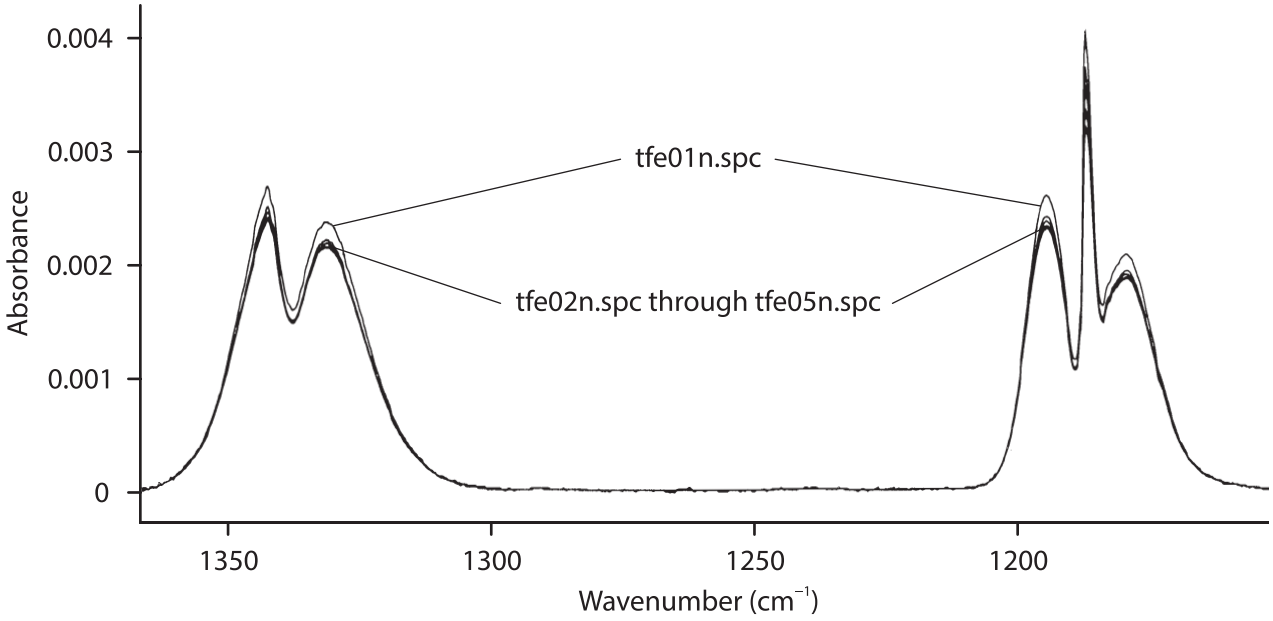

Figure D2. Normalized reference absorbance spectra for TFE.

Table D4 shows the results of a linear least-squares analysis using the *average* normalized spectrum as a single reference spectrum (with CPP 1.00 ppm · m) over the analytical range 1050 cm^{-1} to 1400 cm^{-1}. The bias in the linear method is clearly evident in the fourth column of the table, which indicates that the analysis yields concentrations that are slightly too high at the lowest concentration and slightly too low at the highest concentration. The average of the last column in the table, which represents the absolute percent difference between the actual and calculated concentrations, the "fractional calibration uncertainty" (FCU; see reference 3), is 3.2%. This value represents the average error over the concentration range for these reference spectra to be expected from the linear analysis up to the maximum CPP value used in the analysis (257 ppm · m). If additional accuracy is required, non-linear analyses or corrections such as those discussed above (Appendix B, section B6) can be employed.

Table D4. Results of linear least squares analysis for TFE reference spectra

TFE Reference Spectrum	Calculated Concentration (ppm)	Actual Concentration (ppm)	Actual – Calculated Concentration (ppm)	Absolute Percent Difference
tfe01.spc	2.69	2.50	0.19	7.7
tfe02.spc	6.64	6.63	0.01	0.2
tfe03.spc	12.8	13.0	–0.2	1.4
tfe04.spc	19.8	20.4	–0.6	2.9
tfe05.spc	24.2	25.1	–0.9	3.7

D9. Calculating the LOD

The estimated LODs are the concentrations — for the given system configuration, reference spectra, and analytical region — at which each compound's absorbance area is equal to the RSA. For a specified system configuration and analytical region, an estimate of the LOD (L_D) for a compound can be made

from the absorbance area of a reference spectrum in that region (A_R, cm^{-1}), the reference spectrum CPP (P_{CP}, ppm · m), the sample absorption path length (L, m), and the RSA values (A_{RS}, cm^{-1}) as

$$L_D = \frac{P_{CP} \times A_{RS}}{L \times A_R}. \qquad \text{(Equation D1)}$$

A simple trapezoidal approximation of A_R over the analytical region of interest, including baseline corrections when necessary, is suitable for the LOD estimate. The RSA is formed from the product of the FTIR system's typical root-mean-square noise level in absorbance and the width of the analytical region in cm^{-1} (see APPENDIX B, section B2); the RSA estimate should reflect the error incurred in subtracting known spectral interferences. APPENDIX E, section E1 presents detailed examples of RSA and LOD calculations.

D10. Using Existing Reference Libraries

The analyst may use any of the publicly available reference libraries for quantitative analyses, but it is strongly recommended that quantitative results for analytes be based only on spectra from libraries that meet the requirements discussed in this appendix. If the reference library consists of spectra recorded at a spectral resolution different from that of the field system, the analyst must 1) deresolve the spectra mathematically to that of the field data and 2) ensure that the library data are suitably linear over the desired measurement range *at the spectral resolution of the field system*.

APPENDIX E. EXAMPLE CALCULATIONS

This appendix uses an analysis of TFE and 1,1-difluoroethylene (DFE) in workplace air to illustrate the calculations of RSA and LODs. The topics of designing, applying and verifying, and correcting a spectral analysis are also addressed below.

The FTIR system configuration assumed for this set of calculations is given below. These parameters are consistent with the LOD values presented in Table 2.

System Configuration Parameters	Values/Notes
MIL:	0.5 cm^{-1}
Absorption path length:	10 m
Apodization function:	Triangular
Gas temperature:	293 K
Gas pressure:	101.3 kPa
Zero filling factor:	None
Wavenumbers of water bands:	1918 cm^{-1} and 2779 cm^{-1}
Reference library sources:	NIST, EPA
Integration time:	70 s (64 scans)
Detector type:	MCT
Detector gain - hardware:	Gain jumpers A, D, and H
Detector gain - software:	1.0

E1. RSA, Analysis Design, and LODs

The analysis is to be carried out in workspace air, so the only potential spectral interferences are due to water and carbon dioxide. Figure E1 illustrates example reference spectra of TFE, DFE, and water. (The water spectrum shown is typical of workspace air samples; carbon dioxide does not absorb in any of the spectrum. As a result, the limited spectral region shown in Figure E2 is actually of the greatest interest for an analysis of DFE and TFE in workspace air.

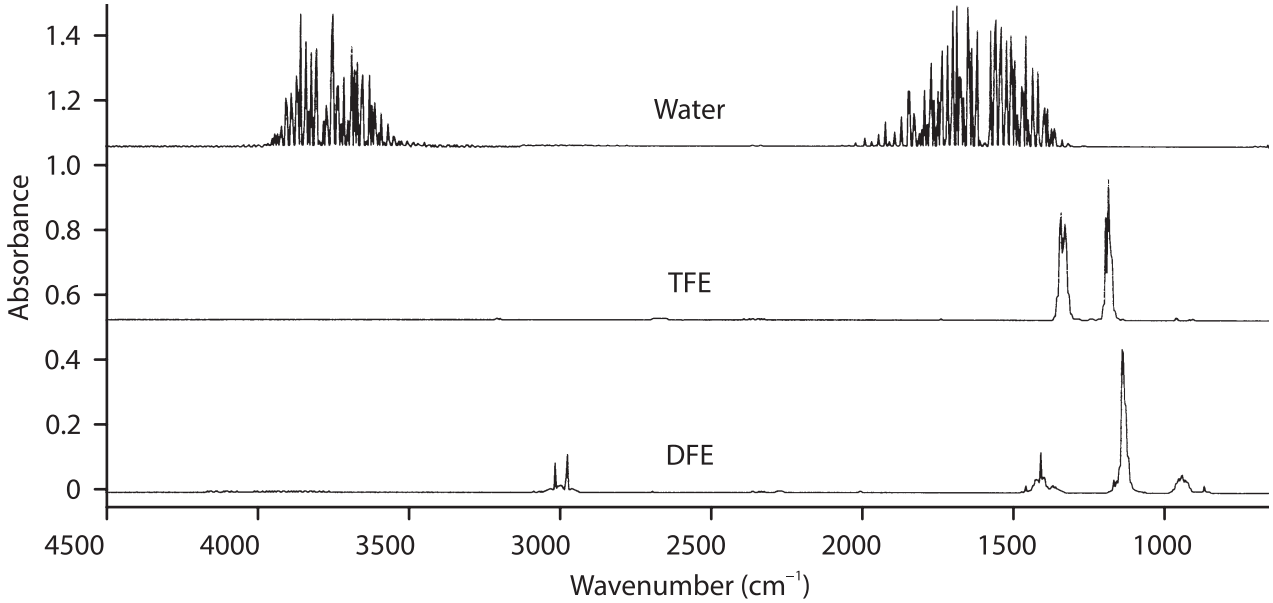

Figure E1. Absorbance reference spectra of TFE, DFE, and water.

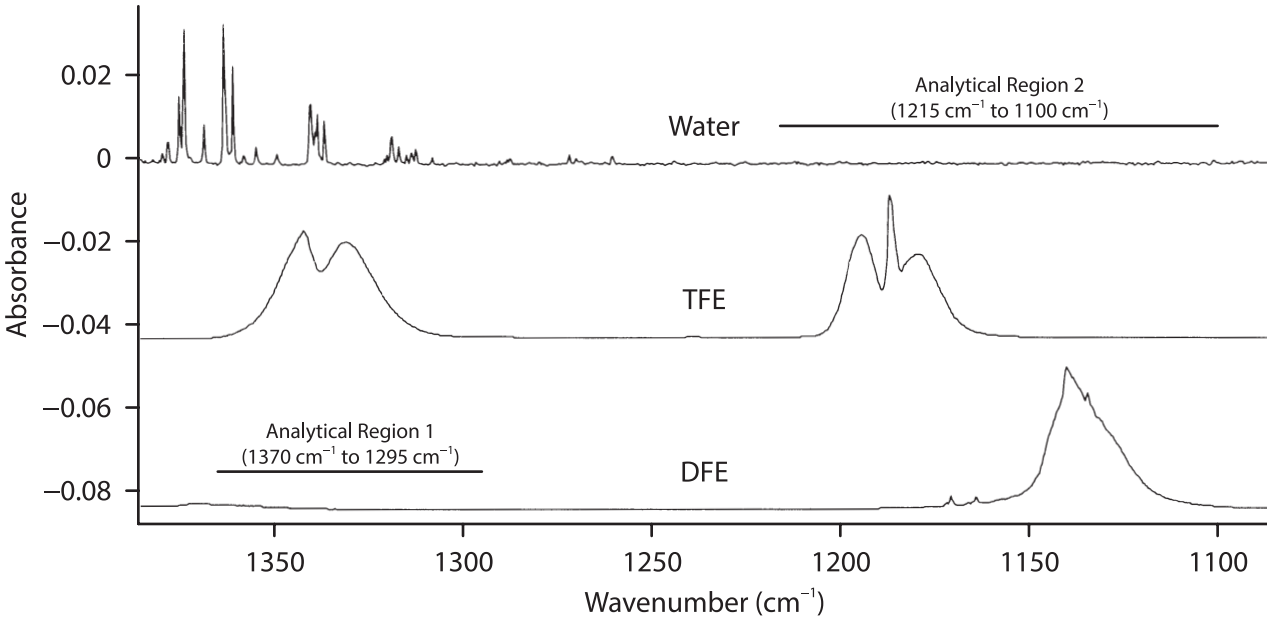

Figure E2. Possible analytical regions.

Shown in greater detail in Figure E2 are the three reference spectra and two possible analytical regions. Analytical region 1, from 1370 cm^{-1} to 1295 cm^{-1}, includes water bands that interfere with the TFE absorbance in the sample spectra. Analytical Region 2 (1215 cm^{-1} to 1100 cm^{-1}) may be the best choice for analyzing samples for both TFE and DFE (though the weaker features near 3000 cm^{-1} remain an option for DFE); it avoids the TFE interference with water, but necessarily includes some spectral overlap between the two analytes. Until the relative TFE, DFE, and water concentrations in the samples are known, it is unclear which of the two regions will provide better concentration estimates for TFE, so calculations for both regions are described below.

Estimation of the LODs for TFE and DFE requires a calculation of the RSA in the actual sample spectra over the selected analytical regions. The RSA represents an estimate, based on the assumed sample matrix and available reference spectra, of the residual absorbance (see Equation C6) that will be used to calculate the concentration uncertainties from the actual sample spectra.

The reader should note that the RSA and derived LOD are only estimates. If the actual sample matrix differs substantially from that of the sample matrix assumed in the performance of these estimates, the actual concentration uncertainties and LODs may differ substantially from the RSA and LOD values obtained in the calculations described below. For workplace air samples, water is the only interfering compound that is certain to appear in any of the analytical regions considered below. A realistic estimate of the RSA is therefore available by forming the mathematical difference of two water spectra — of substantially different water concentrations — recorded using the same FTIR system configuration. For each analyte, this estimate assumes that only water and that analyte will absorb substantially in the actual sample spectra. Later analyses based on the actual sample matrix could lead to either lower or higher concentration, uncertainty, and LOD estimates; examples of such analyses are detailed below.

Figures E3 and E4 illustrate two absorbance spectra recorded using the system configuration described above. They represent spectra of workspace air at approximately 20% and 40% relative humidity. The upper trace in each figure is slightly offset for clarity.

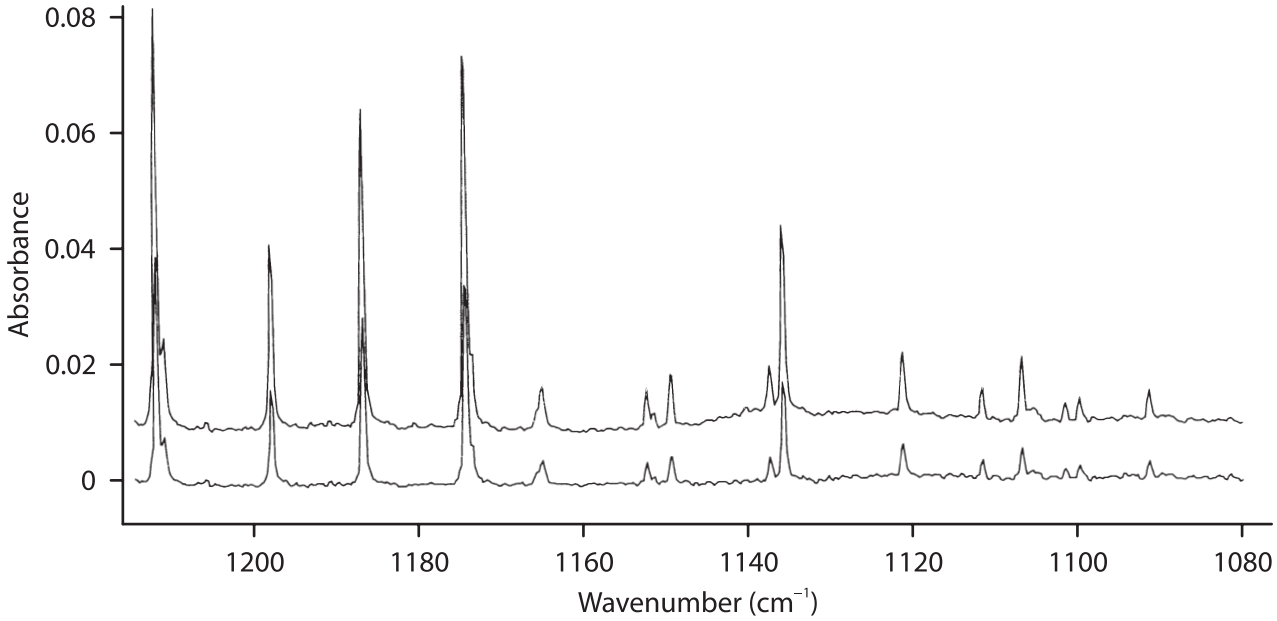

Figure E3. Water spectra 1215 cm^{-1} to 1080 cm^{-1}.

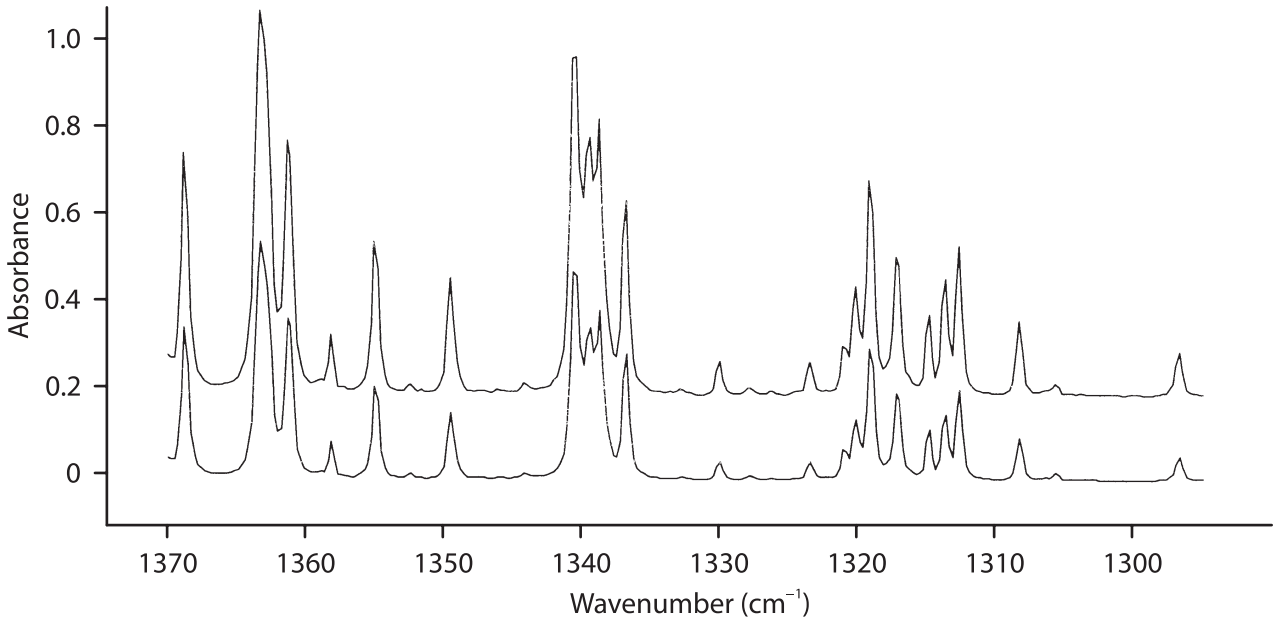

Figure E4. Water spectra 1370 cm^{-1} to 1295 cm^{-1}.

Figure E5 shows two residual spectra formed by subtracting scaled versions of the lower-absorbance spectrum from the higher-absorbance spectrum. The scaling factors were determined in independent LSF analyses over the two analytical regions. Linear baseline corrections (offset and slope) were also determined during the analyses, so the mean value of each residual spectrum is zero. (These calculations were performed by using the ANOVA data analysis tool in Microsoft Excel 97). The RSA values for the residual spectra are defined in Equation C2 and the related calculations are presented in Table E1. (The calculations also were performed in the program Excel by applying the function STDEV to the regression residuals.)

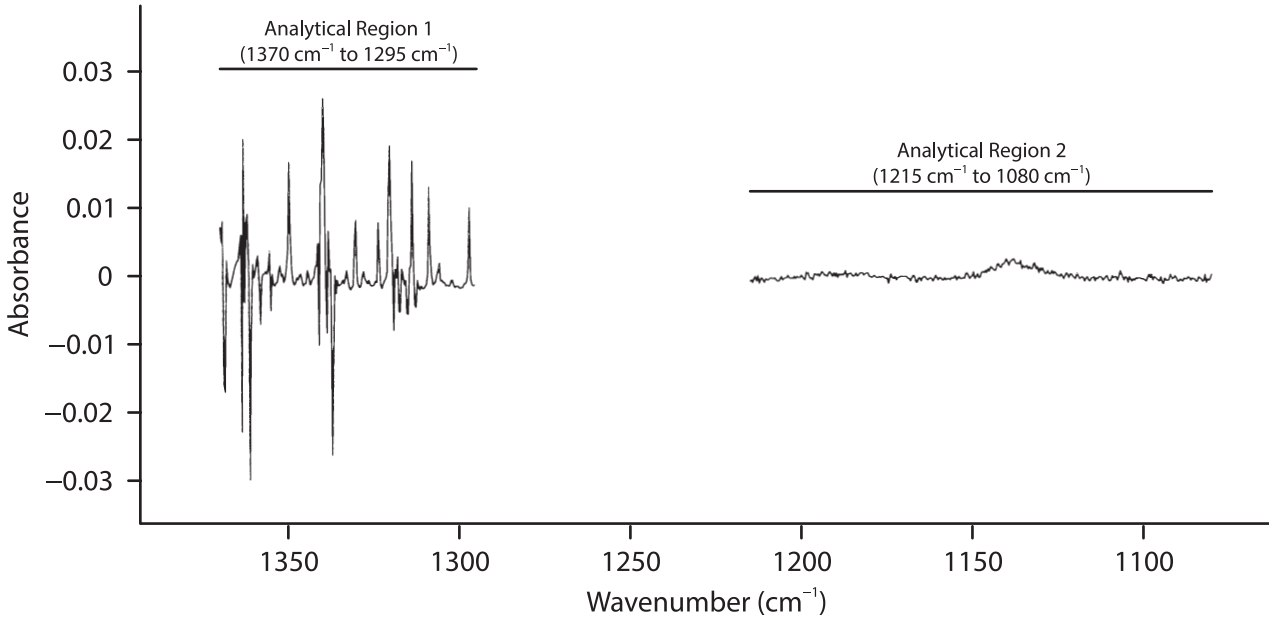

Figure E5. Water residual spectra.

Table E1. Results of RSA analysis from water reference spectra

Analytical Region (cm^{-1})	Calculated Scaling Factor	Scaling Factor Uncertainty (1σ)	Residual RMS Standard Deviation (Absorbance)	RSA; Equation B2 (cm^{-1})
1370 to 1295	1.636	0.003	0.00575	0.431
1215 to 1080	1.870	0.008	0.00069	0.093

An estimate of the LODs (L_D, ppm) for the two compounds — for the specified system configuration — can be made from the absorbance areas of the reference spectra over these analytical ranges (A_R, cm^{-1}), the reference spectra CPPs (P_{CP}, ppm · m), the sample absorption path length L (m), and the RSA values (A_{RS}, cm^{-1}) derived above.

The absorbance areas were determined using a standard trapezoidal approximation without baseline correction. (For these spectra, baseline corrections lead to values that differ from those quoted by less than 3% and have been neglected below.) Figure E6 shows the spectral features of TFE and DFE used to calculate the A_R for the reference spectra tfeav05.spc (CPP = 256.7 ppm · m) and dfeav05.spc (CPP = 197.8 ppm · m).

The estimated LODs are the concentrations — for the given system configuration, reference spectra, and analytical region — at which each compound's absorbance area is equal to the RSA. Mathematically, the LOD estimates are given by

$$L_D = \frac{P_{CP} \times A_{RS}}{L \times A_R}. \qquad \text{(Equation E1)}$$

Table E2 lists the pertinent quantities and resulting LODs for DFE and TFE in the two analytical regions considered. The results indicate that the analytical region from 1215 cm^{-1} to 1080 cm^{-1} is likely to provide the most reliable TFE concentrations.

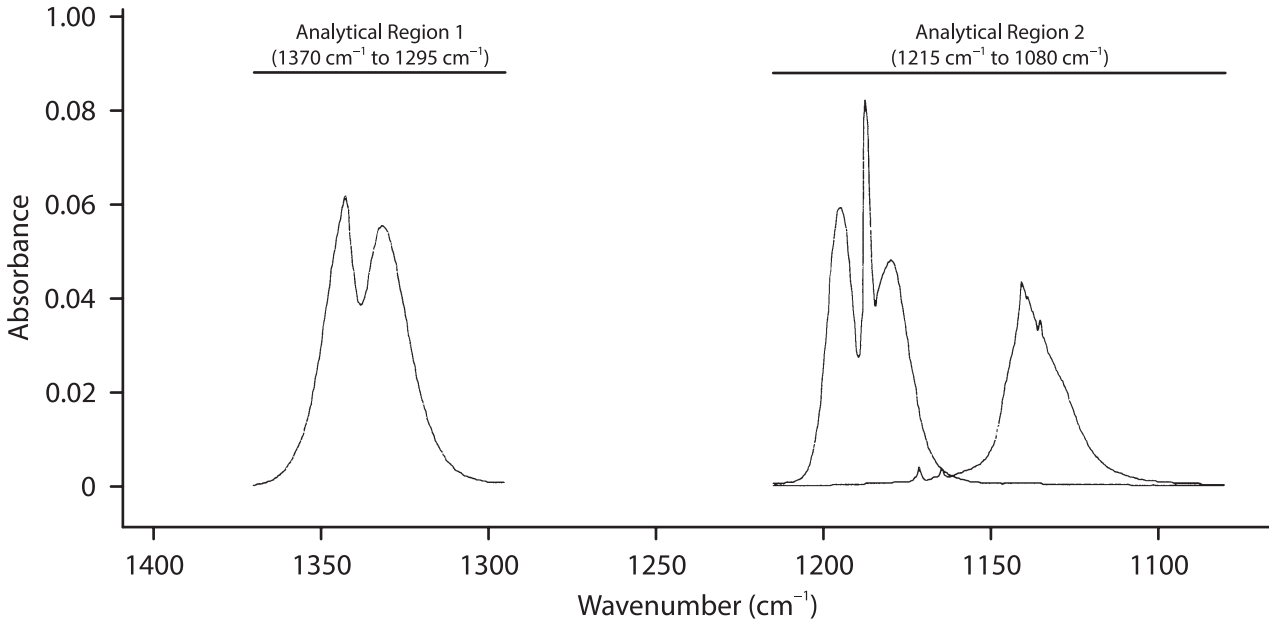

Figure E6. TFE and DFE spectra for absorbance area calculations.

Table E2. LODs for TFE and DFE from RSA analysis of water reference spectra

		Reference Spectra			System Configuration		
Analytical Region (cm^{-1})	Compound	File Name	CPP (ppm · m)	Absorbance Area (cm^{-1})	RSA (cm^{-1})	L (m)	Estimated LOD (ppm)
1370 to 1295	TFE	tfe05.spc	256.7	16.03	0.431	10.0	0.69
1215 to 1080	TFE	tfe05.spc	256.7	13.97	0.093	10.0	0.17
1215 to 1080	DFE	dfe05.spc	197.8	8.72	0.093	10.0	0.21

E2. LSF Determinations of TFE and DFE Concentrations

Presented in this section is a description of an LSF analysis for the two compounds TFE and DFE in ambient air samples. As is always the case before actual measurements are taken, no actual sample data for mixtures of the compounds in the assumed matrix (ambient air) were available as these analyses were performed. Accordingly, the following description is based on synthetic spectra generated from available reference spectra for TFE, DFE, and water.

In order to *not* overestimate the effectiveness of the FTIR technique, the noise levels in the synthetic sample spectra were artificially raised and the reference spectra used are not those most likely to provide an optimal analysis. This is the most prudent course available to an analyst attempting to predict the performance of the FTIR method under essentially unknown conditions and it is the course recommended by the authors to analysts who find themselves in this common situation.

Estimates of the LOD for this sample matrix (see section E1) indicate that the analytical region from 1215 cm^{-1} to 1080 cm^{-1} will likely provide the most reliable TFE and DFE concentrations. The system configuration parameters used in those estimates are assumed to hold in the following description.

E2A. Generation and Analysis of Synthetic Sample Spectra of TFE and DFE

Table E3 describes the mathematical generation of synthetic samples for the following LSF analysis description. Each sample spectrum consists of the sum of scaled reference spectra for TFE (tfe4.spc, CPP = 208.3 ppm · m), DFE (dfeav05.spc, CPP = 197.8 ppm · m) and water (wat02bl.spc). The scaling factors indicated in Table E3 were used to generate synthetic sample spectra at the listed concentrations and the assumed absorption path length of 10.0 m.

Table E3. Parameters used to generate synthetic sample spectra containing TFE, DFE, and water

TFE Scaling Factor	TFE Synthetic Concentration (ppm)	DFE Scaling Factor	DFE Synthetic Concentration (ppm)	Water Scaling Factor	Synthetic Sample Spectrum File Name
0	0	0	0	0.6	S001.spc
0	0	0	0	1.2	S002.spc
1.200	25.0	1.264	25.0	0.6	S551.spc
1.200	25.0	0.253	5.00	0.6	S511.spc
0.240	5.00	1.264	25.0	0.6	S151.spc
1.200	25.0	1.264	25.0	1.2	S552.spc
1.200	25.0	0.253	5.00	1.2	S512.spc
0.240	5.00	1.264	25.0	1.2	S152.spc

A spectrum representing random absorbance noise was added to each synthetic spectrum. The noise spectrum was generated using the function RANDOM within the program GRAMS/32 V4.11 (Galactic, Inc.; see the Array Basic User's Guide, V4.1, page 316); similar functions are also available in other spreadsheet software programs. For the noise spectrum R, with discrete absorbance values R_i for wavenumbers $i = p$ to q, the root mean square (RMS) absorbance noise N_{RMS} (see also Equation B2, which defines the RSA), calculated over the appropriate analytical region(s) according to

$$N_{RMS} = \sqrt{\sum_{i=p}^{i=q} \frac{R_i^2}{q-p}}, \qquad \text{(Equation E2)}$$

was 0.00034 in the region 1438 cm^{-1} to 1282 cm^{-1}; this is very close to the value obtained from actual absorbance spectra (provided by MIDAC Corporation) recorded with the quoted system configuration in the region 1005 cm^{-1} to 932 cm^{-1}. The synthetic spectra represent four different mixtures of TFE and DFE (including one "mixture" that contains neither compound), each at two different moisture levels.

Table E4 lists the results of a LSF analysis (program 4FTIMD V15, Rho Squared; see reference 14) for TFE, DFE, and water in the analytical region 1215 cm^{-1} to 1080 cm^{-1} using the reference spectral files TFE3.spc (CPP = 133.2 ppm · m), dfeav04.spc (CPP = 133.3 ppm · m), and wat01bl.spc. Note that these are not the same reference spectra that were used in the generation of the synthetic sample spectra and that the results for water are in arbitrary units. The analysis included the determination of two baseline correction parameters along with the compound concentrations.

Table E4. Original LSF results for original synthetic sample spectra containing TFE, DFE, and water

Synthetic Sample Spectrum File Name	TFE*			DFE†			Water‡	
	Synthetic Concentration (ppm)	LSF Result (ppm)	LSF 3σ Uncertainty (%)	Synthetic Concentration (ppm)	LSF Result (ppm)	LSF 3σ Uncertainty (%)	LSF Result (arbitrary)	LSF 3σ Uncertainty (%)
S001.spc	0	0.02	52.5	0	0.07	13.7	1.12	1.23
S002.spc	0	0.03	32.2	0	0.14	8.95	2.24	0.80
S551.spc	25.0	24.41	0.26	25.0	24.30	0.29	0.87	11.8
S511.spc	25.0	24.43	0.25	5.00	4.88	1.43	0.87	11.5
S151.spc	5.00	4.88	0.41	25.0	24.33	0.09	1.07	3.04
S552.spc	25.0	24.43	0.26	25.0	24.35	0.29	1.99	5.20
S512.spc	25.0	24.45	0.26	5.00	4.95	1.43	1.99	5.11
S152.spc	5.00	4.90	0.43	25.0	24.39	0.10	2.19	1.56

*For TFE, excluding samples S001 and S002, the average difference between the synthetic concentration and the LSF result was 2.24%. The average 3σ uncertainty was 0.31%.
†For DFE, excluding samples S001 and S002, the average difference between the synthetic concentration and the LSF result was 2.34%. The average 3σ uncertainty was 0.61%.
‡For water, excluding samples S001 and S002, the average 3σ uncertainty was 6.38%.

The LSF results for the non-zero TFE and DFE spectra are consistently good, being different from the synthetic concentrations less than 3% in every case. The concentration uncertainties listed in Table E4 are the statistically determined 3σ values from the LSF analyses. These percent uncertainty parameters and the visual appearance of the LSF residual spectra are important indicators of the quality of the least squares analysis and are discussed further in the following section.

The TFE and DFE results for the two synthetic spectra that contain no absorption features of TFE and DFE (S001 and S002) are of interest and importance. The LSF concentration results are small. (Their maximum is 0.14 ppm). They are smaller in each case than the LOD estimates of Table E2 and their corresponding 3σ uncertainties from this LSF analysis are smaller still. Unfortunately, no consensus exists on the exact mathematical relationship between the LODs calculated as described in this document and the 3σ concentration uncertainties. This statement is supported by the contents of section A2 in reference 4 — a consensus document — that prescribes three different methods for calculating LODs (or, in the terminology of reference 4, "minimum detectable concentrations"). These three prescriptions include one similar to the LOD method prescribed in this document and one that is based on the concentration uncertainties derived from spectra similar to S001 and S002. In this limited example, two of the three prescriptions included in reference 4 provide very different results and they indicate that the LOD calculation described in this document provides the most conservative estimate — that is, the highest estimate — of the three LOD prescriptions of reference 4.

E2B. Analyses of Synthetic Sample Spectra with an Interfering Compound

Every compound-specific quantitative analytical technique, including FTIR spectrometry, can fail to provide accurate results when interfering compounds appear in a sample. However, the results of a mathematical FTIR spectral analysis designed for a particular set of compounds provides clues to its failure in the presence of interferants. An experienced analyst can often adjust the analysis to accommodate the interferants and provide accurate results.

To illustrate this important aspect of FTIR spectrometry, a synthetic interference was introduced to the spectra described in Table E3. Scaled versions of a reference spectrum (hfpav06.spc, 256.6 ppm · m) of the compound hexafluoropropylene (HFP), representing the compound at two concentrations (5.00 and 10.0 ppm), were added to the original synthetic spectra. The resulting final synthetic sample spectra

are described in Table E5 below. The least squares analysis described above for TFE and DFE only, when applied to these spectra containing spectral features of HFP, gives the results shown in Table E6 below.

Table E5. Parameters used to generate synthetic sample spectra containing TFE, DFE, water, and HFP

Original Synthetic Sample Spectrum File Name	HFP Scaling Factor	HFP Synthetic Concentration (ppm)	Final Synthetic Sample Spectrum File Name
S001.spc	0.195	5.00	S0011.spc
S002.spc	0.390	10.0	S0022.spc
S551.spc	0.195	5.00	S5511.spc
S151.spc	0.195	5.00	S1511.spc
S512.spc	0.195	5.00	S5121.spc
S511.spc	0.390	10.0	S5112.spc
S552.spc	0.390	10.0	S5522.spc
S152.spc	0.390	10.0	S1522.spc

Table E6. Original LSF results for final synthetic sample spectra containing TFE, DFE, water, and HFP

Synthetic Sample Spectrum File Name	TFE*			DFE†			Water‡	
	Synthetic Concentration (ppm)	LSF Result (ppm)	LSF 3σ Uncertainty (%)	Synthetic Concentration (ppm)	LSF Result (ppm)	LSF 3σ Uncertainty (%)	LSF Result (arbitrary)	LSF 3σ Uncertainty (%)
S0011.spc	0	1.00	39.6	0	−1.58	26.5	1.65	0.89
S0022.spc	0	2.01	39.5	0	−3.16	26.4	3.29	1.78
S5511.spc	25.0	25.06	1.51	25.0	22.65	1.89	1.43	43.3
S5112.spc	25.0	25.73	2.90	5.00	1.57	53.8	1.99	61.4
S1511.spc	5.00	5.53	6.64	25.0	22.67	1.84	1.63	37.0
S5522.spc	25.0	25.73	2.90	25.0	21.05	4.01	3.10	39.2
S5121.spc	25.0	25.09	1.52	5.00	3.29	13.1	2.55	24.4
S1522.spc	5.00	6.20	11.87	25.0	21.09	3.96	3.30	36.4

*For TFE, excluding samples S001 and S002, the average 3σ uncertainty was 4.56%.
†For DFE, excluding samples S001 and S002, the average 3σ uncertainty was 13.1%.
‡For water, excluding samples S001 and S002, the average 3σ uncertainty was 40.3%.

The average 3σ uncertainties shown in Table E4 (those of the original LSF analysis *without* HFP interference) and Table E6 (those of the original LSF analysis *with* HFP interference) are clearly quite different. Averaged over the six synthetic spectra containing TFE and DFE in each case, the (absolute) percent concentration uncertainties for TFE, DFE, and water are greater for the spectra with HFP interference. For TFE and DFE, the average percent uncertainties of Table E6 are over ten times greater than those of Table E4. This exercise shows that:

- For sample spectra containing substantial TFE and DFE concentrations, the HFP interference causes large increases in the TFE and DFE relative absolute concentration uncertainties.
- For sample spectra containing low or zero concentrations TFE and DFE, the relative absolute uncertainties are NOT a reliable indicator of the HFP interference. However, for such spectra, the concentration results themselves are often clearly unreliable; note that the DFE concentration

results are negative *and* large compared to the LOD estimate for this compound. (Note also that negative concentration results that are *small* compared to the LOD are statistically valid and do not necessarily indicate a failure of the analysis.)

If the concentration results show anomalies such as those noted above, the residual spectra from the analyses will also exhibit anomalous behavior. This is illustrated in Figure E7, which shows the residual spectra for four analyses. Compared to the residual spectra resulting from analyses of spectra without the HFP interference, those with HFP interference show large absorbance features that cannot be modeled by the three reference spectra employed. The analyst needs to identify the interfering compound before proceeding. This can often be done by visually comparing the suspect residual spectra to reference spectra of a number of likely interferants, as illustrated in Figure E8.

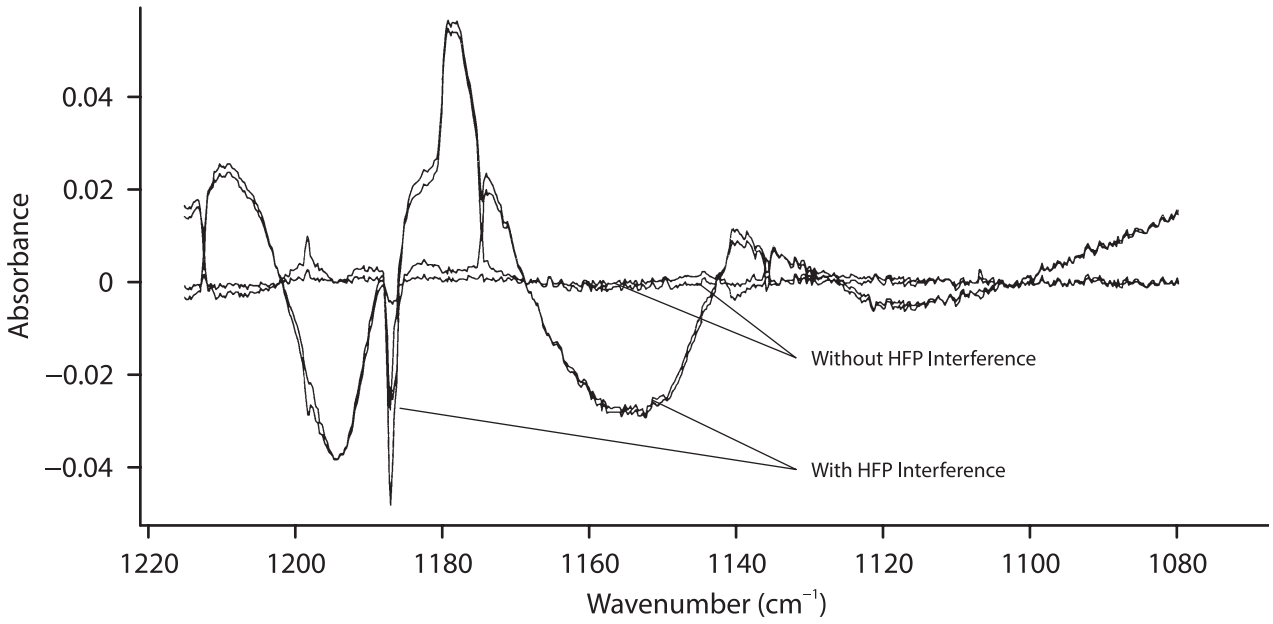

Figure E7. Residual spectra with and without HFP interferance.

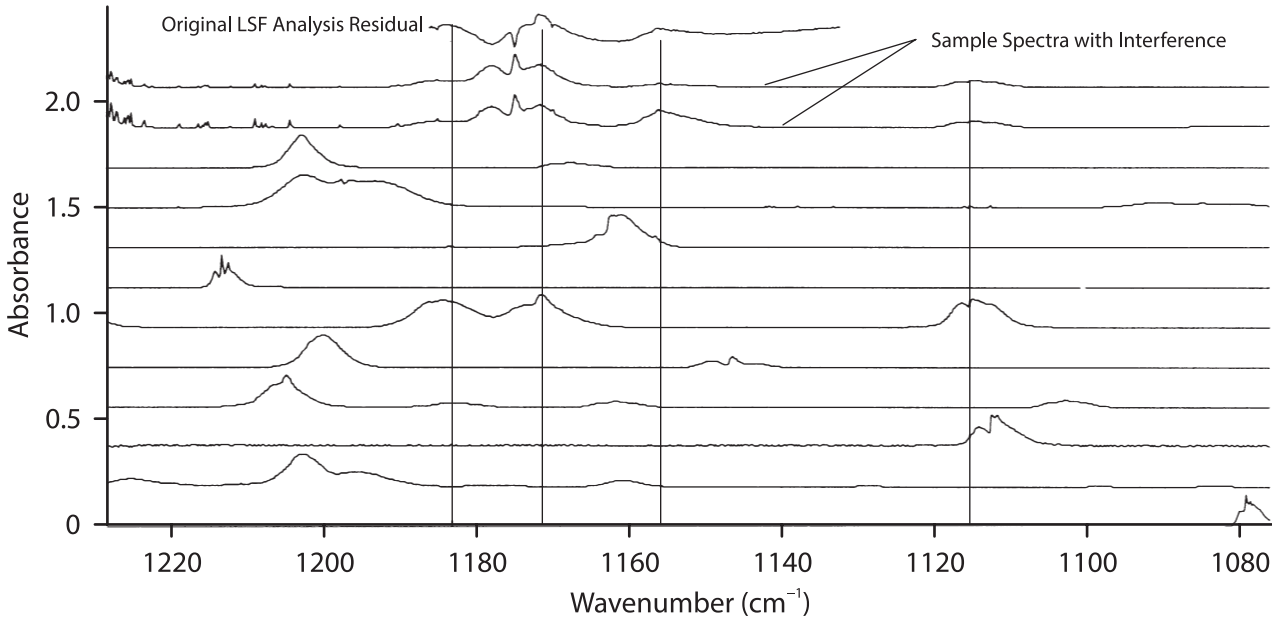

Figure E8. Comparisons of residual, sample, and reference spectra.

Figure E8 shows that the positions of three major relative maxima in the residual spectrum (top trace) correspond well to only one of the nine candidate reference spectra in the lower traces of the figure. (The nine spectra shown are all of light, partially or fully fluorinated hydrocarbons.) An additional absorbance band from this single reference spectrum also corresponds to a large peak in both of the sample spectra (second and third traces from top of the figure).

A closer examination of this reference spectrum — that of HFP, of course — is illustrated in Figure E9. It clearly shows a close relationship between the shape of the residual spectrum and the absorption features of HFP. The relationship is not exact because the sample spectrum has had incorrect amounts of the compounds TFE and DFE subtracted and this distorts the residual spectrum.

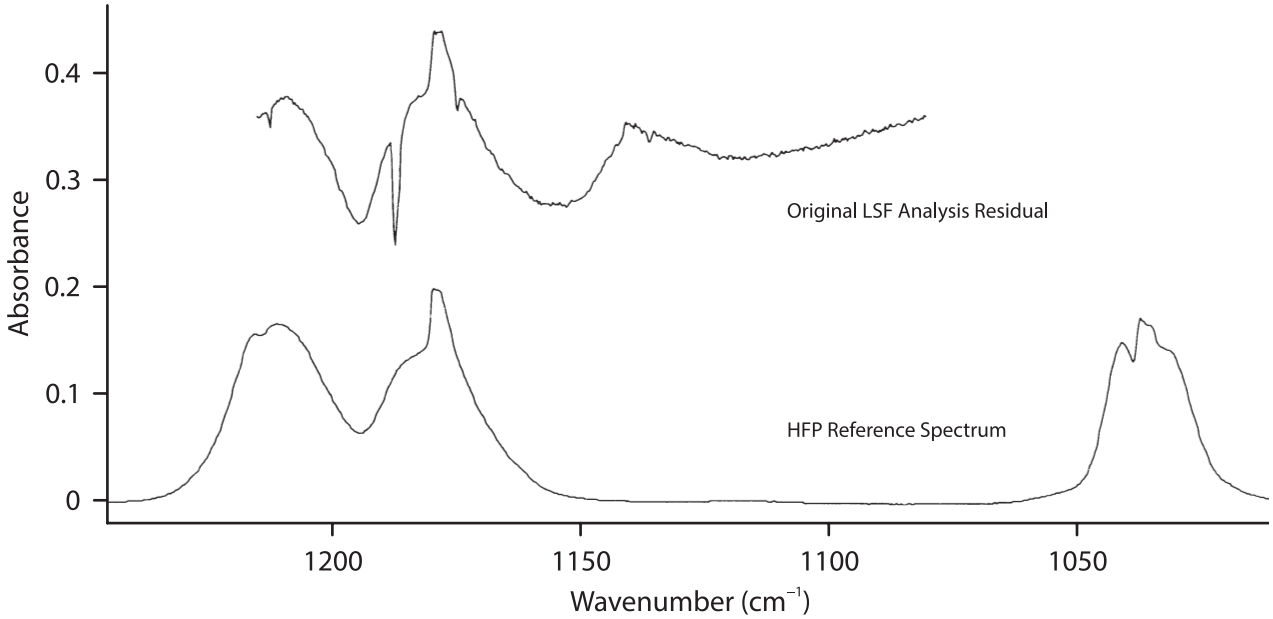

Figure E9. Original LSF residual and HFP reference spectra.

Though this identification is tentative, it can be tested by including HFP in the LSF analysis. Table E7 shows the TFE, DFE, and water concentrations resulting from an analysis identical to those described above except for the addition of HFP as a fourth compound. (As usual, an HFP reference spectrum different from the one used to add the synthetic interference was employed in the analysis.) To facilitate comparisons with the preceding tables, the HFP results have been excluded from Table E7; they were in all cases similar in quality to those obtained for the other compounds.

Table E7. Final LSF results for final synthetic sample spectra containing TFE, DFE, water, and HFP

Synthetic Sample Spectrum File Name	TFE*			DFE†			Water‡	
	Synthetic Concentration (ppm)	LSF Result (ppm)	LSF 3σ Uncertainty (%)	Synthetic Concentration (ppm)	LSF Result (ppm)	LSF 3σ Uncertainty (%)	LSF Result (arbitrary)	LSF 3σ Uncertainty (%)
S0011.spc	0	1.00	39.6	0	−1.58	26.5	1.65	0.89
S0022.spc	0	2.01	39.5	0	−3.16	26.4	3.29	1.78
S5511.spc	25.0	24.43	0.27	25.0	24.27	0.33	0.87	12.1
S5112.spc	25.0	24.45	0.27	5.00	4.81	1.72	0.88	12.34
S1511.spc	5.00	4.91	0.44	25.0	24.27	0.11	1.08	3.23
S5522.spc	25.0	24.46	0.28	25.0	24.27	0.35	1.99	5.51
S5121.spc	25.0	24.45	0.27	5.00	4.92	1.63	1.99	5.25
S1522.spc	5.00	4.94	0.57	25.0	24.29	0.14	2.20	2.05

*For TFE, excluding samples S0011 and S0022, the average 3σ uncertainty was 0.35%.
†For DFE, excluding samples S0011 and S0022, the average 3σ uncertainty was 0.71%.
‡For water, excluding samples S0011 and S0022, the average 3σ uncertainty was 6.74%.

The results show that inclusion of HFP in the analysis yields results of the original (high) quality shown in Table E3 for TFE, DFE, and water. The percent relative uncertainties are slightly higher in the final analysis than in the original analysis; this is to be expected because the same amount of spectral information is being used to determine an additional parameter in the final analysis. The quality of the analysis could probably be further improved by extending the analytical region to include the entire HFP absorbance band shown in Figure E9.

HYDROQUINONE 5004

HOC_6H_4OH MW: 110.11 CAS: 123-31-9 RTECS: MX3500000

METHOD: 5004, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 February 1984 **Issue 3:** 26 February 2016

OSHA: 2 mg/m³
NIOSH: C 2 mg/m³/15 min

PROPERTIES: solid; MP 170 °C; BP 285 °C @ 730 mm; VP 0.0024 Pa (1.8×10^{-5} mm Hg; 0.11 mg/m³) @ 25 °C

SYNONYMS: 1,4-benzenediol; hydroquinol; quinol; 1,4-dihydroxybenzene

SAMPLING

SAMPLER: FILTER (0.8-µm cellulose ester membrane)

FLOW RATE: 1 - 4 L/min

VOL-MIN: 30 L @ 2 mg/m³
-MAX: 180 L

FIELD TREATMENT: transfer filter immediately to jar with 10 mL 1% acetic acid

SHIPMENT: ship sample solutions

SAMPLE STABILITY: at least 7 days @ 25 °C

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 0.8 to 4 mg/m3 [1] (90-L samples)

BIAS: 4.4%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.061

ACCURACY: ± 15.0%

MEASUREMENT

TECHNIQUE: HPLC, UV DETECTION

ANALYTE: hydroquinone

EXTRACTION: 1% acetic acid, 10 mL

INJECTION VOLUME: 100 µL

MOBILE PHASE: 1% acetic acid in H_2O; 1 mL/min

COLUMN: 25 cm x 4.6-mm ID C18/USP L1 column; ambient temperature, 400 to 600 psi (2800-4100 kPa)

DETECTOR: UV @ 290 nm

CALIBRATION: solutions of hydroquinone in 1% aqueous acetic acid

RANGE: 0.06 to 0.8 mg per sample [2]

ESTIMATED LOD: 0.01 mg per sample [3]

PRECISION ($\bar{S}_r$): 0.030 [1]

APPLICABILITY: The working range is 0.7 to 8 mg/m³ for a 90-L air sample or 2 to 25 mg/m³ for a 30-L air sample. This method can be used when significant concentrations of hydroquinone vapor are not present.

INTERFERENCES: None known. Hydroquinone is unstable on the collection media and must be stabilized immediately after collection by dissolution in 1% acetic acid.

OTHER METHODS: This is Method S57 [2] in a revised format. The method also appears in a NIOSH recommended standard [4].

REAGENTS:

1. Hydroquinone, reagent grade.
2. Distilled water.
3. Acetic acid, glacial.
4. Acetic acid, 1%. Dilute 10 mL acetic acid to 1 L with distilled water.
   NOTE: This solution is needed at the sampling site for field treatment of samples.
5. Calibration stock solution, 3.6 mg/mL. Dissolve 0.0900 g hydroquinone in 25 mL 1% acetic acid. Prepare fresh daily, in duplicate.

EQUIPMENT:

1. Sampler: 37-mm cassette containing 0.8-µm cellulose ester membrane filter and cellulose backup pad.
2. Personal sampling pump, 1 to 4 L/min, with flexible connecting tubing.
3. High pressure liquid chromatograph with UV detector at 290 nm, integrator and column (page 5004-1).
4. Jars, 60-mL, ointment, low form, with PTFE film gaskets and screw caps.
5. Syringe, 100-µL, or autosampler for sample injection.
6. Microliter syringes for standard preparation.
7. Volumetric flasks, 10- and 25-mL, and 1-L.

SPECIAL PRECAUTIONS: None

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Sample at an accurately known flow rate between 1 and 4 L/min for a total sample size of 30 to 180 L.
   NOTE: This method will collect hydroquinone aerosol only. The equilibrium vapor pressure is equivalent to 0.11 mg/m^3 at 25 °C and may be a significant factor at elevated temperatures.
3. Immediately after sampling, transfer the filter (do not include backup pad) with tweezers to a 60-mL ointment jar. Add 10 mL 1% acetic acid. Process field blanks similarly.
4. Ship the filters in the ointment jars.

SAMPLE PREPARATION:

5. Transfer the sample solution from the ointment jar to a 25-mL volumetric flask.
6. Rinse the ointment jar twice with 5 mL 1% acetic acid. Add the washings to the volumetric flask. Make up to volume with 1% acetic acid.

CALIBRATION AND QUALITY CONTROL:

7. Calibrate daily with at least six working standards over the range 0.01 to 0.8 mg hydroquinone per sample.
   a. Add known amounts of calibration stock solution to 1% acetic acid in 25-mL volumetric flasks and dilute to the mark.
   b. Analyze together with samples and blanks (steps 9 and 10).
   c. Prepare calibration graph (peak area vs. mg hydroquinone).
   d. Prepare recovery graph (recovery vs. mg hydroquinone).
8. Check recovery with at least three spiked media blanks per sample set.
   a. Add aliquot of calibration stock solution with a microliter syringe directly to a representative filter. Transfer filter to 60-mL ointment jar, add 10 mL 1% acetic acid, and allow to stand overnight.
   b. Prepare and analyze together with working standards (steps 5, 6, 9 and 10).
   c. Calculate recovery [(mg recovered - mg blank)/mg added)].

MEASUREMENT:

9. Set HPLC to conditions given on page 5004-1. Inject 100-mL sample aliquot.

10. Measure peak area. Retention time is ca. 5.2 min under these conditions.

CALCULATIONS:

11. Determine the mass, mg (corrected for recovery) of hydroquinone, found in the sample (W) and in the average media blank (B).
12. Calculate concentration of hydroquinone, C, in the air volume sampled, V (L):

$$C = \frac{(W - B)x10^3}{V}, mg/m^3$$

EVALUATION OF METHOD:

Method S57 [2] was issued on November 26, 1976, and validated over the range 0.8 to 4 mg/m^3 at 20 °C and 762 mm Hg using 90-L air samples [1,5]. Overall precision, $\hat{\mathbf{S}}_{\mathbf{rT}}$, was 0.061 with average recovery 105%, representing a non-significant bias. The atmospheres were generated by atomization of an aqueous solution of hydroquinone into dry air; aerosol concentrations were independently verified by direct UV spectrophotometry on filter samples. Average collection efficiency was 100% at 4 mg/m^3. No loss of hydroquinone was seen from filters spiked with 720 µg hydroquinone, and then used to sample 180 L clean air, indicating the hydroquinone vapor pressure is not significant at these conditions. At elevated temperature, however, contribution from vapor may be significant. Storage studies were conducted by storing exposed filters in 1% acetic acid at ambient temperature for seven days. No change in hydroquinone concentration was seen.

REFERENCES:

[1] NIOSH [1976]. Backup data report No. S57. In: Ten NIOSH analytical methods, set 2. Unpublished. Available as Order No. PB 271-464, from NTIS, Springfield, VA.

[2] NIOSH [1977]. Hydroquinone: Method S57. In: Taylor DG, ed. NIOSH manual of analytical methods. 2nd ed. (vol 2) Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 77-157-B.

[3] A.D. Little, Inc. [1983]. User check. NIOSH Sequence #4121Q. Unpublished.

[4] NIOSH [1978]. Criteria for a recommended standard-occupational exposure to hydroquinone. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 78-155.

[5] NIOSH [1980]. NIOSH research report-development and validation of methods for sampling and analysis of workplace toxic substances. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 80-133.

METHOD REVISED BY:

Jerome Smith, Ph.D., NIOSH; S57 originally validated under NIOSH Contract 210-76-0123.

THIRAM 5005

$((CH_3)_2NC(=S)S-)_2$ MW: 240.43 CAS: 137-26-8 RTECS: JO1400000

METHOD: 5005, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 February 1984 **Issue 3:** 15 March 2016

OSHA: 5 mg/m³
NIOSH: 5 mg/m³; Group I Pesticide

PROPERTIES: white crystalline powder; d 1.29 g/mL; MP 155 °C; VP not significant

SYNONYMS: bis(dimethylthiocarbamoyl)disulfide; tetramethylthiuram disulfide; tetramethylthioperoxydicarbonic diamide

SAMPLING

SAMPLER: FILTER (1-µm PTFE membrane)

FLOW RATE: 1 to 4 L/min

VOL-MIN: 10 L
-MAX: 400 L

SHIPMENT: routine

SAMPLE STABILITY: 7 days at 25 °C

BLANKS: 2 to 10 field blanks per set

BULK SAMPLES: desirable; 1 to 5g

ACCURACY

RANGE STUDIED: 3 to 12 mg/m³ [1] (240-L samples)

BIAS: -0.18%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.055 [1]

ACCURACY: ± 10.67%

MEASUREMENT

TECHNIQUE: HPLC, UV DETECTION

ANALYTE: Thiram

EXTRACTION: (filter) 10 mL CH_3CN, 30 min; (cassette top) 10 mL CH_3CN rinse

INJECTION VOLUME: 5 µL

MOBILE PHASE: 60% acetonitrile/40% water, 1 mL/min

COLUMN: C18 (30 cm x 3.9-mm-ID stainless steel); ambient temperature

DETECTOR: UV @ 254 nm, 1-cm cell

CALIBRATION: standard solutions of Thiram in acetonitrile

RANGE: 0.1 to 3 mg per sample [1]

ESTIMATED LOD: 0.005 mg per sample [1]

PRECISION ($\bar{S}_r$): 0.012 [1]

APPLICABILITY: The working range is 0.5 to 15 mg/m³ for a 200-L air sample. NIOSH researchers have used this method at facilities that use Thiram as an insecticide.

INTERFERENCES: None known.

OTHER METHODS: This is Method S256 [2] in a revised format. An earlier spectrophotometric method, P&CAM 228 [3], has not been revised because of excessive analytical variability [4].

REAGENTS:

1. Acetonitrile, HPLC grade.*
2. Water, distilled, deionized.
3. Thiram, reagent grade.*
4. Air or nitrogen, compressed, for drying syringes.
5. Calibration stock solution, 0.75 mg/mL. Dissolve an accurately weighed 7.5 mg Thiram in acetonitrile and dilute to 10 mL. Prepare fresh daily in duplicate.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: 1-µm polytetrafluoroethylene (PTFE) membrane filter, 37-mm diameter, two-piece polystyrene cassette filter holder with backup pad, sealed with tape or a shrinkable band.
2. Personal sampling pump, 1 to 4 L/min, with flexible connecting tubing.
3. Liquid chromatograph, UV detector at 254 nm, integrator and column (page 5005-1).
4. 13 mm x 5 µm PTFE filters and stainless steel filter holder to protect the LC column.
5. Vials, 20-mL, glass, PTFE-lined screw caps.
6. Syringe, 1-mL, with luer lock style fitting.
7. Pipets, 10-mL, with pipet bulb.
8. Tweezers.
9. Volumetric flasks, 10-mL.

SPECIAL PRECAUTIONS: Acetonitrile is toxic and flammable; work with it only in a hood. Thiram is an irritant of skin and mucous membranes, a skin sensitizer, and suspected teratogen [5].

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Sample at 1 to 4 L/min for a total sample size of 10 to 400 L. Do not exceed 2 mg total dust loading on the filter.
3. Collect a bulk sample (1 to 5 g) in a glass vial with PTFE-lined cap; ship separately from filters.

SAMPLE PREPARATION:

4. Remove filter from cassette with tweezers and place in 20-mL vial.
5. Add 10 mL acetonitrile. Cap the vial.
6. Rinse the inside top of cassette with 10 mL acetonitrile into a 20-mL vial. Cap the vial.
7. Agitate samples during the 30-min desorption period.

CALIBRATION AND QUALITY CONTROL:

8. Calibrate daily with at least six working standards over the range 0.005 to 3 mg Thiram per sample.
   a. Add known amounts of calibration stock solution to acetonitrile in 10-mL volumetric flasks and dilute to the mark.
   b. Analyze together with samples and blanks (steps 9 and 10).
   c. Prepare calibration graph (peak area vs. mg Thiram).

MEASUREMENT:

9. Set liquid chromatograph to conditions on page 5005-1. Inject 10-µL sample aliquot. Rinse and dry syringe between injections.
10. Measure peak area.

CALCULATIONS:

11. Read the mass, mg, of Thiram found in the sample filter (W_f) and top rinse (W_t) and in the average media blank (B) from calibration graph.
12. Calculate the concentration of Thiram, C (mg/m^3), in the air volume sampled, V (L):

$$C = \frac{\left(W_f + W_t - B\right) \cdot 10^3}{V}, mg/m^3$$

EVALUATION OF METHOD:

Method S256 was issued on June 8, 1979 [2], and validated by collecting 18 samples (six each at 0.5, 1 and 2 times the OSHA standard) from dynamically-generated test atmospheres using Thiram 65 (65% Thiram; Mayer Chemical Co.), as well as a set of six samples which was stored at room temperature for seven days to establish stability [1,4]. The stored sample results were within 2.1% of samples analyzed after one day, indicating adequate storage stability for seven days. Eighteen more samples were spiked directly (six each at 0.5, 1 and 2 times the OSHA standard). The pooled relative standard deviation for these three sets of samples was found to be 0.012. The average recovery for all three levels was 99.8%; therefore, there is no bias for this method. The pooled relative standard deviation for the three sets of samples collected from test atmospheres was 0.022. Test atmospheres at 12 mg/m^3 Thiram were sampled with PTFE filters followed by bubblers containing acetonitrile; no detectable Thiram (LOD = 0.005 mg) was found in the bubblers indicating that vapor pressure of Thiram was insignificant.

REFERENCES:

[1] Stanford Research Institute [1979]. Backup Data Report: Method S256. Menlo Park, CA: Stanford Research Institute. NIOSH contract 210-76-0123. Available as order no. PB-81-244634 from NTIS.

[2] NIOSH [1979]. Thiram in air: Method S256. In: Taylor DG, ed. NIOSH manual of analytical methods. 2nd. ed. (Vol 5). Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) 79-141.

[3] NIOSH [1976]. Thiram in air: Method P&CAM 228. In: Taylor DG, ed. NIOSH manual of analytical methods. 2nd ed. (Vol 1). Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 77-157-A.

[4] IIT Research Institute [1976]. Failure Report: Method S256. Chicago, IL: IIT Research Institute. NIOSH contract no. 99-74-45. Unpublished.

[5] NIOSH [1978] NIOSH criteria for a recommended standard: occupational exposure during manufacture and formulation of pesticides, Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 78-174.

[6] NIOSH [1980]. NIOSH research report – development and validation of methods for sampling and analysis of workplace toxic substances. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 80-133.

METHOD REVISED BY:

Yvonne T. Gagnon, NIOSH; S256 originally validated under NIOSH Contract 210-76-0123.

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ROTENONE 5007

$C_{23}H_{22}O_6$ MW: 394.43 CAS: 83-79-4 RTECS: DJ2800000

METHOD: 5007, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 February 1984
Issue 3: 26 February 2016

OSHA: 5 mg/m³
NIOSH: 5 mg/m³; Group II Pesticide

PROPERTIES: solid, MP 163 °C or 181 °C; BP 220 °C @ 0.5 mm Hg; d ca. 1 g/cm³; VP not significant

SYNONYMS: tubatoxin; cube

SAMPLING

SAMPLER: FILTER (1-mm PTFE membrane)

FLOW RATE: 1 - 4 L/min

VOL-MIN: 8 L
-MAX: 400 L

SHIPMENT: routine

SAMPLE STABILITY: at least 7 days @ 25 °C in dark

BLANKS: 2 to 10 field blanks per set

BULK SAMPLE: desirable; 1g

ACCURACY

RANGE STUDIED: 1 to 11 mg/m³ [1] (100-L sample)

BIAS: -0.6%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.079

ACCURACY: ± 13.5%

MEASUREMENT

TECHNIQUE: HPLC; UV DETECTION

ANALYTE: Rotenone

EXTRACTION: 4 mL acetonitrile; 30 min

INJECTI ON VOLUME: 10 µL

MOBILE PHASE: 60% methanol/40% water, 2 mL/min

DETECTOR: UV @ 290 nm; 0.1A full-scale; 1-cm cell

COLUMN: C18 (30 cm x 3.9-mm ID stainless steel); ambient temperature

CALIBRATION: solutions of Rotenone in acetonitrile

RANGE: 0.04 to 1 mg per sample

ESTIMATED LOD: 4 µg per sample [1, 2]

PRECISION ($\bar{S}_r$): 0.024 [1]

APPLICABILITY: The working range is 0.4 to 10 mg/m³ for a 100-L air sample and the method is applicable to commercial formulations.

INTERFERENCES: None known. Rotenone, a naturally occurring insecticide, is adequately separated by HPLC from other compounds (e.g., sumatrol, α-toxicarol, deguelin, elliptone, malaccol, and tephrosin [3]) present in commercial cube root extracts [4]. Rotenone is sensitive to photodecomposition.

OTHER METHODS: This is Method S300 [2] in a revised format.

REAGENTS:

1. Acetonitrile, HPLC grade.*
2. Methanol, HPLC grade.
3. Rotenone, 97% purity.
4. Water, distilled, HPLC grade.
5. Calibration stock solution, 3 mg/mL.
   Dissolve 0.075 g Rotenone in 25 mL acetonitrile. Prepare fresh daily in duplicate.
6. Recovery stock solution, 50 mg/mL.
   Dissolve 0.500 g Rotenone in acetone. Dilute to 10 mL. Prepare fresh daily.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: 37-mm, two-piece cassette containing 1-µm PTFE membrane filter with backup pad.
   NOTE: Use an opaque cassette or otherwise shield the filter from light to minimize photodecomposition of Rotenone during and after sampling.
2. Personal sampling pump, 1 to 4 L/min, with flexible connecting tubing.
3. HPLC, UV detector, integrator and column (page 5007-1).
4. Jars, ointment, 60-mL, with PTFE-lined caps.
5. Vials, 4-mL, with PTFE-lined caps.
6. Syringes, 5-mL.
7. Filtration device, 13-mm with 1-µm PTFE filters, or PTFE syringe filters.
8. Volumetrics, 10- and 25-mL.
9. Syringes, microliter, for sample injection and standard preparation.
10. Pipet, 4-mL, with pipet bulb.

SPECIAL PRECAUTIONS: Avoid breathing acetonitrile vapors; may cause skin irritation.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Sample at an accurately known flow rate between 1 and 4 L/min for a total sample size of 8 to 400 L. Do not exceed 2 mg total dust loading on the filter.
3. Collect a bulk sample (1 g) in a glass vial with PTFE-lined cap; ship separately from filters.

SAMPLE PREPARATION:

4. Open filter cassette; transfer filter to ointment jar.
5. Add 4.0 mL acetonitrile; gently swirl for 30 min.
6. Filter each sample using a 5-mL syringe with PTFE syringe filter or filtration device. Deliver filtrate to a 4-mL vial.

CALIBRATION AND QUALITY CONTROL:

7. Prepare at least six working standards daily in the range 0.01 to 1 mg Rotenone per sample.
   a. Add known amounts of calibration stock solution to acetonitrile in 10-mL volumetric flasks and dilute to the mark.
   b. Analyze together with samples and blanks (steps 9 and 10).
   c. Prepare calibration graph (peak area vs. mg Rotenone).

8. Check recovery (R) with at least three spiked media blanks per sample set in the calibration range (step 7).
   a. Add aliquots of recovery stock solution to blank filters with a microliter syringe. Air dry.
   b. Analyze together with working standards (steps 4 through 6, 9 and 10).
   c. Calculate recovery [(mg recovered - mg blank)/mg added].
   d. Prepare recovery graph (R vs. mg Rotenone).

MEASUREMENT:

9. Set HPLC system according to manufacturer's recommendations and to conditions given on page 5007-1. Inject 10-µL sample.
   NOTE: If peak area is above linear range of calibration graph, dilute, reanalyze, and apply appropriate dilution factor in calculations.
10. Measure peak area.

CALCULATIONS:

11. Read the mass, mg (corrected for recovery) of Rotenone found on the filter (W) and average media blank (B) from the calibration graph.
12. Calculate the concentration, C (mg/m^3), of Rotenone in the air volume sampled, V (L):

$$C = \frac{(W - B)x10^3}{V}, mg/m^3$$

EVALUATION OF METHOD:

Method S300 [2] was issued on May 11, 1979, and validated over the range 1.16 to 11.1 mg/m^3 at 25°C and 760 mm, using 100-L samples [1, 5]. Overall precision, $\hat{S}_{rT}$, was 0.079 with average recovery 100.4%, representing a non-significant bias. The concentration of Rotenone (generated by Wright dust feeder using Ortho Rotenone Dust [1%; Chevron Chemical Co.] enriched to 10% Rotenone with analytical grade Rotenone [Aldrich Chemical Co.]) was independently verified by collection in dioxane and HPLC analysis. Recovery was 0.98 in the range 250 to 1000 µg Rotenone per sample. Collection efficiency of the PTFE filter was found to be greater than 99% and no detectable Rotenone (LOD = 4 µg) was found on Chromosorb 102 tubes placed behind the PTFE filters at 11.8 mg/m^3. No loss was seen from spiked filters stored in the dark at room temperature for seven days.

REFERENCES:

[1] NIOSH. Backup data report. Unpublished. Available as Order No. PB 82-114729 from NTIS, Springfield, VA.

[2] NIOSH [1979]. Rotenone: Method S300. In: Taylor DG, ed. NIOSH manual of analytical methods. 2nd ed. (Vol 5). Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 79-141.

[3] Gunther FA, Blinn RG [1975]. Analysis of insecticides and acaricides. NY: Interscience, pp 419-420.

[4] Bushway RJ, Engdahl BS, Colvin BM, Hanks AR [1975]. Separation of rotenoids and the determination of rotenone in pesticide formulations by high-performance liquid chromatography. J Assoc Off Anal Chem *58*(5):965-970.

[5] NIOSH [1980]. NIOSH research report-development and validation of methods for sampling and analysis of workplace toxic substances. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 80-133.

METHOD REVISED BY:

Jerome Smith, Ph.D., NIOSH; S300 originally validated under NIOSH Contract 210-76-0123.

PYRETHRUM 5008

$C_{20}H_{28}O_3$ to $C_{22}H_{30}O_5$ (Table 1) MW: 316.4-372.4 (active constituents) CAS: 8003-34-7 RTECS: UR4200000

METHOD: 5008, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 May 1985 **Issue 3:** 25 February 2016

OSHA: 5 mg/m³
NIOSH: 5 mg/m³; Group II pesticide

PROPERTIES: viscous brown resin or solid; VP not significant

SYNONYMS: Active constituents include pyrethrin I and II, jasmolin I and II, and cinerin I and II.

SAMPLING

SAMPLER: FILTER (glass fiber, 37 mm)

FLOW RATE: 1 - 4 L/min

VOL-MIN: 20
-MAX: 400 L

SHIPMENT: routine; ship bulk sample separately

SAMPLE STABILITY: at least 1 week @ 25 °C [1]

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 1.4 to 8.5 mg/m³ [1] (132-L samples)

BIAS: -4.5%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.070 [1]

ACCURACY: ± 13.8%

MEASUREMENT

TECHNIQUE: HPLC, UV DETECTION

ANALYTE: six active constituents of pyrethrum

EXTRACTION: 10 mL acetonitrile; stand 30 min
INJECTION

VOLUME: 25 µL

COLUMN: C18, reverse phase, 10-µm packing, 25 to 30 cm

MOBILE PHASE: 85% acetonitrile/15% water, isocratic, 1.0 mL/min, room temperature, 2000 kPa (400 psi)

DETECTOR: UV absorption @ 225 nm

CALIBRATION: solutions of pyrethrum in acetonitrile

RANGE: 0.1 to 1.8 mg/sample

ESTIMATED LOD: 0.01 mg/sample

PRECISION ($\bar{S}_r$): 0.040 [1]

APPLICABILITY: The working range is 0.5 to 10 mg/m³ for a 200-L air sample.

INTERFERENCES: Specific interferences have not been studied. Mass spectrometry or gas-liquid chromatography with electron-capture detection may be needed for confirmation [1].

OTHER METHODS: This method is S298 [2] in a revised format. For bulk samples, gas-liquid chromatography with electron-capture detection has been recommended [3]. A modified HPLC method (C8 column, programmed methanol/water or acetonitrile, isocratic) has been used [4].

REAGENTS:

1. Pyrethrum*, analytical standard solution (commercially available).
   NOTE: Store away from direct light. Active constituents of pyrethrum oxidize in air and photo- decompose.
2. Acetonitrile, HPLC grade.*
3. Water, HPLC grade.
4. Isopropanol.
5. Calibration stock solution,* 60 mg/mL, in isopropanol.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: 37-mm glass fiber filter and cellulose backup pad in filter holder held together with tape or shrinkable band.
2. Personal sampling pump, 1 to 4 L/min, with flexible connecting tubing.
3. High pressure liquid chromatograph with UV absorption detector at 225 nm, integrator and column (page 5008-1).
4. Ointment jars, 2-oz, squat form, with polytetrafluoroethylene (PTFE)-lined screw caps.
5. Tweezers.
6. Pipet, TD, 10-mL, with pipet bulb.
7. Volumetric flasks, 10-mL.
8. Syringe, 10-mL, with syringe filter.
9. Syringes or pipets, 5- to 100-µL.

SPECIAL PRECAUTIONS: *p*-Chlorophenol is toxic by skin absorption, inhalation, or ingestion. It also is a strong irritant to tissue and is combustible with a flash point of 121 °C.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Sample at an accurately known flow rate between 1 and 4 L/min for a total sample size of 20 to 400 L.

SAMPLE PREPARATION:

3. Transfer the filter carefully to an ointment jar using tweezers.
4. Add 10.0 mL acetonitrile. Seal and gently swirl the jar to wet the filter. Let stand 30 min with occasional swirling.
5. Filter the sample solution through a syringe filter.

CALIBRATION AND QUALITY CONTROL:

6. Calibrate daily with at least six working standards over the range 0.01 to 1.8 mg pyrethrum per sample.
   a. Add known amounts of calibration stock solution, or a dilution thereof, to acetonitrile in 10-mL volumetric flasks and dilute to the mark.
   b. Analyze together with the samples and blanks (steps 9, 10 through 11).
   c. Prepare calibration graph (peak area vs. mg pyrethrum/10 mL).
7. Determine recovery (R) at least once for each batch of filters used for sampling in the range of the samples. Prepare three filters at each of five levels plus three media blanks.
   a. Deposit a known amount of calibration stock solution, or a dilution thereof, onto the filters. Allow filters to air-dry.
   b. Store samples overnight in ointment jars.
   c. Prepare (steps 4 and 5) and analyze together with working standards (steps 9 through 11).
   d. Prepare a graph of R vs. mg pyrethrum recovered.
8. Analyze three quality control blind spikes and three analyst spikes to ensure that the calibration graph and R graph are in control.

MEASUREMENT:

9. Set HPLC system according to manufacturer's recommendations and to conditions on page 5008-1.
10. Inject sample aliquot using syringe, fixed volume sample loop, or autosampler.
11. Measure peak area.
    NOTE: Pyrethrum is a mixture of at least six components which elute in two major peaks (t_r = 5 to 7 min under these conditions). The minor peaks have been shown by mass spectrometry not to be pyrethrums. The components may be separated by gas chromatography [1,4].

CALCULATIONS:

12. Determine the mass, mg (corrected for R) of pyrethrum found in the sample (W) and in the average media blank (B) from the calibration graph.
13. Calculate concentration, C, of pyrethrum in the air volume sampled, V (L):

$$C = \frac{(W - B)x10^3}{V}, mg/m^3$$

EVALUATION OF METHOD:

Method S298 [2] was issued on August 3, 1979, and validated over the range 1.4 to 8.5 mg/m^3 using atmospheres generated from Premium Pyrocide 175 (McLaughlin Gormley King Co.) [1]. Standards and collected filter samples were analyzed by GC/MS. Lab testing was done with spiked filters and atmospheres dynamically generated by atomization of a hydrocarbon solution; verified by PTFE filter/isooctane bubbler analyzed by gas chromatography with electron capture detector (absence of pyrethrum in the bubbler was established by mass spectrometry). Samples containing 0.7 mg pyrethrum collected from a test atmosphere were stable for seven days at ambient conditions (average recovery = 98.2%). Collection efficiency equal 99.7% for 120-L samples collected at 1 L/min at 9 mg/m^3. Precision and accuracy are given on page 5008-1.

REFERENCES:

[1] NIOSH [1979]. Backup Data Report: Method S298. Unpublished.

[2] NIOSH [1980]. Pyrethrum: Method S298. In: Taylor DG, ed. NIOSH manual of analytical methods. 2nd ed. (Vol 6) Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 80-125.

[3] Association of Official Analytical Chemists (AOAC) [1982]. Changes in official methods of analysis. J Assoc Off Anal Chem *65*: 455-456.

[4] Hultquist A, Izumi RM [1982]. NIOSH sequence reports 3481-J and 4151-J. Salt Lake City, UT: Utah Biomedical Test Laboratory. Unpublished.

[5] NIOSH [1981]. Occupational health guidelines for chemical hazards. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 81-123.

METHOD REVISED BY:

James E. Arnold, NIOSH

Table 1. Active constituents of Pyrethrum.

Compound	Formula	M.W.	CAS #
Cinerin I	$C_{20}H_{28}O_3$	316.44	25402-06-6
Cinerin II	$C_{21}H_{28}O_5$	260.45	121-20-0
Jasmolin I	$C_{21}H_{30}O_3$	330.47	4466-14-2
Jasmolin II	$C_{22}H_{30}O_5$	374.48	1172-63-0
Pyrethrin I	$C_{21}H_{28}O_3$	328.45	121-21-1
Pyrethrin II	$C_{22}H_{28}O_5$	372.46	121-29-9

BENZOYL PEROXIDE 5009

$(C_6H_5CO)_2O_2$ MW: 242.22 CAS: 94-36-0 RTECS: DM85750000

METHOD: 5009, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 February 1984 **Issue 3:** 26 February 2016

OSHA: 5 mg/m³
NIOSH: 5 mg/m³

PROPERTIES: solid; MP 103 °C; d 1.334 g/mL @ 25 °C; VP not significant; auto ignition temperature 80 °C

SYNONYMS: dibenzoyl peroxide, benzoyl superoxide

SAMPLING

SAMPLER: FILTER (0.8-µm cellulose ester membrane)

FLOW RATE: 1 - 3 L/min

VOL-MIN: 40 L @ 5 mg/m³
-MAX: 400 L

SHIPMENT: refrigerated

SAMPLE STABILITY: 9% loss from filter after 1 week @ 25 °C

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 3 to 9 mg/m³ [1]; (90-L samples)

BIAS: -0.52%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.06 [1]

ACCURACY: ± 11.82%

MEASUREMENT

TECHNIQUE: HPLC, UV DETECTION

ANALYTE: benzoyl peroxide

EXTRACTION: ethyl ether, 10 mL

PRESSURE-COLUMN: 9000 KPa (1300 psi)

MOBILE PHASE: 70/30 methanol/water; 1.6 mL/min

COLUMN: 250 mm x 3 mm-ID stainless steel; spherical silica particles with 5% bonded coating of octadecyl groups, US Pharmacopeia (USP) L1

DETECTOR: UV photometer @ 254 nm

CALIBRATION: benzoyl peroxide in ethyl ether

RANGE: 0.2 to 1.7 mg per sample [1]

ESTIMATED LOD: 0.01 mg per sample [2]

PRECISION ($\bar{S}_r$): 0.024 [1]

APPLICABILITY: The working range is 2 to 19 mg/m³ for a 90-L air sample.

INTERFERENCES: None identified

OTHER METHODS: This is Method S253 [3] in a revised format. A non-specific gravimetric method and a non-specific colorimetric method appear in the criteria document [4].

REAGENTS:

1. Benzoyl peroxide, 99% pure.*
2. Ethyl ether, purified, without stabilizer.*
3. Methanol, distilled in glass.
4. Water, deionized and distilled.
5. Calibration stock solution, 10 mg/mL. Dissolve 250 mg benzoyl peroxide in ethyl ether and dilute to 25 mL. Stable at least one week at 4 °C.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: cellulose ester membrane filter, 0.8-µm pore size, 37-mm diameter, with backup pad in cassette filter holder.
2. Personal sampling pump, 1 to 3 L/min, with flexible connecting tubing.
3. Refrigerant, water solution, sealed, refreezable, reusable.
4. Vials, 20-mL, polytetrafluoroethylene (PTFE)-lined caps.
5. High performance liquid chromatograph, 254-nm UV detector, sample injection valve with a 20-µL external sample loop, syringe filter, integrator and column (page 5009-1) or autosampler.
6. Tweezers.
7. Microliter syringes, 10- and 100-µL.
8. Volumetric flasks, 10- and 25-mL, assorted sizes.
9. Pipet, 10-mL, with pipet bulb.

SPECIAL PRECAUTIONS: Benzoyl peroxide is a flammable solid and may explode when heated; it will attack some plastics, rubber, and coatings [4]. Ethyl ether is highly flammable and forms explosive peroxides on exposure to air.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Sample at an accurately known flow rate between 1 and 3 L/min for a total sample size of 40 to 400 L. Do not exceed 2 mg particulate loading on the filter.
3. Ship samples in an insulated container with bagged refrigerant.

SAMPLE PREPARATION:

4. Immediately upon receipt at laboratory, refrigerate the samples.
5. As soon as possible after receipt, transfer each filter to a clean vial with tweezers.
6. Pipet 10 mL ethyl ether into each vial; screw on cap. Swirl to mix.

CALIBRATION AND QUALITY CONTROL:

7. Calibrate daily with at least six working standards covering the range 0.01 to 1.7 mg per sample.
   a. Add calibration stock solution with a microliter syringe to ethyl ether in a 10-mL volumetric flask and dilute to the mark.
   b. Analyze together with samples, blanks and control samples (steps 10 through 12).
   c. Prepare calibration graph of peak area vs. mass (mg) of benzoyl peroxide per sample.
8. Determine recovery of benzoyl peroxide from filters at least once for each lot of samplers in the calibration range (step 7). Prepare three filters at each of five levels plus media blanks.
   a. Add aliquot of calibration stock solution with a microliter syringe directly onto a media blank filter in a vial.
   b. Prepare and analyze together with working standards (steps 5, 6 and 10 through 12).
   c. Prepare a graph of recovery vs. mg benzoyl peroxide recovered.

9. Analyze three quality control blind spikes and three analyst spikes to ensure that the calibration graph and recovery graph are in control.

MEASUREMENT:

10. Set high performance liquid chromatograph according to manufacturer's recommendations and to conditions given on page 5009-1.
11. Flush sample loop thoroughly with sample (0.1 mL) and inject sample or autosampler.
12. Measure peak area.

CALCULATIONS:

13. Read mass, mg (corrected for recovery), of benzoyl peroxide found on sample filters, W (mg), and on average blank filters, B (mg), from calibration graph.
14. Calculate concentration, C (mg/m^3), of benzoyl peroxide in the air volume sampled, V (L):

$$C = \frac{(W - B)x10^3}{V}, mg/m^3$$

EVALUATION OF METHOD

Method S253 was issued on January 21, 1977 [3], and validated over the range 3.1 to 19.1 mg/m^3 at 26 °C and 764 mm Hg, using 90-L samples [1, 5]. The collection efficiency of the filter was determined to be 1.00, since no benzoyl peroxide was detected on a backup filter mounted directly behind the front filter. Storage stability studies on the filters held in the filter cassettes indicated a 9.3% decrease in the amount of benzoyl peroxide recovered after one week. Benzoyl peroxide was stable in ethyl ether at room temperature for at least one week. Overall precision, $\widehat{S}_{rT}$, was 0.060. Recovery was 0.97 in the range 0.225 to 0.900 mg per sample for 18 spiked samples.

REFERENCES:

[1] NIOSH [1976]. Backup data report: S253 for Benzoyl Peroxide. In: Ten NIOSH analytical methods (Set 2). Available as order No. PB 271-464 from NTIS. Unpublished.

[2] Wade R [1980]. Memorandum: UBTL analytical laboratory report for benzoyl peroxide, Sequence #2182-J. Salt Lake City, UT: Utah Biomedical Test Laboratory. Unpublished.

[3] NIOSH [1978]. Benzoyl peroxide: Method S253. In: NIOSH manual of analytical methods. 2nd ed. (Vol 4). Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 78-175.

[4] NIOSH [1977]. NIOSH criteria for a recommended standard: occupational exposure to benzoyl peroxide. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 77-166.

[5] Gunderson EC, Anderson CC [1980]. Development and validation of methods for sampling and analysis of workplace toxic substances. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 80-133.

METHOD REVISED BY:

Charles Neumeister, NIOSH.

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STRYCHNINE 5016

$C_{21}H_{22}N_2O_2$ MW: 334.42 CAS: 57-24-9 RTECS: WL2275000

METHOD: 5016, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 May 1985
Issue 3: 26 February 2016

OSHA: 0.15 mg/m³
NIOSH: 0.15 mg/m³/10h; Group I Pesticide

PROPERTIES: solid; MP 268 °C; VP not significant

SYNONYMS: strychnidin-10-one

SAMPLING

SAMPLER: FILTER (glass fiber, 37-mm)

FLOW RATE: 1 - 3 L/min

VOL-MIN: 70 L @ 0.15 mg/m³
-MAX: 1000 L

SHIPMENT: routine

SAMPLE STABILITY: at least 7 days @ 25 °C [1]

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 0.073 to 0.34 mg/m³ [3] 180-L samples)

BIAS: 4.4%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.059 [1]

ACCURACY: ± 14.6%

MEASUREMENT

TECHNIQUE: HPLC, UV DETECTION

ANALYTE: strychnine

DESORPTION: 5 mL mobile phase

INJECTION VOLUME: 20 µL

MOBILE PHASE: aqueous 1-heptane sulfonic acid + CH3CN; pH 3.5; 1 mL/min @ ambient temperature

COLUMN: 25 cm x 4.2-mm ID, packed with C18/US Pharmacopeia (USP) L1, 10-µm particle size

DETECTOR: UV absorption @ 254 nm

CALIBRATION: solutions of strychnine in mobile phase

RANGE: 10 to 70 µg per sample

ESTIMATED LOD: 0.8 µg per sample [1,2]

PRECISION ($\bar{S}_r$): 0.042 @ 13 to 62 µg per sample [1]

APPLICABILITY: The working range is 0.05 to 10 mg/m³ for a 200-L air sample.

INTERFERENCES: None known

OTHER METHODS: This revises Method S302 [2].

REAGENTS:

1. Strychnine, 98%.*
2. Acetonitrile, chromatographic quality.
3. Water, chromatographic quality, distilled.
4. Acetonitrile:water, 1:1 (v/v). Mix equal volumes of acetonitrile and distilled water.
5. Acetic acid, glacial.*
6. Acetic acid, 0.01 N. Dilute 0.6 mL glacial acetic acid to 1 L with distilled water.
7. 1-Heptanesulfonic acid sodium salt, 95%.
8. Calibration stock solution, 1 mg/mL strychnine in 0.01 N acetic acid. Use an ultrasonic bath to aid dissolution.
9. Mobile phase: Dissolve 1.1014 g 1-heptanesulfonic acid sodium salt in 980 mL 1:1 acetonitrile:water. Adjust pH to 3.5 with glacial acetic acid. Dilute to 1 L with 1:1 acetonitrile:water. Filter through 0.45-µm PTFE filter and refrigerate. Prepare fresh weekly and if cloudiness appears.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: glass fiber filter, 37-mm diameter, in cassette filter holder.
2. Personal sampling pump, 1 to 3 L/min, with flexible connecting tubing.
3. HPLC, UV absorption detector at 254 nm, recorder, integrator and column (page 5016-1).
4. Syringe filter, polypropylene housing, nylon membrane, 0.2-µm pore size.
5. Syringe, 20-µL.
6. Micropipets or syringes, 10- to 100-µL.
7. Jars, glass, squat-form ointment, with polytetrafluoroethylene (PTFE)-lined screw caps.
8. Volumetric flasks, glass, 10-mL.
9. Pipet, 5-mL delivery, with pipet bulb.
10. Tweezers.
11. Ultrasonic bath.

SPECIAL PRECAUTIONS: Strychnine is a potent convulsant. Use impervious clothing, gloves and face shields when handling it [3,4]. Avoid skin contact with acetic acid as it may cause severe burns.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Sample at an accurately known flow rate between 1 and 3 L/min for a total sample size of 70 to 1000 L.

SAMPLE PREPARATION:

3. Transfer the filter carefully using tweezers to an ointment jar.
4. Add 5.0 mL mobile phase. Seal and gently swirl the jar to wet the filter.
5. Filter the sample solution through a syringe filter.

CALIBRATION AND QUALITY CONTROL:

6. Calibrate daily with at least six working standards over the range 1 to 70 µg strychnine per sample (0.2 to 14 µg/mL).
   a. Add known amounts of calibration stock solution to mobile phase in 10-mL volumetric flasks and dilute to the mark.
   b. Analyze together with the samples and blanks (steps 9, 10, and 11).
   c. Prepare calibration graph (peak area vs. µg strychnine).
7. Determine recovery (R) at least once for each lot of filters used for sampling in the calibration range. Prepare three filters at each of five levels plus three media blanks.
   a. Deposit a known amount of calibration stock solution onto the filter. Allow filters to air dry.
   b. Store samples overnight in ointment jars.
   c. Prepare for analysis (steps 3 through 5) and analyze together with working standards (steps 9 through 11).

d. Prepare a graph of R vs. µg strychnine recovered.

8. Analyze three quality control blind spikes and three analyst spikes to ensure that the calibration graph and R graph are in control.

MEASUREMENT:

9. Set HPLC system according to manufacturer's recommendations and to the conditions given on page 5016-1.
10. Inject sample aliquot using syringe, fixed volume sample loop or autosampler.
11. Measure peak area.

CALCULATIONS:

12. Determine the mass, µg (corrected for R) of strychnine found in the sample (W) and in the average media blank (B) from the calibration graph.
13. Calculate concentration, C, of strychnine in the air volume sampled, V (L):

$$C = \frac{W - B}{V}, mg/m^3$$

EVALUATION OF METHOD:

Method S302 was issued on February 17, 1978 [2], and evaluated over the range 0.073 to 0.34 mg/m^3 using a 180-L sample [1,5]. Overall precision, $\widehat{S}_{rT}$, was 0.059 with an average recovery of 100.9%, representing a non-significant bias. The concentration of strychnine was independently verified by analysis of filter samples with a UV spectrophotometer at 254 nm. Recovery was 0.98 in the range of 13.5 to 54.1 µg per sample. Collection efficiency was determined to be at least 98.8% for 180-L sample at a concentration to be 0.15 µg/mL. Average recovery for one-day old samples was 105% vs. 98.8% for seven-day old samples stored at room temperature. Since the filter samples for the recovery and stability studies were prepared with strychnine acetate rather than the free base, the recovery of the free base and the stability of such samples is unknown.

REFERENCES:

[1] NIOSH [1976]. Back-up data report for Strychnine. In: Ten NIOSH analytical methods. Available as order No. PB288-629 from NTIS. Unpublished.

[2] NIOSH [1979] Strychnine: Method S302. In: Taylor, DG ed. 2nd ed. (Vol 5). NIOSH manual of analytical methods. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 79-141.

[3] NIOSH [1978]. NOSH criteria for a recommended standard: occupational exposure during the manufacture and formulation of pesticides. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 78-174. Available as order No. PB81-227001 from NTIS.

[4] NIOSH [1981]. Occupational health guidelines for chemical hazards. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 81-123.

[5] NIOSH [1980]. Development and validation of methods for sampling and analysis of workplace and toxic substances. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 80-133.

METHOD REVISED BY:

M.J. Seymour, NIOSH

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ARSENIC, organo- 5022

(1) $CH_3AsO_3H_2$	MW: (1) 139.96	CAS: (1)124-58-3	RTECS: (1) PA1575000
(2) $(CH_3)_2AsO_2H$	(2) 137.99	(2)75-60-5	(2) CH7525000
(3) $H_2NC_6H_4AsO_3H$	(3) 217.07	(3) 98-50-0	(3) CF7875000

METHOD: 5022, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 May 1985 **Issue 3:** 3 March 2016

OSHA: 0.5 mg/m³ (as As)
NIOSH: None

PROPERTIES: (1) Solid; MP 161 °C
(2) Solid; MP 195 °C
(3) Solid; MP 232 °C

SYNONYMS: (1) Methylarsonic acid: methanearsonic acid. (2) Dimethylarsinic acid: cacodylic acid; hydroxydimethyl arsine oxide. (3) *p*-Aminophenyl arsonic acid: *p*-arsanilic acid; atoxylic acid.

SAMPLING

SAMPLER: FILTER (1-µm PTFE)

FLOW RATE: 1 - 3 L/min

VOL-MIN: 50 L @ 0.1 mg/m³
-MAX: 1000 L

SHIPMENT: routine

SAMPLE STABILITY: stable

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 0.005 to 0.2 mg/m³ [1,2]

BIAS: none significant

OVERALL PRECISION ($\hat{S}_{rT}$): 0.047 @ 0.02 mg/m³ [1]; 0.14 @ 0.005 mg/m³ [1]

ACCURACY: ± 20% @ 0.02 mg/m³

MEASUREMENT

TECHNIQUE: ION CHROMATOGRAPHY/HYDRIDE ATOMIC ABSORPTION

ANALYTE: anions (IC); AsH_3 (AAS)

EXTRACTION: borate-carbonate buffer, 25 mL

ION CHROMATOGRAPHY:
INJECTION LOOP VOLUME: 0.8 mL

COLUMNS: two, 3 x 150-mm anion

ELUENT: borate-carbonate buffer; 2.5 mL/min; 3450 kPa (500 psi); ambient temperature

AAS:
QUARTZ FURNANCE: 800 °C

WAVELENGTH: 193.7 nm (no D_2)

CALIBRATION: organoarsenicals in water

RANGE: 0.5 to 2 µg As per sample

ESTIMATED LOD: 0.2 µg As per sample [1]

PRECISION ($\bar{S}_r$): Table 1

APPLICABILITY: The working range is 0.005 to 10 mg/m³ (as As) for a 100-L air sample. The method is designed to quantitate particulate organo-arsenic compounds.

INTERFERENCES: Inorganic arsenic (III) co-elutes with dimethylarsenic acid using Eluent A but the two may be separated with Eluent B. Other ions at high concentrations in the sample can interfere with the chromatographic separation of the arsenicals. As_2O_3 is not efficiently sampled by this sampler; for quantitation of that compound see Method 7901.

OTHER METHODS: This is P&CAM 320 in revised format [2]. Method 7200 measures total As by hydride/AAS. Method 7901 measures As_2O_3, which can exist as a vapor and aerosol.

REAGENTS:

1. Deionized water.
2. Hydrochloric acid, conc.
3. Eluent A (2.4 mM HCO_3^-/1.9 mM CO_3^{2-}/1.0 mM $B_4O_7^{2-}$). Dissolve 0.8067 g $NaHCO_3$, 0.8055g Na_2CO_3, and 1.5257 g $Na_2B_4O_7 \cdot 10H_2O$ in 4 L deionized water.
4. Eluent B (5 mM $B_4O_7^{2-}$). Dissolve 7.6284 g $Na_2B_4O_7 \cdot 10\ H_2O$ in 4L deionized waster.
5. Potassium persulfate solution,* $K_2S_2O_8$, saturated in 15% (v/v) HCl.
6. Sodium borohydride, 1% $NaBH_4$ (w/v) in 0.2% KOH (w/v). Add 5 g $NaBH_4$ and 1 g KOH to deionized water; dilute to 500 mL. Prepare fresh weekly.
7. Stock standards, 1000 µg As/mL:
   a. Methylarsonic acid.* Dissolve 0.9341 g $CH_3AsO_3H_2$, in deionized water; dilute to 500 mL.
   b. Dimethylarsenic acid.* Dissolve 0.9210 g $(CH_3)_2AsO_2H$ in deionized water; dilute to 500 mL.
   c. *p*-Aminophenylarsonic acid.* Dissolve 1.4485 g *p*-$H_2NC_6H_4AsO_3H_2$ in 5 mL 1 N NaOH. Dilute to 500 mL with deionized water. Protect from light.
   d. Arsenic trioxide.* Dissolve 0.6602 g As_2O_3 in 5 mL 1 N NaOH. Dilute to 500 mL with deionized water.
   e. Arsenic pentoxide.* Dissolve 0.7669 g As_2O_5 in 5 mL 1 N NaOH. Dilute to 500 mL with deionized water.
8. Calibration stock solution, 1 µg/mL mixed analyte. Dilute 0.1 mL of each stock standard (REAGENTS, 7.) with Eluent A in a 100-mL volumetric flask. Prepare fresh daily.
9. Argon.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: PTFE polyethylene-backed membrane filter, 1-µm pore size, 37-mm diameter with backup pad; in cassette filter holder.
2. Personal sampling pump, 1 to 3 L/min, with flexible connecting tubing.
3. Ion chromatograph with suppressor and detector bypassed. Route column effluent via PTFE tubing (0.3mm ID x 0.6mm OD) directly into arsine generator (Figure 1).
4. Syringes, plastic, 10-mL, with male luer lock style fittings.
5. Arsine generator: proportioning pump with flow-rated pump tubes and 1.5-mm ID x 3-mm OD manifold mixing coils, 5-turn and 20-turn, 1.5-mm ID x 3.5-mm OD glass "T" connectors; gas-liquid separator and expansion chamber (Figure 2); 1 m of 1/4" OD PTFE tubing; three PTFE 1/4" ID Swagelok fittings; and rotometer (100 to 900 mL/min).
6. Atomic absorption spectrophotometer (reciprocal linear UV dispersion 0.65 nm/mm); As electrodeless discharge lamp and power supply; and atomization cell (16-cm x 13-mm ID windowless quartz tube with 18-cm x 4-mm ID inlet tube fused in the center), wound with Nichrome wire (14 Ω/m, spaced 2 to 3 mm between turns and wrapped with heat resistant tape) (Figure 3). Temperature in the cell is measured by a thermocouple (800 °C). Mount the cell on top of a single-slot AAS burner head and align with burner alignment controls.
7. Beakers, 50-mL.**
8. Ultrasonic waterbath.
9. Volumetric flasks, 10-, 100- and 500-mL.**
10. Pipets, 25-µL and 0.1- to 1-mL.

**Soak all glassware in mild detergent, rinse with deionized water, 10% HNO_3, and deionized water.

SPECIAL PRECAUTIONS: Wear gloves, lab coat, and safety glasses while handling chemicals. All work should be performed in a fume hood. Potassium persulfate is a powerful oxidizing agent. Arsine gas is extremely toxic and can be fatal. The arsenic compounds used in the stock standards are poisonous [3].

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Sample at an accurately known flow rate between 1 and 3 L/min for a total sample volume of 50 to 1000 L.
3. Cap the cassettes and pack securely for shipment.

SAMPLE PREPARATION:

4. For each sample, pipet 25 mL Eluent A into a clean 50-mL beaker.
5. Open the cassette, remove the PTFE filter with clean forceps, and transfer it to the beaker. Place the exposed side of the filter in contact with the solution. Cover beaker.
6. Agitate contents of the beaker for 30 min in an ultrasonic water bath. If the extracts will not be analyzed immediately, store at ca. 4 °C until measurement.

CALIBRATION AND QUALITY CONTROL:

7. Calibrate daily with at least six working standards over the range 0.2 to 2 µg As per sample (0.008 to 0.08 µg As/mL).
   a. Add known amounts of calibration stock solution to Eluent A in 10-mL volumetric flasks and dilute to the mark.
   b. Analyze together with the samples and blanks (steps 8 through 12).
   c. Prepare calibration graph for each arsenic species (peak area or height vs. µg As).

MEASUREMENT:

8. Set the ion chromatograph to the conditions given on page 5022-1. Allow the columns to equilibrate with eluent >1 h before connecting effluent to the arsine generator.
   NOTE: Eluent A allows the separation of methylarsonic acid (retention time (t_r) = 2 min), *p*-aminophenylarsonic acid (t_r = 4 min), and As(V) (t_r = 7.5 min); As(III) and dimethylarsenic acid (t_r = 1 min) are not resolved. If a signal is obtained at the approximate retention time of the latter two compounds, or if both compounds are known to be present in the sample, perform a second analysis using Eluent B (lower ionic strength). If either of the two compounds is known not to be present, Eluent A will effectively determine the remaining compounds. With Eluent B the other species have very long retention times and will accumulate on the column, tying up active resin sites. Therefore, flush the column with Eluent A after each 10 to 15 samples and reequilibrate with Eluent B before further analysis.
9. Connect the IC effluent to the arsine generator into which the following flow:
   Saturated $K_2S_2O_8$ solution: 0.8 mL/min
   $NaBH_4$ solution: 2.0 mL/min
   Ar carrier gas: 300 mL/min
   NOTE: The gaseous arsines formed in the arsine generator are first separated from liquid solution using the gas-liquid separator (Figure 2) and then transferred by argon carrier gas through PTFE tubing to the heated quartz furnace.
10. Set the AAS according to manufacturer's recommendations and to the conditions given on page 5022-1. Align the quartz cell in the optical path. Heat the quartz cell gradually to 800 °C using a variable transformer and thermocouple.
11. Using a syringe, inject a sample aliquot (ca. 2 to 3 mL) into the chromatograph, flushing the injection loop to avoid contamination from the previous injection. Rinse the syringe with deionized water and dry it between samples, or use disposable syringes.
12. Identify the component peaks. Measure peak height or area.

Calculations

13. From the calibration graphs, calculate the amount (µg) of arsenic for each species in the sample (W) and in the average media blank (B).
14. Calculate the arsenic concentrations, C, (mg/m^3) in the air volume sampled, V (L):

$$C = \frac{W - B}{V}, mg/m^3$$

EVALUATION OF METHOD:

The measurement precision obtained under the conditions recommended in this procedure is presented in Table 1 [1]. The overall precision of the method was tested using filters loaded in a dynamic aerosol generation/sampling system with particulates of the three organoarsenical compounds. The concentration levels tested for each species were 5, 10, and 20 µg As/m^3 of air. Depending on the concentration and species, the relative standard deviation ranged from 14.4% at the lowest level to 4.7% at the highest level.

The collection efficiency of the method for organoarsenicals in the range of 5 to 20 µg/m^3 using a 300-L sample was found to be >99%. The collection efficiency of the method for inorganic arsenic was not determined.

The accuracy of the overall method was determined by analyzing additional aerosol samples from each set using Neutron Activation (NAA) and X-ray Fluorescence (XRF) analyses. Since NAA and XRF techniques provide only the total elemental arsenic, the total arsenic obtained from the IC-AAS analysis was used for comparison. The accuracy ranged from 90 to 120% of the values obtained by NAA and XRF.

REFERENCES:

[1] Colovos G, Hester N, Ricci GR, Shepard, LS. [1980]. Development of a method for the determination of organoarsenicals in air. NIOSH Contract #210-77-0134, NTIS No. PB83-180794.

[2] NIOSH [1980]. Particulate arsenicals: Method P&CAM 320. In: Taylor, DG, ed. NIOSH manual of analytical methods, 2nd ed. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 80-125.

[3] Budavari S, [1989]. Merck Index. 11th ed. Rahway, NJ: Merck & Co., Inc.

METHOD REVISED BY:

Mary Ellen Cassinelli, NIOSH;
P&CAM 320 originally developed under NIOSH Contract 210-77-0134.

TABLE 1. Sensitivity, detection limit and working range data for analysis of particulate arsenicals [1].

Arsenical	Sensitivity (ng/mL/ 1% Abs)	Detection limit (as As) for 300 L sample volume (µg/m³)	Detection limit (as As) for solution (ng/mL)	Range* for 300 L sample volume (µg/m³)	Range* for solution (ng/mL)	Measurement precision (% $\overline{S}_r$)
Dimethylarsenic acid	1.3	0.62	7	1.7-6.7	20-80	11.2
Arsenic (III)	2.1	0.71	8	1.7-6.7	20-80	11.2
Methylarsonic acid	2.1	0.72	9	1.7-6.7	20-80	8.1
p-Aminophenylarsonic acid	6.3	0.64	8	1.7-6.7	20-80	6.0
Arsenic (V)	13.0	0.46	6	1.7-6.7	20-80	10.8

*The upper limit of the range can be increased by using higher concentration standards which are injected via loops of smaller volume. Although not tested with air samples, the useful range can be extended from 5 µg/m³ down to 1.7 µg/m³ based upon the measurement range.

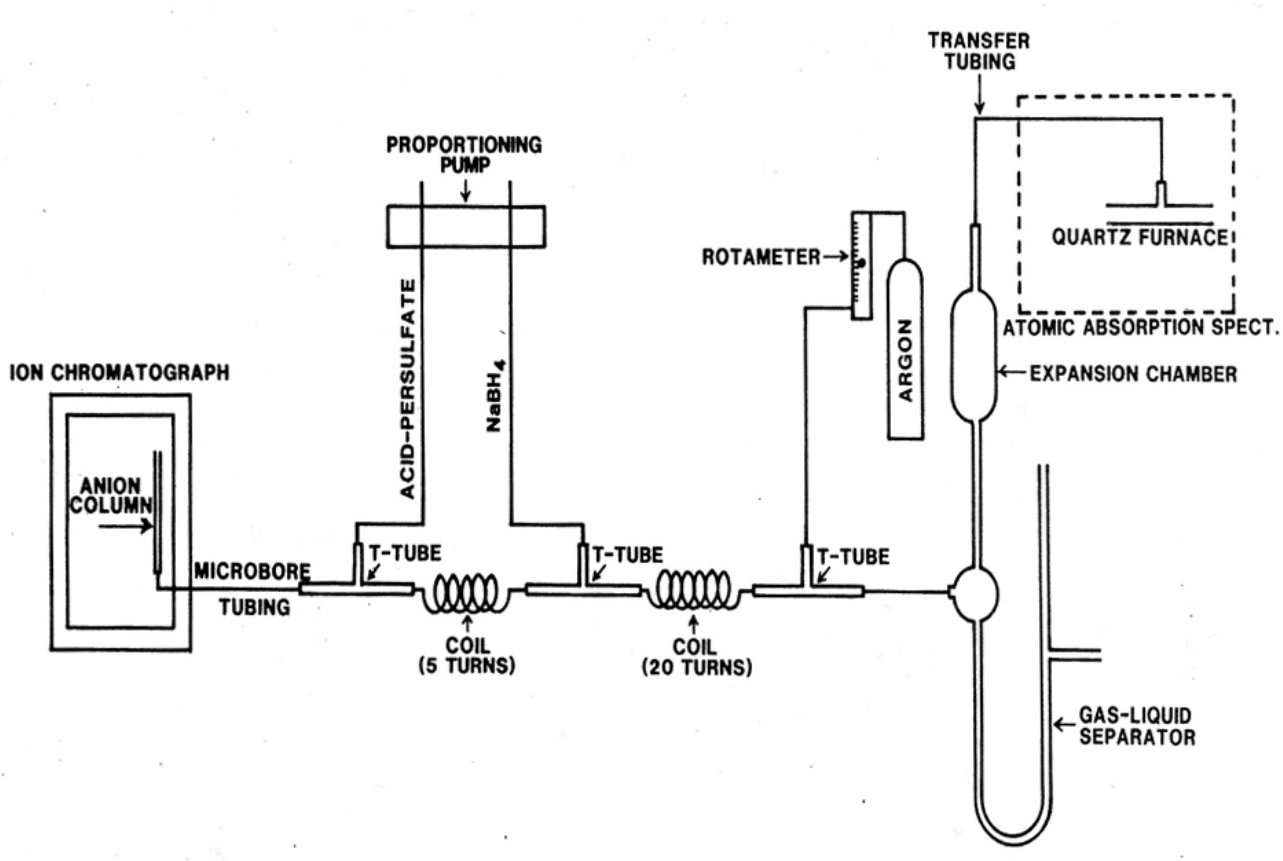

FIGURE 1. IC/AAS Analytical System.

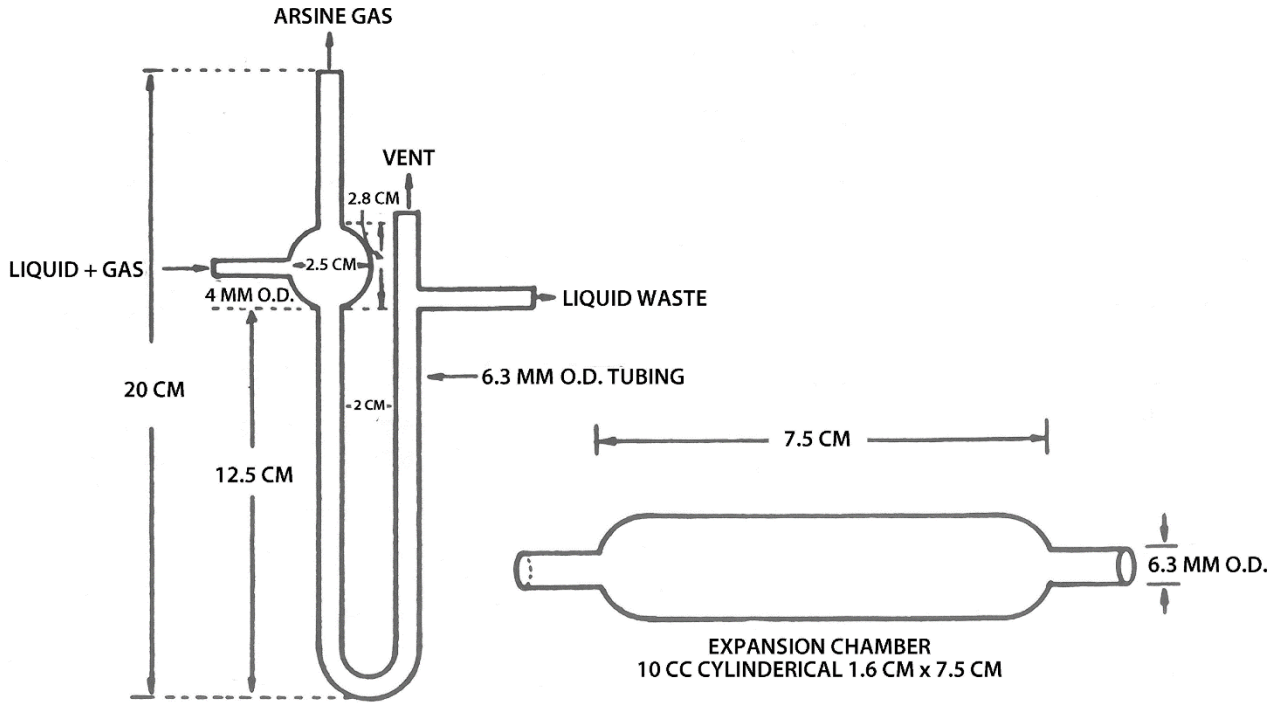

FIGURE 2. Gas-Liquid Separator and Expansion Chamber.

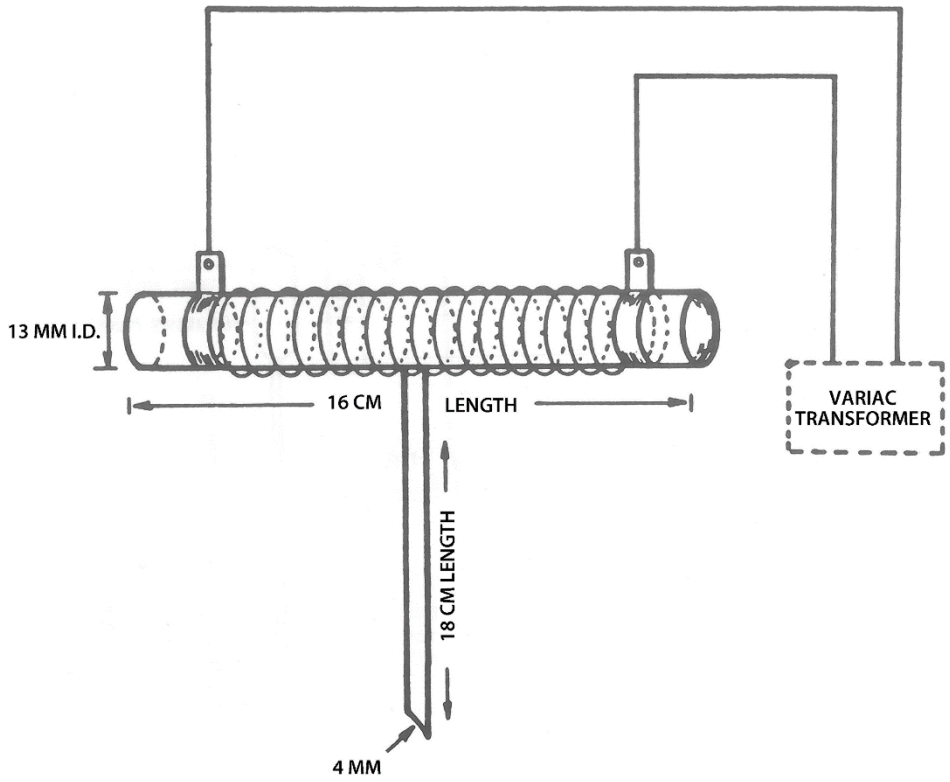

FIGURE 3. Quartz Furnace Atomization Cell.

p-NITROANILINE 5033

$H_2NC_6H_4NO$ MW: 138.14 CAS: 100-01-6 RTECS: BY7000000

METHOD: 5033, Issue 2 **EVALUATION:** FULL **Issue 1:** 15 August 1994
Issue 2: 29 February 2016

OSHA: 6 mg/m³ (skin)
NIOSH: 3 mg/m³ (skin)

PROPERTIES: yellow crystals; MP 146 °C; BP 332 °C; VP 0.02 Pa (1.5 x 10^{-4} mm Hg) @ 20 °C

SYNONYMS: 4-nitrobenzenamine, *p*-aminonitrobenzene, *p*-nitrophenylamine

SAMPLING

SAMPLER: FILTER (0.8 µm mixed cellulose ester membrane)

FLOW RATE: 1 - 3 L/min

VOL-MIN: 16 L @ 6 mg/m³
-MAX: 350 L

SHIPMENT: routine

SAMPLE STABILITY: 7 days @ 25 °C

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 3.9 to 12.9 mg/m³ (90-L samples) [1]

BIAS: -1.7%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.054 for range studied [1]

ACCURACY: ± 11%

MEASUREMENT

TECHNIQUE: HPLC, UV DETECTION

ANALYTE: *p*-nitroaniline

EXTRACTION: **5** mL isopropanol

MOBILE PHASE: 40% isopropanol/60% hexane isocratic, 1 mL/min

COLUMN: silica (25-cm x 4.6-mm x 6.4- mm stainless steel, US pharmacopeia (USP) L18)

DETECTOR: UV @ 375 nm

CALIBRATION: solutions of *p*-nitroaniline in isopropanol

RANGE: 100 to 2000 µg per sample [1]

ESTIMATED LOD: 20 µg/sample [1]

PRECISION ($\bar{S}_r$): 0.020 [1]

APPLICABILITY: The working range is 1.1 to 22 mg/m³ for a 90-L air sample. This method is applicable to *p*-nitroaniline aerosol but not for environments where vapor may be present.

INTERFERENCES: None identified

OTHER METHODS: This revises Method S7 [2].

REAGENTS:

1. *p*-Nitroaniline, 99%.*
2. Isopropanol, distilled in glass.*
3. Hexane, distilled in glass.*
4. Calibration stock solution, 10 mg/mL. Dissolve 0.100 g p-nitroaniline in 10 mL 2-propanol.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: mixed cellulose ester (MCE) membrane filter (37-mm) and cellulose backup pad (37- mm) in a 2-piece filter holder held together by shrinkable band.
2. Personal sampling pump, calibrated, capable of operating 8 h at 1 to 3 L/min, with flexible connecting tubing.
3. HPLC with UV detector (375 nm), silica column (USP L18), injector, and electronic integrator (5033-1).
4. Microliter syringes, various sizes.
5. Volumetric flasks, various sizes.
6. Squat form ointment jars with polytetrafluoroethylene (PTFE) gaskets and screw caps.
7. Pipet, 5-mL, with pipet bulb.
8. Tweezers.

SPECIAL PRECAUTIONS: *p*-Chlorophenol is toxic by skin absorption, inhalation, or ingestion. It also is a strong irritant to tissue and is combustible with a flash point of 121 °C. Work should be performed in hood

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Remove the front and rear plugs immediately before sampling and attach sampler to personal sampling pump with flexible tubing. Sample at a known flowrate between 1 and 3 L/min and collect a total sample of 16 to 350 L of air.
3. Cap the filters, record sample identity and all relevant sample data (duration, ambient temperature and pressure).
4. Prepare blank sample filters by handling in the same manner (open, seal, and transport) as samples except that no air is sampled through the blanks.
5. Ship in suitable container with blanks.

SAMPLE PREPARATION:

6. Open the filter holder and using tweezers, transfer each mixed cellulose ester filter to an ointment jar.
7. Add 5 mL isopropanol, cap, and swirl the jar to ensure that the filter is thoroughly wetted.

CALIBRATION AND QUALITY CONTROL:

8. Calibrate daily with at least six working standards.
   a. Dilute aliquots of *p*-nitroaniline stock solution with isopropanol in volumetric flasks to encompass the range of interest.
   b. Prepare calibration graph (peak area vs. µg *p*-nitroaniline per sample).
9. Determine the recovery (R) of the filters at least once for each lot of filters used in the range of interest.
   a. Using a microliter syringe, spike 6 filters at each of 3 concentration levels with *p*-nitroaniline in isopropanol. Allow the filters to dry overnight for solvent evaporation.
   b. Analyze the spiked filters. Prepare graph of µg recovered vs. µg spiked.

10. Analyze three quality control blind spikes and three analyst spikes to ensure that the calibration graph and recovery graph are in control.

MEASUREMENT:

11. Set HPLC according to manufacturer's recommendations and to conditions on page 5033-1.
12. Separation is achieved on a silica column using a mobile phase of 40% isopropanol/60% hexane at 1 mL/min. Inject 20-µL sample aliquot.
    NOTE: If peak area is above the linear range of the working standards, dilute with isopropanol and apply the appropriate dilution factor in calculations.
13. Measure peak areas.

CALCULATIONS:

14. Determine the mass of *p*-nitroaniline, µg (corrected for recovery), for the sample (W) and average media blank (B).
15. Calculate the concentration of *p*-nitroaniline, C (mg/m^3), in the air volume sampled, V (L):

$$C = \frac{W - B}{V}, mg/m^3$$

EVALUATION OF METHOD:

The method is not applicable to environments where p-nitroaniline vapor is present. However, experiments indicate that less than 0.04 mg/m^3 of p-nitroaniline would exist as a vapor at 40 °C [1]. Extraction efficiencies of spiked filters containing 0.278, 0.556, or 1.112 mg of p-nitroaniline were 96.6%, 94.7%, and 94.6%, respectively [1]. Samples generated to measure the filter's collection efficiency at 1.5 L/min for concentration of 3.9, 6.75, and 12.88 mg/m^3 showed recoveries of 95.9%, 98.8%, and 100.9% respectively [1]. The average recovery for 7-day-old samples was 98.6% [1].

REFERENCES:

[1] NIOSH [1977]. Back-up data report for *p*-Nitroaniline: Method S7. Unpublished.

[2] NIOSH [1977]. *p*-Nitroaniline: Method S7. In: Taylor DG, ed. NIOSH manual of analytical methods. 2nd ed. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 77-157-B.

[3] NIOSH [1981]. Occupational health guidelines for chemical hazards. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 81-123. Available as #PB 83-154609 from NTIS.

METHOD REVISED BY:

Charles Neumeister, NIOSH.

DIESEL PARTICULATE MATTER (as Elemental Carbon)

5040

C | MW: 12.01 | CAS: none | RTECS: none

METHOD: 5040, Issue 4 | **EVALUATION:** FULL | **Issue 1:** 15 May 1996 | **Issue 2:** 10 March 2016

OSHA: None
NIOSH: None

PROPERTIES: nonvolatile solid

SYNONYMS: diesel particulate matter, diesel exhaust, diesel soot, diesel emissions

SAMPLING

SAMPLER: FILTER: quartz-fiber, 37-mm or 25-mm; size-selective sampler may be required [1]

FLOW RATE: 2 to 4 L/min (typical)

VOL-MIN: 142 L @ 40 µg/m^3
-MAX: 19 m^3 (for filter load of ~ 90 µg/cm^2)

SHIPMENT: Routine.

SAMPLE STABILITY: Stable.
.

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 23 to 240 µg/m^3 (See also ref. [1].)

BIAS: None (See also ref. [1].)

OVERALL PRECISION ($\hat{S}_{rT}$): 0.07

ACCURACY: ± 16.7% at 23 µg/m^3 (See also ref. [1].)

MEASUREMENT

TECHNIQUE: Thermal-optical analysis; flame ionization detector (FID)

ANALYTE: Elemental carbon (EC). Total carbon is determined, but an EC exposure marker was proposed. See [1] for details.

FILTER PUNCH SIZE: 1.5 cm^2 (or other [1])

CALIBRATION: Methane injection

RANGE: 1 to 105 µg per filter portion (See also [1].)

ESTIMATED LOD: 0.3 µg per filter portion

PRECISION ($\bar{S}_r$): 0.19 @ 1 µg C, 0.01 @ 10 to 72 µg C

APPLICABILITY: The working range is approximately 6 to 630 µg/m^3, with an LOD of ~ 2 µg/m^3 for a 960-L air sample collected on a 37-mm filter with a 1.5 cm^2 punch from the sample filter. If a lower LOD is desired, a larger sample volume and/or 25-mm filter may be used (e.g., a 1920-L sample on 25-mm filter gives an LOD of 0.4 µg/m^3). The split between organic carbon (OC) and EC may be inaccurate if the sample transmittance is too low. The EC loading at which this occurs depends on laser intensity. In general, the OC-EC split may be inaccurate when EC loadings are above 20 µg/cm^2. High loadings can give low (and variable) EC results because the transmittance remains low and relatively constant until some of the EC is oxidized. The split should be reassigned (prior to EC peak) in such cases [2]. An upper EC limit of 800 µg/m^3 (90 µg/cm^2) can be determined. Low EC loadings (e.g., near the LOD) also may require a manual split to improve accuracy [1].

INTERFERENCES: Total carbon (as OC and EC) is determined by the method, but EC was recommended as a measure of workplace exposure because OC interferences may be present [1,2]. Cigarette smoke and carbonates ordinarily do not interfere in the EC determination. Less than 1% of the carbon in cigarette smoke is elemental. If heavy loadings of carbonate or organic dusts are anticipated, a size-selective sampler (impactor and/or cyclone) should be used [1]. For measurement of diesel-source EC in coal mines, a cyclone and impactor with a submicrometer cutpoint are required to minimize collection of coal dust. A cyclone and/or impactor may be necessary in other workplaces if EC-containing dusts are present.

OTHER METHODS: Other methods for determination of EC and OC have been employed, but these are not equivalent to the method described herein. Information on other methods is summarized elsewhere [1]. The method procedures are unchanged from the 4th edition supplement to NMAM, but the corresponding diesel guidance chapter was updated for the 5th edition.

REAGENTS:

1. Aqueous solutions of reagent grade (99+%) sucrose, 0.1 to 3 mg C per mL solution. Ensure filter spike loading range brackets that of samples.
2. Ultrapure H_20, Type I, or equivalent.
3. UHP helium (99.999%), scrubber also required for removal of oxygen.
4. Hydrogen, purified (99.995%), cylinder or hydrogen generator source.
5. Ultra Zero air (low hydrocarbon).
6. 10% oxygen in helium balance, both gases UHP, certified mix.
7. 5% methane in helium balance, both gases UHP, certified mix.

EQUIPMENT:

1. Sampler: Quartz-fiber filter, precleaned (in low temperature asher 2 to 3 h, or muffle furnace for 1 to 2 h at ~ 800 °C), 37-mm, in a 3-piece cassette with filter support (stainless steel screen, cellulose pad, or a second quartz filter). Alternative samplers may be required in dusty environments. See ref. [1] for details.
   NOTE 1: High purity, high efficiency, binder- free quartz-fiber filters must be used (e.g., Pall Gelman Sciences Pallflex Tissuequartz 2500QAT-UP. Precleaned filters are available from several laboratories. Filters also can be purchased and cleaned in-house. Filters should be cleaned in a muffle furnace operated at 800-900 °C for 1- 2 hours. Check (analyze) filters to ensure removal of OC contaminants. A shorter cleaning period may be effective. OC results immediately after cleaning should be below 0.1 µg/cm^2. OC vapors readily adsorb on to clean filters. Even when stored in closed containers, OC loadings may range from 0.5 µg/cm^2 after several weeks.
   NOTE 2: Cellulose supports give higher OC blanks than screens and quartz filters. Bottom quartz filters can be used to correct for adsorbed vapor; see ref. [1].
2. Personal sampling pump with flexible tubing.
3. Thermal-optical analyzer; see ref. [1].
4. Metal punch for removal of 1.5 cm^2 rectangular portion of filter.
   NOTE: A smaller portion (e.g., taken with cork borer) may be used, but the area must be large enough to accommodate the entire laser beam (i.e., beam should pass through the sample, not around it). The area of the portion must be accurately known, and the sample must be carefully positioned (the filter transmittance will decrease dramatically when the sample is properly aligned). A filter portion ≥ 0.5 cm^2 with diameter or width ≤ 1 cm is recommended.
5. Syringe, 10-µL.
6. Aluminum foil.
7. Needle (for lifting filter punch portion).
8. Forceps
9. Volumetric flasks, Class A.
10. Analytical balance.

SPECIAL PRECAUTIONS: Hydrogen is a flammable gas. Users must be familiar with the proper use of flammable and nonflammable gases, cylinders, and regulators. According to the instrument manufacturer, the instrument is a Class I Laser Product. This designation means there is no laser radiation exposure during normal operation. Weakly scattered laser light is visible during operation, but does not pose a hazard to the user. The internal laser source is a Class IIIb product, which poses a possible hazard to the eye if viewed directly or from a mirror-like surface (i.e., specular reflections). Class IIIb lasers normally do not produce a hazardous diffuse reflection. Repairs to the optical system, and other repairs requiring removal of the instrument housing, should be performed only by a qualified service technician.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
   NOTE: Both open and closed-faced cassettes have been used. Both configurations generally give even deposits. At higher flow rates (e.g., 4 L/min), small spots occasionally have been observed in the center of the filters when closed-faced cassettes are used. This material likely consisted of impacted diesel agglomerates and/or non-diesel particulate matter. EC results for multiple portions of the filters were in good agreement, so the spots had little analytical impact. Other samplers also can be used (see ref. [1]) provided an even deposit of diesel particulate results. An even deposit is necessary because the sample portion analyzed must be representative of the entire deposit. If the deposit is not homogeneous, the entire sample must be analyzed. An impactor/cyclone may be needed in some cases [1].
2. Attach sampler outlet to personal sampling pump with flexible tubing.
3. Sample at an accurately known flow rate. Typical rates are 2-4 L/min (note: Lower flows (e.g., 1 L/min) have been used in mines to prevent overloading).
4. After sampling, replace top piece of cassette, if removed, and pack securely for shipment to laboratory.
   NOTE: Diesel particulate samples from occupational settings generally do not require refrigerated shipment unless there is potential for exposure to elevated temperatures (that is, well above collection temperature). Filter samples normally are stable under laboratory conditions. Some OC loss may occur over time if samples contain OC from other sources (for example, cigarette smoke). Sorption of OC vapor after sample collection has not occurred, even with samples having high (e.g., 80%) EC content.

SAMPLE PREPARATION:

5. Place sample filter on a freshly cleaned aluminum foil surface. Isopropyl alcohol or acetone can be used to clean the foil. Allow residual solvent to vaporize from the surface prior to use. Punch out a representative portion of the filter. Take care not to disturb deposited material and avoid hand contact with sample. A needle inserted at an angle is useful for removal of the filter portion from the punch body. Newer instruments have an externally mounted bracket to support the quartz sample holder while the previous sample is removed and a new one is loaded. Through a hole in the side of the standard punch, a needle can be used to push the filter portion from the punch onto the sample holder. Alternative approaches also can be used, depending on the user's preference, as long as contamination is avoided.

CALIBRATION AND QUALITY CONTROL:

6. Analyze at least one replicate sample. For sets of up to 50 samples, replicate 10 % of the samples. For sets over 50 samples, replicate 5 % of the samples. If a filter deposit appears uneven (this should not be the case if the cassette is sealed properly), take a second portion (step 5) for analysis to check evenness of deposition.
   NOTE: Precision of replicate analyses of a filter is usually better than 5% (1 to 3% is typical).
7. Analyze three quality control blind spikes and three analyst spikes to ensure that instrument calibration is in control. Prepare spike as follows:

a. With 10-µL (or other) syringe, apply an aliquot of OC standard solution directly to filter portion taken (step 5) from a precleaned filter. For best results, the precleaned filter punch should be cleaned again in the sample oven prior to application of the aliquot.
   NOTE: With small aliquots (e.g., ≤ 10 µL), disperse standard solution over one end of filter portion to ensure standard is in laser beam. To prevent possible solution loss to surface, hold the portion off the surface. Larger volumes can easily penetrate to the underside of the filter portion.
b. Allow water to evaporate and analyze spikes with samples and blanks (steps 9 and 10).
   NOTE: A pronounced decrease in filter transmittance during the *first* temperature step of the analysis indicates water loss. Allow portions to dry longer if this occurs. Spiked punches also can be dried in the oven, if desired. For quick drying, the 'clean oven' command on the menu can be selected and canceled after about 4 seconds. The time allowed may depend on instrument, but oven temperatures should be below 100 °C to avoid boiling the solution. This approach is convenient and prevents potential adsorption of organic vapors in laboratory air. Some software versions may not have this feature.

8. Determine instrument blank (results of analysis with freshly cleaned filter portion) for each sample set.

MEASUREMENT:

9. Adjust analyzer settings according to manufacturer's recommendations (see instrument operation manual and background information in ref. [1]). Place sample portion into sample oven.
   NOTE: Forms of carbon that are difficult to oxidize (e.g., graphite) may require a longer period and higher temperature during the oxidative mode to ensure that all EC is removed (the EC peak should never merge with the calibration peak.) Adjust time and temperature accordingly. A maximum temperature above 940 °C should not be required.
10. Determine EC (and OC) mass, µg. Analyzer results are reported in units µg/cm^2 of C. The reported values are normally based on a sample portion of about 1.5 cm^2, which is the area of the standard punch provided by the manufacturer. If the portion area used differs from the value entered in the ocecpar.txt file, multiply the result by 1.5 (or value in ocecpar.txt file) and divide the product by the actual area analyzed to obtain the area-corrected result (i.e., reported result x 1.5 /portion area = corrected result in µg/cm^2). This is most easily done in the data spreadsheet. Alternatively, the correct results will be obtained with the data calculation program if the portion area is entered in the parameter file (ocecpar.txt), but this approach is error prone and tedious when punches of different areas are used for a sample set because correct results will not be obtained for all punch sizes. Updated software avoids this potential problem by prompting entry of the sample punch area prior to the analysis.

CALCULATIONS

11. Multiply the reported (or area-corrected) EC result (µg/cm^2) by filter *deposit area*, cm^2, (typically 8.5 cm^2 for a 37-mm filter) to calculate total mass, µg, of EC on each filter sample (W_{EC}). Do the same for the blanks and calculate the mass found in the average field blank (W_b). The mass of OC is calculated similarly, but the mean OC field blank may underestimate the amount of OC contributed by adsorbed vapor. A quartz filter placed beneath the sample filter can provide a better estimate of the adsorbed OC [1].
12. Calculate the EC concentration (C_{EC}) in the air volume sampled, V (L):

$$C_{EC} = \frac{W_{EC} - W_b}{V}, mg/m^3$$

EVALUATION OF METHOD:

Details on the evaluation of this method are provided in an NMAM guidance chapter on diesel [1]. The chapter includes a summary of interlaboratory comparison work conducted since the initial publication of the method. Background information and guidance on method use, including sampling requirements, also are provided. In general industry, 37-mm or 25-mm cassettes are normally suitable for air sampling, but there are exceptions. A cyclone in series with an impactor having a submicrometer cutpoint must be used in coal mines, and the Mine Safety and Health Administration (MSHA) has recommended use of a cyclone-impactor sampler in metal and nonmetal mines [3]. The impactor is commercially available through SKC, Inc. A size-selective sampler (either impactor and/or cyclone) also may be required in other dusty environments [1], particularly if the dust is carbonaceous. If a sample contains carbonate, the carbonate carbon (CC) will be quantified as OC. A carbonate-subtracted result can be obtained through acidification of the sample portion or through separate integration of the carbonate peak [1] (Note: Trona and other compounds containing sodium can etch the quartz oven wall during the analysis. Avoid spillage in the sample oven and frequent analysis of these materials.) These procedures are described in a Chapter of this Manual [1]. The thermal-optical method is applicable to nonvolatile carbon species (i.e., particulate OC, CC and EC). The method is not appropriate for volatile or semivolatiles, which require sorbents for efficient collection.

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METHOD REVISED BY:

M. Eileen Birch, Ph.D., NIOSH

CARBON BLACK 5100

C MW: 12.01 CAS: 1333-86-4 RTECS: FF5800000

METHOD: 5100, Issue 1 **EVALUATION: FULL** **Issue 1: 30 April 2015**

OSHA: 3.5 mg/m³[1]
NIOSH: 3.5 mg/m³ (in presence of PAHs: carcinogen/PAHs to 0.1 mg/m³, cyclohexane extractable fraction) [2]
For other OELs and guidelines: See references [3,4]

PROPERTIES: Solid; may contain polynuclear aromatic hydrocarbons (PAHs)

SYNONYMS: Acetylene black; amorphous carbon; furnace black; lamp black

SAMPLING

SAMPLER: INTERNAL CAPSULE, (tared 37-mm, 2- to 5-µm PVC filter melded to PVC housing) in 37-mm 2-piece cassette

FLOW RATE: 1 to 2 L/min

VOL-MIN: 75 L @ 3.5 mg/m³
-MAX: 1400 L @ 3.5 mg/m³

SHIPMENT: Routine

SAMPLE STABILITY: 28 days minimum

BLANKS: Minimum of 2 field blanks per batch

ACCURACY

RANGE STUDIED: 0.1 to 4 mg/sample

BIAS: 0.058 [5]

OVERALL PRECISION ($\hat{S}_{rT}$): 0.059 [5]

ACCURACY: ± 15.5%

MEASUREMENT

TECHNIQUE: GRAVIMETRIC (INTERNAL CAPSULE WEIGHT)

ANALYTE: Carbon black

BALANCE: 0.001 mg sensitivity; use same balance before and after sample collection

CALIBRATION: National Institute of Standards and Technology (NIST), Class S-1.1 weights or ASTM Class 1 weights

RANGE: 0.25 to 5 mg per sample

ESTIMATED LOD: 0.075 mg per sample

PRECISION ($\overline{S}_r$): 0.031 at 2 mg per sample [5]

APPLICABILITY: The working range is 1.5 to 25 mg/m³ for a 200-L air sample. This method is not applicable for the determination of "cyclohexane-solubles" [3]. The method is nonspecific; information on any other particulate materials that may be present should be assessed.

INTERFERENCES: Moisture and static electricity can affect gravimetric measurements. Humidity control and minimization of static effects are addressed in this procedure. The presence of co-sampled airborne particulate material is a positive interference since this is a gravimetric method.

OTHER METHODS: This method is preferred over Method 5000, Issue 2 [6], and is similar to Method 0501 for particulates not otherwise regulated [8]. OSHA method PV2121 describes a similar procedure (but for respirable sampling) using an alternative sampler design [9].

EQUIPMENT:

1. Sampler: Internal capsule, 37-mm PVC, 2- to 5-µm pore size membrane or equivalent hydrophobic filter attached to PVC housing and supporting pad in 37-mm 2-piece cassette filter holder
   NOTE: The cassettes should be fabricated so as to ensure complete sealing of the internal capsule after sample collection.
2. Personal sampling pump, 1 to 2 L/min, with flexible connecting tubing
3. Microbalance capable of weighing to ±0.001 mg
4. Static neutralizer; e.g. ^{210}Po; replace no more than nine months after production date
5. Tool for handling internal capsules, e.g., forceps (preferably plastic)
6. Environmental chamber or room for balance (e.g. 20 ± 1 °C and 50 ± 5% RH)

SPECIAL PRECAUTIONS: Carbon black containing polynuclear aromatic hydrocarbons (cyclohexane - extractable materials) in excess of 0.1% (w/w) should be treated as a suspect carcinogen [3].

PREPARATION OF FILTER CAPSULES BEFORE SAMPLING:

1. Equilibrate the PVC filter capsules in an environmentally controlled weighing area or chamber for at least 24 h.
   NOTE: An environmentally controlled chamber is desirable, but not required.
2. Place backup pads in filter cassette bottom sections.
3. Weigh the filter capsules in an environmentally controlled area or chamber. Record the capsule tare weight, W_1 (mg).
   a. Zero the balance before each weighing.
   b. Handle the filter capsule with forceps. Pass the capsule over an antistatic radiation source. Repeat this step if the capsule does not release easily from the forceps or if it attracts balance pan. Static electricity can cause erroneous weight readings.
4. Assemble the filter capsules in the filter cassettes and close firmly so that leakage around the internal capsule will not occur. Place a plug in each opening of the filter cassette. Place a cellulose shrink band around the filter cassette, allow to dry, and label the cassette with indelible ink.

SAMPLING:

5. Calibrate each personal sampling pump with a representative sampler in line.
6. Sample at 1 to 2 L/min for a total sample volume of 75 to 1400 L. Do not exceed a filter capsule loading of approximately 5 mg total dust. Take two to four replicate samples for each batch of field samples for quality assurance on the sampling procedure.

SAMPLE PREPARATION:

7. Wipe dust from the external surface of the filter cassette with a moist paper towelette to minimize contamination. Discard the towelette.
8. Remove the top and bottom plugs from the filter cassette. Equilibrate for at least 24 h in the balance room.
9. Using forceps, open the cassette and remove the internal capsule gently to avoid loss of dust or damage to the capsule.

CALIBRATION AND QUALITY CONTROL:

10. Zero the microbalance before all weighings. Use the same microbalance for weighing filter capsules before and after sample collection. Calibrate the balance with National Institute of Standards and Technology Class S-1.1 or ASTM Class 1 weights.
11. Process laboratory blanks, spiked QC samples and field blanks at a minimum frequency of 1 per 20 field samples. Internal capsules used for QC samples should come from the same lot. Spiked QC samples, loaded with 0.25 to 4 mg of material per internal capsule, should be prepared using weight-stable material such as Arizona Road Dust [10].

MEASUREMENT:

12. Weigh each capsule, including field blanks. Record the post-sampling weight, W_2 (mg). Record anything remarkable about a capsule (e.g., overloading, leakage, wet, torn, etc.).

CALCULATIONS:

13. Calculate the concentration, C (mg/m^3), of carbon black in the air volume sampled, V (L):

$$C = \frac{(W_2 - W_1) - (B_2 - B_1)}{V} 10^3 \quad , \text{mg/m}^3$$

where: W_1 = tare weight of capsule before sampling (mg)
W_2 = post-sampling weight of sample-containing capsule (mg)
B_1 = mean tare weight of blank capsules (mg)
B_2 = mean post-sampling weight of blank capsules (mg)

EVALUATION OF METHOD:

Lab testing was carried out using blank internal capsules and with capsules spiked with 0.1 – 4 mg of NIST SRM 1648 (Urban Particulate Matter) and Arizona Road Dust (Air Cleaner Test Dust) [5]. Precision and accuracy data are given on page 5100-1. Weight stability over 28 days was verified for both blanks and spiked capsules [5]. Independent laboratory testing on blanks and field samples have verified long-term weight stability as well as sampling and analysis uncertainty estimates [5].

REFERENCES:

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METHOD WRITTEN BY: Kevin Ashley, Ph.D., NIOSH/DART

ORGANOTIN COMPOUNDS (as Sn) 5504

Table 1 MW: Table 1 CAS: Table 1 RTECS: Table 1

METHOD: 5504, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 August 1987
Issue 3: 4 February 2016

OSHA: 0.1 mg/m^3
NIOSH: 0.1 mg/m^3 (skin)

PROPERTIES: Table 1

SYNONYMS: Table 1

SAMPLING

SAMPLER: FILTER + SORBENT (glass fiber + XAD-2, 80 mg/40 mg)

FLOW RATE: 1 to 1.5 L/min

VOL-MIN: 50 L
-MAX: 500 L

SHIPMENT: ship assembled sampler in dry ice

SAMPLE STABILITY: stable 7 days @ 0 °C [1]

FIELD BLANKS: 2 to 10 field blanks per set

MEDIA BLANKS: 12 per sample set

ACCURACY

RANGE STUDIED: 0.07 to 0.2 mg/m^3 [1] (300-L samples)

BIAS: see EVALUATION OF METHOD

OVERALL PRECISION ($\hat{S}_{rT}$): 0.07 to 0.10 [1]

ACCURACY: see EVALUATION OF METHOD

MEASUREMENT

TECHNIQUE: HPLC/ATOMIC ABSORPTION, GRAPHITE FURNACE

ANALYTE: tin

DESORPTION: 10 mL 0.1% acetic acid/H_3CN; ultrasonic, 30 min

SEPARATION: HPLC (C18 or cation exchange column)

GRAPHITE FURNACE: dry 30 sec @ 80 °C; atomize 5 sec @ 2750 °C (gas interrupt mode)

INJECTION VOLUME: 20 µL

WAVELENGTH: 286.3 nm, with background correction

CALIBRATION: standard solutions of organotin compounds in acetic acid/CH_3CN

RANGE: 5 to 50 µg Sn per sample

ESTIMATED LOD: 1 µg Sn per sample [1]

PRECISION ($\bar{S}_r$): 0.07 to 0.08 [1]

APPLICABILITY: The working range is 0.015 to 1 mg/m^3 (as Sn) for a 300-L air sample. The method was validated using TeBT, TBTC, TCHH, and BuIOMA as surrogates for the most important classes of organotin compounds [1]. If speciation of organotin compounds is not required and if inorganic tin compounds are absent, the HPLC separation may be deleted. Use special care to avoid losses of TeBT and other volatile tetra-substituted organotin compounds

INTERFERENCES: Organotin compounds not separated chromatographically will mutually interfere. Other compounds with similar retention times will not interfere unless they contain tin.

OTHER METHODS: This replaces the colorimetric criteria document method [2].

REAGENTS:

1. Zirconium acetate oxide, reagent grade.
2. Ammonium acetate, reagent grade.
3. Diammonium citrate, reagent grade.
4. Acetonitrile, chromatographic grade.
5. Deionized water.
6. Acetic acid, glacial, reagent grade.
7. Methanol, chromatographic grade.
8. Acetic acid, 0.1% (v/v) in acetonitrile.
9. Acetate buffer solution (v/v) 70% methanol, 27% deionized water, 3% aqueous 1 M ammonium acetate.
10. Citrate buffer solution (v/v) 70% methanol, 26.8% deionized water, 3% aqueous 1 M diammonium citrate in 0.2% (v/v) glacial acetic acid.
11. Organotin standard solutions, 1000 µg/mL (as Sn), prepared from pure organotin compounds in 0.1% (v/v) acetic acid in acetonitrile.
12. Calibration stock solution, 10 µg/mL (as Sn). Prepare a standard mixture of the organotin compounds of interest. Pipet 0.1 mL of each organotin standard solution into a 10-mL volumetric flask. Dilute to the mark with 0.1% (v/v) acetic acid in acetonitrile. Prepare fresh daily.

EQUIPMENT:

1. Sampler: glass fiber filter, 37-mm (commercially available) in cassette filter holder followed by XAD-2 sorbent tube, 80 mg front section/40 mg back section separated and retained by silanized glass wool (commercially available).
2. Personal sampling pump, 1 to 1.5 L/min, with flexible connecting tubing.
3. Shipping container, refrigerated, with dry ice.
4. High performance liquid chromatograph (HPLC), interfaced with autoinjection system (Fig. 1), with binary solvent capability, solvent gradient capability and columns:
   a. non-tetraorganotin species: cation exchange column.
   b. tetraorganotin compounds: C18 column
5. Atomic absorption spectrophotometer (AAS) having recorder output proportional to absorbance units, graphite furnace accessory (pyrolytic with Zr coating, coated L'vov platform may be required; see APPENDIX), sample autoinjection system with moving sample tube rack or carrousel (Fig. 1), automatic micropipettor for accurately injecting 20-µL sample aliquots into graphite furnace, background correction (e.g., D_2 or H_2 lamp) capability, and tin electrodeless discharge lamp or hollow cathode lamp.
6. Bath, ultrasonic.
7. Volumetric flasks, 10-mL.
8. Syringe, 20-µL, readable to 0.5 µL.
9. Beakers, Phillips, 125-mL.
10. Pipets, 5- and 10-mL; 10- and 100-µL.
11. Oven or muffle furnace, 200°C.
12. Plastic film.

SPECIAL PRECAUTIONS: None.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Break the ends of the sorbent tube immediately before sampling and connect to the filter with a short piece of tubing. Attach sampler to personal sampling pump with flexible tubing.
3. Sample at an accurately known flow rate between 1 and 1.5 L/min for a total sample size of 50 to 500 L.
4. Cap the samplers. Pack securely for shipment in dry ice.
   NOTE: The cassette and sorbent tube should remain connected for storage. Store samples at less than 0 °C. Analyze within seven days after collection.

SAMPLE PREPARATION:

5. Open the cassette filter holder. With tweezers, carefully transfer the filter to a 125-mL beaker.
6. Place the front sorbent section and front glass wool plug into a second beaker. Place the back sorbent section and remaining glass wool plugs into a third beaker.
7. Pipet 10.0 mL acetonitrile and 10 µL acetic acid into each beaker. Cover with plastic film.
8. Agitate beakers in ultrasonic bath for 30 min.

CALIBRATION AND QUALITY CONTROL:

9. Calibrate daily with at least six working standards.
   a. Add known amounts of calibration stock solution to 0.1% (v/v) acetic acid in acetonitrile in 10-mL volumetric flasks and dilute to the mark. Use serial dilutions as needed to obtain concentrations of each organotin compound in the range 0.1 to 5 µg/mL (as Sn).
   b. Analyze with samples and blanks (steps 12 through 15), alternating samples and standards with similar responses.
   c. Prepare calibration graphs (peak height vs. µg Sn) for each organotin compound.
10. Determine recovery (R) in the range of interest. Prepare three samplers at each of three levels plus three media blanks.
    a. Remove and discard back sorbent section of a media blank sampler.
    b. Inject a known amount (2 to 20 µL) of organotin standard solution directly onto front sorbent section and a separate aliquot onto the filter, with a microliter syringe.
    c. Cap the sampler. Allow to stand overnight.
    d. Desorb (steps 5 through 8) and analyze with working standards (steps 12 through 15).
    e. Prepare a graph of R vs. µg Sn recovered for each organotin compound.
11. Analyze three quality control blind spikes and three analyst spikes to ensure that the calibration graphs and recovery graphs are in control.

MEASUREMENT:

12. Set the AAS and graphite furnace according to manufacturer's recommendations and to conditions on page 5504-1. Adjust the sample injection/dry/atomize cycle so that it occurs exactly once every 60 sec.
13. Operate the HPLC according to manufacturer's recommendations and the following conditions:
    a. For non-tetraorganotin compounds:
       (1) Column: strong cation exchange (EQUIPMENT, 4a).
       (2) Flush column with 50 to 60 mL acetate buffer prior to sample injection.
       (3) Eluent: flowrate = 2 mL/min
       (4) Eluent Gradient:

Time (min)	% Acetate Buffer	% Citrate Buffer
0-15	100	0
15-18	100-0	0-100
18-40	0	100

       (5) After the chromatogram is complete, re-equilibrate the HPLC system to initial conditions by pumping acetate buffer through the column for 15 min.
       (6) Inject 100-µL sample aliquot.

b. For tetraorganotin compounds:
   (1) Column: C18.
   (2) Flush column with 50 to 60 mL of 100% acetonitrile prior to sample injection.
   (3) Eluent: flowrate = 2 mL/min, isocratic, 100% acetonitrile.
   (4) Inject a 100-µL aliquot of sample solution.

14. Collect HPLC eluent at the rate of 1 fraction (2 mL) per minute in AAS autosampler (Fig. 1).
    NOTE: In this example system, the column effluent is fed directly into one of the sample cups. After 1 min, the sample holder rotates and the eluted sample is in a position to be sampled for AA measurement. The furnace injection device withdraws a portion of the sample and places it in the furnace while the next sample is being eluted and collected.
15. Measure total AAS peak area for each organotin compound.
    NOTE 1: The recorder output will consist of AA peaks which form a chromatographic peak for each organotin compound if a line is drawn connecting the highest points of the AA peaks. Determine total absorbance for a species by the sum of the absorbencies of the corresponding AA peaks.
    NOTE 2: The characteristics of the graphite tube can influence the results drastically. Pay careful attention to the response of the standards and replace the graphite tube if erratic results and non-reproducible peak areas occur.

CALCULATIONS:

16. Read the mass, µg Sn (corrected for R), for each organotin compound found on the filter (W) and front sorbent (W_f) and back sorbent (W_b) sections, and on the average media blanks [filter (B) and front sorbent (B_f) and back sorbent (B_b) sections] from the calibration graphs.
17. Calculate concentration, C (mg/m^3), for each organotin compound as Sn in air as the sum of the particulate concentration and the vapor concentration in the air volume sampled, V (L):

$$C = \frac{W - B + W_f + W_b - B_f - B_b}{V}, mg/m^3$$

NOTE: W_f and W_b will include any analyte originally collected on the filter as particulate, then volatilized during sampling or storage.

EVALUATION OF METHOD:

The method was validated with tetrabutyltin (TeBT), tributyltin chloride (TBTC), tricyclohexyltin hydroxide (TCHH), and dibutyltin bis(isooctylmercaptoacetate) (BuIOMA) [1]. The working ranges, validation ranges, and estimated linear working ranges (as tin) for 300-L air samples of these organotin species at an atmospheric temperature and pressure of 20 °C and 756 mm Hg, respectively, appear below:

Species	Validation Range (mg/m^3)	Estimated linear Working Range (mg/m^3)	Estimated linear Working Range (µg/mL)	Measurement Precision (%)	Bias (%·)	Overall Precision (±%)	Accuracy
TeBT	0.027-0.112	0.02-0.17	0.05-5.0	8.1	+1.8	10.0	21.4
TBTC	0.042-0.191	0.01-0.34	0.3-10	5.9	·6.7	9.9	26.1
TCHH	0.071-0.218	0.01-0.34	0.3-10	6.9	·2.3	7.1	16.2
BuIOMa	0.070-0.220	0.01-0.34	0.3-10	7.7	·1.2	7.4	15.7

The methods were developed using a Partisil-10 strong cation exchange column and a Solvecon precolumn kit (Whatman, Inc.) for the analysis of the non-tetraorganotin compounds. For the tetraorganotin compounds, a LiChrosorb RP-18 HPLC column (Whatman, Inc.) was used.

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METHOD REVISED BY:

Eugene R. Kennedy, Ph.D., NIOSH

APPENDIX: Preparation of Zr-Coated Graphite Furnace Tube and Platform

1. Zirconium coating: soak pyrolytic graphite tubes and platforms overnight in 4.5% (w/v) zirconium acetate oxide solution; then dry in a muffle furnace for 2h at 200 °C.
2. Pyrolytic zirconium-coated graphite furnace tubes are acceptable for measurements of all organotin compounds. However, a pyrolytic zirconium-coated graphite platform (e.g., L'vov platform) is recommended for better precision at low levels and improved atomization response for volatile species such as TeBT. Platforms may be purchased commercially or prepared from pyrolytic graphite tubes, as shown in Fig. 2. Special care must be exercised during placement of the platform in the tube (Fig. 3) and in optical alignment

Table 1. Formulae and Physical Properties

Compound/ RTECS	Formula	M.W.	% Sn	Synonym
Dibutyltin bis(isooctyl mercaptoacetate) WH6719000	$C_{28}H_{56}O_4S_2Sn$	639.57	18.6	BuIOMA; CAS #25168-24-5
Tetrabutyltin WH8605000	$C_{16}H_{36}Sn$	347.16	34.2	Stannane, tetrabutyl-; TeBT; CAS #1461-25-2
Tributyltin chloride WH6820000	$C_{12}H_{27}ClSn$	325.49	36.5	Stannane, chlorotributyl-; TBTC; CAS #1461-22-9
Tricyclohexyltin hydroxide WH8750000	$C_{18}H_{34}OSn$	385.16	30.8	Stannane, tricyclohexylhydroxy-; TCHH; CAS #13121-70-5

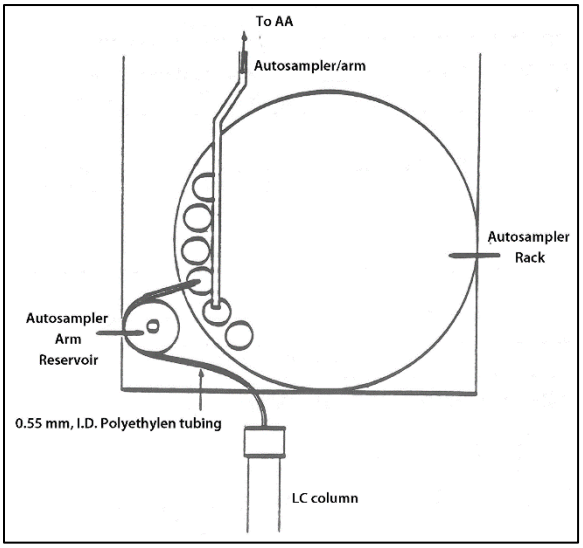

Figure 1 HPLC/AAS interface system

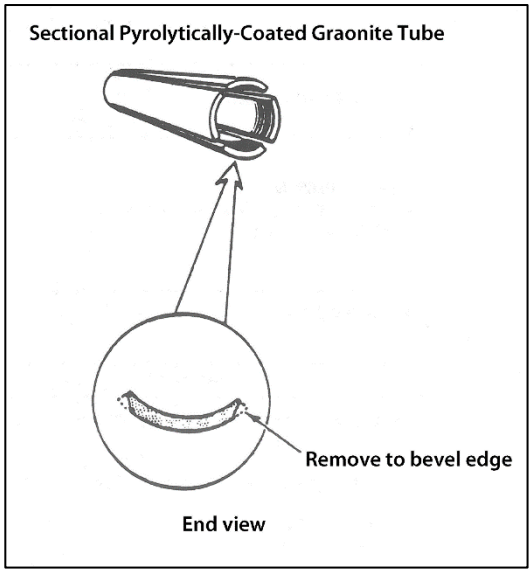

Figure 2 Construction of a laboratory made platform

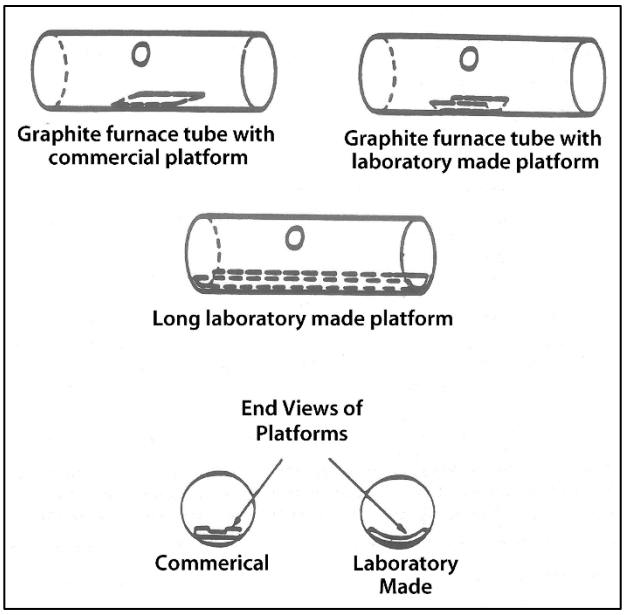

Figure 3 Placement of commercial and "laboratory-made" graphite L'vov platforms in furnace tubes.

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BENZIDINE and 3,3′-DICHLOROBENZIDINE

5509

(1) $(C_6H_4NH_2)_2$ MW: (1) 184.23 CAS: (1) 92-87-5 RTECS: (1) DC9625000
(2) $(C_6H_3ClNH_2)_2$ (2) 253.13 (2) 91-94-1 (2) DD0525000

METHOD: 5509, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 May 1989
Issue 3: 29 February 2016

OSHA: lowest feasible; carcinogen (29 CFR 1910.1010)
NIOSH: lowest feasible; carcinogen (29 CFR 1910.1010)

PROPERTIES: (1) solid; MP 127 °C; BP 400 °C
(2) solid; MP 132 °C

SYNONYMS: (1) [1,1'-biphenyl]-4,4'-diamine; *p*-diaminodiphenyl and (2) 3,3′-Dichloro[1,1′-biphenyl]-4-4′-diamine

SAMPLING

SAMPLER: FILTER (13-mm glass fiber)

FLOW RATE: 0.2 L/min

VOL-MIN: 20 L @ 10 µg/m³
-MAX: 100 L

SHIPMENT: ship benzidine samples in dry ice

SAMPLE STABILITY: (1) 11 days @ 15 °C [1]
(2) 12 days @ 23 °C [1]

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: (1) 21 to 63 µg/m³ [1]
(2) 20 to 130 µg/m³ [1]

BIAS: (1) -3%
(2) -4.0%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.07 [1]

ACCURACY: (1) ± 13.7%
(2) ± 15.2%

MEASUREMENT

TECHNIQUE: HPLC, UV DETECTION

ANALYTE: benzidine or 3,3'-dichlorobenzidine

DESORPTION: 0.5 mL 0.17% (v/v) trimethylamine in methanol; stand 60 min

INJECTION VOLUME: (1) 10 µL
(2) 15 µL

MOBILE PHASE: (1) 60% methanol/40% water
(2) 70% acetonitrile/30% water

FLOW RATE: 1.5 mL/min; ambient temperature

COLUMN: C18 US Pharmacopeia (USP) L1, 10 µm particles, 4-mm ID by 30-cm long

DETECTOR: UV @ 254 nm

CALIBRATION: solutions of analyte(s) in eluent

RANGE: 0.2 to 7 µg/sample

ESTIMATED LOD: 0.05 µg/sample [1]

PRECISION ($\bar{S}_r$): ≤0.07 [1]

APPLICABILITY: The working range for benzidine or 3,3'-dichlorobenzidine is 4 to 200 µg/m³ for a 50-L air sample. Benzidinium sulfate and 3,3'-dichlorobenzidine dihydrochloride will be collected and converted to benzidine and 3,3'-dichlorobenzidine, respectively, during sample preparation.

INTERFERENCES: Aniline interferes in the determination of benzidine but may be resolved [2]. 4,4'-Methylenebis(2-chloroaniline) interferes in the determination of 3,3'-dichlorobenzidine [1]. A number of compounds were shown not to interfere [1, 2] (see step 12, NOTE 2).

OTHER METHODS: This combines and replaces P&CAM 243 and P&CAM 246 [3].

REAGENTS:

1. Methanol, HPLC grade.
2. Acetonitrile, HPLC grade.
3. Triethylamine.
4. Water, distilled, deionized.
5. Benzidine.*
6. 3,3'-Dichlorobenzidine.*
7. Eluent: 0.17% (v/v) triethylamine in methanol. Dilute 170 µL triethylamine to 100 mL with methanol.
8. Calibration stock solution, 0.5 µg/µL. Dissolve 50 mg analyte in 100 mL eluent.
9. Recovery (R) stock solution, 0.5 µg/µL. Dissolve 50 mg analyte in 100 mL methanol.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: 13-mm, Type AE, glass fiber filter in a 13-mm filter holder.
2. Personal sampling pump, 0.2 L/min, with flexible connecting tubing.
3. High-performance liquid chromatograph, UV detector, integrator and column (page 5509-1).
4. Test tubes, 1-mL, with polyethylene stoppers.
5. Syringes, glass, 10- and 25-µL, readable to 0.1 µL.
6. Pipets, delivery, 0.5- and 5-mL, graduated in 0.1 mL.
7. Flasks, volumetric, 10- and 100-mL.
8. Centrifuge.
9. Test tube shaker, vortex type.

SPECIAL PRECAUTIONS: Benzidine is a recognized human carcinogen and can be absorbed through the skin [4,5,6]. 3,3'-Dichlorobenzidine is a carcinogen [4,6]. Take appropriate precautions to avoid personal and area contamination.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Sample at 0.2 L/min for a total sample size of 20 to 100 L.
3. Cap the sampler.
4. Ship and store samples at -15 °C if benzidine may be present.
   NOTE: Samples may be stored at room temperature if only 3,3'-dichlorobenzidine is present.

SAMPLE PREPARATION:

5. Place glass fiber filter in a test tube.
6. Add 0.5 mL eluent to each test tube. Seal each test tube and shake them on a test tube shaker.
7. Allow samples to stand for 1 h with intermittent shaking.
8. Centrifuge each sample for 10 min.

CALIBRATION AND QUALITY CONTROL:

9. Calibrate daily with at least six working standards over the range 0.05 to 7 µg analyte per sample.
   a. Deliver aliquots of calibration stock solution with microliter syringe to eluent in 10-mL volumetric flasks and dilute to the mark.
   b. Analyze together with the samples and blanks (steps 12 through 14).
   c. Prepare calibration graph (peak area vs. µg analyte).
10. Determine recovery (R) at least once per year for each lot of filters. Prepare four filters at each of five levels, plus three media blank filters.
    a. Place sample filters into separate test tubes.
    b. Inject an aliquot of R stock solution, or a dilution thereof in methanol, directly onto the filter.
    c. Cap the test tubes. Allow to stand overnight.
    d. Prepare (steps 5 through 8) and analyze (steps 12 through 14) with working standards.
    e. Prepare a graph of R for each filter vs. µg analyte recovered.

11. Analyze three quality control blind spikes and three analyst spikes to ensure that the calibration and R graphs are in control.

MEASUREMENT:

12. Set the liquid chromatograph to conditions given on page 5509-1 for analyte of interest.
    NOTE 1: If aniline is present, use a C18 column and follow the procedures found in reference [2].
    NOTE 2: The following compounds were found not to interfere with the determination of either compound: *o*-, *p*- and *m*-chloroaniline; 4,4'-methylenedianiline and ß-naphthylamine. 2-Chloro-4-methylaniline; 3,3'-dichlorobenzidine; 4,4'-methylenebis(2-chloroaniline); hydrazobenzene; and 1,2- and 1,4-naphthoquinone do not interfere in the determination of benzidine. Benzidine, aniline, *N*-methylaniline, 2-toluidine and 3,3'-dimethylbenzidine will not interfere in the determination of 3,3'-dichlorobenzidine [1].
13. Inject an aliquot (see page 5509-1 for appropriate size).
14. Measure peak area.

CALCULATIONS:

15. Read the mass, µg (corrected for R), of analyte found on the sample filter (W) and on the media blank filter (B) from the calibration graph.
16. Calculate concentration, C, of analyte in the air volume sampled, V (L):

$$C = \frac{W - B}{V}, mg/m^3$$

EVALUATION OF METHOD:

This method was evaluated over the range 21 to 63 µg/m^3 for benzidine and the range 20 to 130 µg/m^3 for 3,3'-dichlorobenzidine. The generated atmospheres for both compounds were at 30 °C and 80% relative humidity. The sampling rate was 0.8 L/min. The pooled overall precision ($\hat{S}_{rT}$) was 0.07 for 29 benzidine samples and 0.07 for 28 3,3'-dichlorobenzidine samples. The sampling methods were evaluated for effects of temperature (25, 30, and 35 °C) and relative humidity (20 and 80%). No detectable quantities of either benzidine or 3,3'-dichlorobenzidine were found on backup silica gel tubes [1]. At 180 °C, vapors of these carried by a stream of dry nitrogen at 0.3 L/min did not break through the backup silica gel in 3 h [1].

The average recovery of benzidine from filters was determined to be 97% over the range 0.2 to 2.0 µg when stored at -15 °C for 11 days. Recoveries dropped to 89% and 75% after 15 days and 21 days, respectively. Recoveries of benzidine and benzidinium sulfate from filters and silica gel indicated that the compounds were unstable in these matrices at ambient temperature. Recoveries over the range of 0.5 to 5 µg 3,3'-dichlorobenzidine and its dihydrochloride were 96% after 21 days from both filters and silica gel stored at -15 °C and at ambient temperature [1].

REFERENCES:

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[2] Kennedy ER, Seymour MJ [1981]. Development of an analytical method for benzidine-based dyes. In: Chemical hazards in the Workplace, ACS symposium series: Vol. 149. Washington, DC: American Chemical Society, pp 21-35.

[3] NIOSH [1977] P&CAM 243 and P&CAM 246. In: Taylor DG, ed. NIOSH manual of analytical methods, 2nd ed. (Vol. 1) Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Centers for Disease Control, National institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 77-157-B.

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[5] NIOSH/NCI [1978]. Current intelligence bulletin 24: Direct Blue 6, Direct Black 38, and Direct Brown 95 benzidine-derived dyes. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 78-148.

[6] NIOSH [1981]. Occupational health guidelines for chemical hazards. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 81-123.

METHOD REVISED BY:

M. J. Seymour, NIOSH.

METALWORKING FLUIDS (MWF) ALL CATEGORIES 5524

DEFINITION: Metalworking fluids CAS: None RTECS: None

METHOD: 5524, Issue 2 **EVALUATION: FULL** **Issue 1: 15 March 2003**
Issue 2: 29 December 2014

OSHA : No PEL
NIOSH: 0.4 mg/m^3 as thoracic fraction
(0.5 mg/m^3 as 'total' aerosol)
Other OELs: [1,2]*

PROPERTIES: Not defined. Fluids may contain varying amounts of mineral oil, emulsifiers, water, alkanolamines, polyethoxyethanols, biocides, surfactants, pressure additives and boron compounds.

SYNONYMS: Metalworking fluids (MWF), metal removal fluids, machining fluids, mineral oils, straight fluids, soluble fluids, synthetic fluids and semi-synthetic fluids

SAMPLING

SAMPLER: Thoracic particles: FILTER + CYCLONE (tared 37-mm, 2-µm polytetrafluoroethylene (PTFE) filter + thoracic cyclone)
Total particulate: tared 37-mm, 2-µm PTFE filter

FLOW RATE: Thoracic – 1.6 L/min,
Total – 2 L/min

VOL-MIN: 768 L at 0.4 mg/m^3 or 0.5 mg/m^3
MAX: Not determined

SHIPMENT: Ship overnight in a refrigerated container

SAMPLE STABILITY: Refrigerate upon receipt; analyze within 2 weeks of collection

BLANKS: At least 5 field blanks per set

BULK SAMPLE: One for each fluid at each site for solubility testing

ACCURACY

RANGE STUDIED: 0.05 to 0.9 mg/sample

BIAS: Not determined

OVERALL PRECISION ($\hat{S}_{rT}$): Total weight- 0.06
Extracted weight - 0.07

ACCURACY (Estimated): Total weight - 0.12
Extracted weight - 0.14

MEASUREMENT

TECHNIQUE: Gravimetric

ANALYTE: Airborne metalworking fluid aerosol

EXTRACTION: Ternary solvent: dichloromethane: methanol:toluene (1:1:1)
Binary solvent: methanol: water (1:1)

BALANCE: 0.001 mg sensitivity; use same balance before and after sample collection

CALIBRATION: National Institute of Standards and Technology Class S-1.1 weights or ASTM Class 1 weights

RANGE: 0.05 to 2 mg per sample

ESTIMATED LOD: Total weight - 0.03 mg per sample [3]
Extracted weight - 0.03 mg per sample weight [3]

PRECISION ($\overline{S}_r$): Total weight - 0.04 (≥ 0.2 mg/sample) [4]
Extracted weight - 0.05 (≥ 0.2 mg/sample) [4]

APPLICABILITY: The method is applicable to all metalworking fluids-straight, soluble, synthetic and semi-synthetic as long as they are soluble in the extraction solvent regimen [4,5]. Only one MWF (Glacier, Solutia Inc.) has thus far been found to be insoluble in the ternary extraction solvent; however, that MWF is soluble in the binary blend and tests have shown that the binary solvent in combination with the ternary solvent is effective in extracting this fluid [6]. **Thoracic samplers** meeting the International Standard ISO 7708 thoracic convention within the performance specifications of the European Standard EN13205, parts 1 through 6 [2] may be considered for this method if they have been validated for the collection of MWF. Depending on the type of thoracic sampler used, the recommended flow rate may differ from that specified above. Sampling at flow rates exceeding those recommended here may result in increased evaporative loss of sample. Welding fume may significantly interfere with proper operation of certain impactor-style samplers.

INTERFERENCES: None identified. However, any material that is collected on the filter and is soluble in the extraction solvents may interfere (positively) with the analysis.

OTHER METHODS: This method is similar to NMAM Method 0500 for Particulates Not Otherwise Regulated [7] and replaces NMAM Method 5026 as a general technique for analysis of MWF. NMAM Method 5026, which employs infrared analysis, may be used solely for the analysis of (straight) MWF that produce mineral oil mists; that method is not recommended for use with water-based fluids [8]. ASTM D7049 is another method that may be used to analyze metalworking fluids [9].

REAGENTS:

1. Dichloromethane, distilled-in-glass (DIG) (See Note)‡
2. Methanol, distilled-in-glass (See Note)‡
3. Toluene, distilled-in-glass (See Note)‡
4. Water, filtered, double deionized (18 MΩ·cm resistivity)
5. Calcium sulfate, desiccant
6. Ternary solvent blend‡: Mix equal volumes of dichloromethane, methanol and toluene in a clean dust-free container. Use a bottle with a screw cap (e.g., a clean, empty solvent bottle): Mix the solvents by gentle swirling, not by violent shaking.
7. Binary solvent blend‡: Mix equal volumes of methanol and water in a clean dust-free container. Use a bottle with a screw cap (e.g., a clean, empty solvent bottle): Mix the solvents by gentle swirling, not by violent shaking.

NOTE: Lower grade solvents have not been evaluated for this method. If it is desired to use ACS or liquid chromatographic grade solvents, in the interest of economy, the user must demonstrate that these solvents perform equally to the DIG grade (blanks ≤ those obtained with the DIG grade).

‡ See SPECIAL PRECAUTIONS

EQUIPMENT:

1. Sampler: 37-mm PTFE, 2-µm pore size membrane filter (see Appendix 1 for PTFE filter cleanup procedure) and PTFE supporting pad in 37-mm cassette filter holder. Use a 2-piece (closed face) cassette for sampling 'total' aerosol. For sampling the thoracic fraction, use a 3-piece cassette with thoracic cyclone that samples at 1.6 L/min at the thoracic cutpoint. See Evaluation of Method. Also, see page 5524-1 for discussion of alternative thoracic sampling.
2. Personal sampling pump, 1.6 to 2 L/min, with flexible connecting tubing
3. Cassette shrink bands, cellulose, 37-mm size
4. Microbalance, capable of weighing to 0.001mg
5. Static neutralizer: e.g., ^{210}Po; replace nine months after the production date
6. Forceps (preferably nylon or chrome-plated steel)
7. Extraction funnel, See Figure 1 for specifications p. 5524-10
8. Desiccator
9. Wash Bottle, PTFE
10. Vials, 20-mL and 10-mL, glass, with leak-proof PTFE-lined caps
11. Syringe, gas-tight with large bore needle, e.g., 16-gauge needle
12. Graduated cylinder, glass, 20 mL
13. Paper towels
14. Metal screen for drying filters following extraction, approximately 550 cm^2 or other convenient size. Grid size approximately 12 to 18 mm. Pre-wash screen with ternary blend solvent and allow to dry.

SPECIAL PRECAUTIONS: Dichloromethane is an inhalation hazard and is a suspect carcinogen. Handle all solvents in a fume hood. The solvents are flammable and have associated adverse health effects. Avoid breathing vapors. Avoid skin contact. Use extreme caution when blending the solvents together. The heat of mixing can cause pressure to develop as the solvents are blended, e.g., blowing a stopper from a glass-stoppered container. Use clean containers sealed with PTFE-lined screwcaps.

CALIBRATION AND QUALITY CONTROL:

1. Zero the microbalance before all weighings. Use the same microbalance for weighing filters before and after sample collection. Maintain and calibrate the balance with National Institute of Standards and Technology Class S-1.1 or ASTM Class 1 weights.
2. Process at least three tared media blanks through the measurement process for 'total' aerosol and the extractable materials.

PREPARATION OF FILTERS BEFORE SAMPLING:

3. Number the backup pads with indelible ink and place them, numbered side down, in the filter cassette bottom sections.
4. Pre-weigh the filters by the weighing procedure given in step 5. Record the mean tare weight of sample filters, W_1 and field blanks, B_1 (mg).
5. Weighing procedure:
   a. Equilibrate the filters in an environmentally controlled weighing area or chamber for 1 hour (minimum.)
   b. Zero the balance before each weighing. Using forceps, pass each filter over a static neutralizer. Repeat this step if the filter does not release easily from the forceps or attracts the balance pan. (Static electricity can cause erroneous weight readings.)
   c. Weigh each filter until a constant weight is obtained (i.e., two successive weighings within 10 µg.)
   d. Record the mean of the last two weights to the nearest microgram.
6. Assemble the filter in the 2- or 3-piece filter cassettes and close firmly so that leakage around the filter will not occur. Place a plug in each opening of the filter cassette. Place a cellulose shrink band around the filter cassette and allow to dry. Alternatively, use heavy duty elastic tape instead of the shrink band. Mark with the same number as the backup pad.

SAMPLING:

Bulks: For solubility testing, obtain liquid samples of pure uncut bulk metal-working fluids (MWF) that are expected to be sampled in worker breathing zone. Place these samples in small (e.g., 10 mL) leak-proof glass container(s) that are sealed with a leak-proof PTFE-lined screwcap. Then place them inside of a resealable plastic bag and ship these samples to the laboratory along with the sample filter cassettes.

Air: For collection of a thoracic sample, insert the cyclone into the inlet of a 3-piece cassette. For collection of a "total" sample, do not use the cyclone.

7. Calibrate each personal sampling pump with a representative sampler in line.
8. For thoracic measurements, sample at 1.6 L/min for 8 hours. For 'total' aerosol measurements, sample at 2 L/min for 8 hours. Do not exceed a total filter loading of approximately 2 mg.
9. Submit at least 5 blank filter samples as field blanks and 3 filters for media blanks for each set of samples collected per day. Handle the field blanks in the same way as the field samples; i.e., open each in a non-contaminated environment, then close the sampler and ship it to the lab along with the remaining samples. Media blanks are not opened.
10. Refrigerate all samples that are to be stored overnight (or longer) prior to shipment to the laboratory. Ship all samples in refrigerated containers to the laboratory via overnight express delivery service.
11. Refrigerate the samples immediately upon receipt at the lab until ready for analysis.
12. Analyze the samples within two weeks of receipt at the laboratory.

SAMPLE PREPARATION AND MEASUREMENT:

13. Solubility test of bulk MWF:
    a. Shake the container of bulk MWF to ensure that a homogeneous sample is obtained.
    b. Place 10 mL of the ternary solvent blend in a 20-mL glass vial.
    c. Using a large-bore gas-tight syringe, inject 50 µL of the bulk MWF into the ternary solvent blend. Cap the vial and shake as necessary to dissolve the MWF. The fluid is soluble if the resulting solution is clear and free of precipitates and phase separation.
    d. If the MWF is soluble in the ternary blend, the samples can be extracted with the ternary blend.
14. Wipe dust from the external surface of each filter cassette (containing either samples or blanks) with a moist paper towel to minimize contamination. Discard the paper towel.
15. Remove the top and bottom plugs from the filter cassette. Equilibrate the filters (in the cassettes) for no more than 2 hours in a desiccator that uses calcium sulfate.
16. Remove from the desiccator. Equilibrate for at least 1 hour in the balance room or chamber.
17. Remove the cassette band, pry open the cassette, and remove the filter gently to avoid loss of sample.
    NOTE: If the filter adheres to the underside of the cassette top, very gently lift it away by using the dull side of a scalpel blade. This must be done carefully or the filter will tear.
18. Weigh and record (steps 5b through 5d) the post-sampling weight of each filter, W_2 (mg) and blank, B_2 (mg). Record anything remarkable about the filter (e.g., overload, leakage, wet, or torn). Perform the extraction as soon as possible. Store in a clean dust free environment until ready to perform the extraction, etc.

EXTRACTION:

19. Perform all extractions in an exhaust hood. General guidelines (see NOTE below):
    NOTE: Samples weighing less than 0.4 to 0.5 mg (for a 1 m^3 sample) may be extracted as desired. The reason that the cutoffs of 0.4 and 0.5 mg (per 1000 L sample) have been specified is to assure compliance with the occupational exposure limit (OEL). If the gross sample weight indicates that the OEL has not been exceeded, there may be no reason to extract the sample. Otherwise, the usefulness of any extraction data obtained at levels less than 0.4 to 0.5 mg per sample is guided by the limit of quantitation (LOQ) of the extraction procedure. Extraction data obtained at levels between the limit of detection (LOD) and the LOQ of the extraction procedure should be used with appropriate caution due to the imprecision associated with such data.
20. Do not presume that a fluid that is soluble only in the binary-blend should be extracted using only the binary blend. The possibility of mixed exposures always dictates that the extraction procedure with both the binary and ternary solvent blends should be followed. If the weights of samples exceed the amount expected to be collected at the REL, e.g., 0.4 mg (thoracic fraction) or 0.5 mg ('total' aerosol) for a 1 m^3 air sample, then extract the samples and blanks as follows:
    a. Place each filter (membrane side up) in the filter funnel assembly connected to the vacuum source.
    b. Pour one 10-mL aliquot of the *ternary solvent* down the inside wall of the funnel over the filter. Allow the solvent to contact the filter for no more than 5 to 10 minutes. Remove the solvent under slight vacuum.
    c. Pour one 10-mL aliquot of the *binary solvent* down the inside of the funnel over the filter. Allow the solvent to contact the filter for no more than 5 to 10 minutes. Remove the solvent under slight vacuum.
    d. Pour a second 10-mL aliquot of the *ternary solvent* down the inside of the funnel over the filter. Allow at least 30 seconds of contact time. Remove the solvent under slight vacuum. Wash the inner wall of the filter funnel with 1 to 2 mL of the ternary blend contained in a PTFE wash bottle. Remove the solvent under slight vacuum.

e. Turn off the vacuum to the filter funnel.
f. Carefully remove the filter from the filter funnel, place it on the clean metal screen, and allow to dry on the metal screen for at least 2 hours in a fume hood. Do not remove the filter from the funnel while vacuum is applied or the filter may delaminate.

NOTE: One metalworking fluid, Glacier (Solutia Chemical, St Louis), was insoluble in the ternary blend but was soluble in the binary blend. Tests have shown that this fluid is extracted efficiently from the filters using steps 20a through 20e [5].

21. Weigh each filter, including field blanks, following steps 5a through 5d. Record the post-extraction weight, W_3 (mg), of the extracted sample filters and B_3 (mg), for the extracted blank filters. Record anything remarkable about the extracted filter (e.g., torn, wet, delamination, etc.).

CALCULATIONS:

22. Calculate the concentration of 'total' aerosol or thoracic fraction, C (mg/m^3), in the air volume sampled, V (L):

$$C = \frac{(W_2 - W_1) - (B_2 - B_1) * 10^3 L/m^3}{V}, (mg/m^3)$$

where: W_1 = mean tare weight of filter before sampling (mg) (step 5)
W_2 = mean post-sampling weight of sample-containing filter (mg) (step 18)
B_1 = mean tare weight of all blank filters (mg) (step 5)
B_2 = mean post-sampling weight of all blank filters (mg) (step 18)

23. Calculate the concentration of extracted MWF aerosol C_{MWF} (mg/m^3), in the air volume sampled, V (L):

$$C_{MWF} = \frac{(W_2 - W_3) - (B_2 - B_3) * 10^3 L/m^3}{V}, (mg/m^3)$$

where: W_2 = mean post-sampling weight (pre-extraction weight) of sample-containing filter (mg) (step 18)
W_3 = mean post-extraction weight of sample-containing filter (mg) (step 21)
B_2 = mean post-sampling weight of all blank filters (mg) (step 18)
B_3 = mean post-extraction weight of all blank filters (mg) (step 21)

24. Report the concentration C as 'total' aerosol or thoracic fraction weight; report the concentration C_{MWF} as the weight of the MWF aerosol.

EVALUATION OF METHOD:

The 'total' weight procedure permits an estimate of the 'total' collected particulate aerosol, including nuisance dust, airborne metal particulate and metal working fluid. If the extraction procedure is used, the technique permits an estimate of the 'total' collected metalworking fluid to which the worker is exposed. The development of the ternary solvent used in this method is described in reference 3. This method was initially tested with representative samples of straight, soluble, semi-synthetic, and synthetic metalworking fluids (MWFs). Samples were spiked onto tared polytetrafluoroethylene (PTFE) membrane filters, stored overnight, and analyzed the following day. The samples were weighed, then the MWF was extracted from the filter with a 1:1:1 blend of dichloromethane:methanol:toluene. The fractions extracted (FE or mass recovered/mass spiked) exceeded 94% for all fluids extracted from the filters over the range from 200 µg to 815 µg for the straight fluid, from 223 µg to 878 µg for the soluble

fluid, from 51 µg to 189 µg for the semi-synthetic fluid, and from 102 µg to 420 µg for the synthetic fluid. For those weights of all four fluids spiked at levels ≥ 200 µg, the relative standard deviation was estimated to be 4% for the total weight procedure and 5% for the extraction procedure. If the sampling imprecision of 5% is included, these estimates become 6% and 7% respectively for the total weight and extraction procedures. Limits of quantitation, estimated from blanks carried through the entire analytical procedure, were 30 µg for the weighing technique and 60 µg for the extraction technique. No estimate of the bias was available [4]. The filters are desiccated to remove excess water from water-based MWF samples.

In a more rigorous test of this method for a 79-plant survey [2], the average limits of quantitation were estimated to be 0.1 mg for both the total and extracted weight procedures. However, there was high variability in these estimates for the sites sampled. The upper 95% confidence limit for the LOQs for both the total weight and extracted weight measurements was 0.3 mg. In order to assess the effectiveness of the extraction step, a secondary extraction of the most heavily-loaded filters obtained in this survey was conducted; on average, less than 5% of the sample weight was removed during the second extraction, indicating that the majority of extractable material had been removed during the first extraction. Samples were refrigerated upon receipt at the laboratory [2,10].

During the 79-plant survey, all thoracic sampling was conducted with a BGI Mdl 2.69 Thoracic sampler. This sampler has a thoracic cut point of 10 µm at 1.6 L/min. The stability of quality assurance (QA) samples, spiked separately with a straight, a soluble, a semi-synthetic, and a synthetic fluid, indicated that the QA samples all lost weight according to simple linear decay equations. This loss in weight was likely due to evaporation of the spiking solvent and water (for soluble, semi-synthetic and synthetic MW fluids.) These decay equations were used to estimate the amounts expected to be reported for QA filters by the performing laboratory. For storage periods ranging from 17 to 26 days, the total weight of samples recovered for all QA samples were greater than or equal to 80% of those expected from the decay equations. For these QA samples, the fractions extracted of all four fluid types were greater than or equal to 90%.

The binary solvent extraction step has been added to assure complete extraction of MWF components that may be incompletely removed by the ternary blend. In addition, the binary solvent extends the procedure to samples that contain ternary blend-soluble fluids co-mingled with ternary blend-insoluble fluids, e.g., Glacier (Solutia Inc.) Tests of the extraction of five MWF (including Glacier) showed that extraction efficiencies using the ternary blend in combination with the binary blend were comparable to those reported in reference 1 using the ternary blend alone (FE greater than 90 %; CV less than 0.10). The binary solvent extractant liquor obtained from the Glacier samples generally contained potassium and phosphorous at levels approximately expected for the mass spiked onto the filters. The binary solvent extracts of the four other test fluids were analyzed for sodium, potassium or boron marker elements. Sodium was present in the extract of the soluble fluid at greater than background levels. The boron marker was not detected in the extract from the semi-synthetic fluid. The potassium marker was not detected in the extract from the synthetic fluid [5].

This method was further evaluated in a six-laboratory round robin study using synthetically generated atmospheres of an aerosol of a soluble MWF at the 0.5 mg/sample level. The data were evaluated according to ASTM standard E691-99. Pooled estimates of the total coefficients of variation were 0.13 for both the total and extracted weight samples. Overall there was no significant bias in the results. LOQs were comparable to those reported above [11].

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METHOD WRITTEN BY:

R. Glaser, NIOSH/DART and edited by Y. T. Gagnon, NIOSH/DART.

* NOTE: Because exposure limits and guidelines may change over time, NIOSH recommends referring to the following sources for updated limits and guidelines. [1,2]

Appendix 1. Procedure to remove PTFE filter contaminants that are soluble in and extracted with the ternary blend.

Use this procedure to prevent high blanks from being obtained following extraction of PTFE filters. The filters are rinsed with ternary solvent (1:1:1 dichloromethane:methanol:toluene) described in NMAM Method 5524. The filters are air-dried and protected from airborne contamination prior to weighing and assembly into cassettes for field sampling. See evaluation of procedure which follows these instructions.

EQUIPMENT, SUPPLIES, REAGENTS AND STANDARDS

1. 250 mL glass beaker(s)
2. 500 mL of ternary solvent 1:1:1 ratio of dichloromethane:methanol:toluene in a stoppered container
3. A fume hood
4. Watch glasses to fit the beakers
5. Glass stir rod
6. One box (or as many as required) of 2 micron PTFE filters to be cleaned; recommend cleaning no more than 1 package of 50 filters per 100 mL of solvent
7. Stainless steel forceps to manipulate filters
8. Large, lint-free paper towels
9. Clean, stainless steel metal trays or screen approximately 45 cm x 60 cm (18 inch x 24 inch)
10. Nitrile gloves
11. Clean, wide mouth glass container e.g., ointment jar with Teflon cap or French square bottle

PROCEDURE

Perform all of the following tasks inside a fume hood!

1. Wear nitrile gloves throughout this procedure to protect yourself from the solvent and to protect the filters from skin oil during handling.
2. Pour approximately 100 mL of ternary solvent into a 250 mL glass beaker.
3. Remove the PTFE filters from the package and remove the plastic spacers from between the filters. Place the filters individually (sample side up) into the beaker filled with ternary solvent. Be careful that the filters stay separated from each other and do not clump together.
4. Carefully stir the filters with the glass stir rod; do not allow the filters to turn over. Cover the beaker with the watchglass. Allow the filters to extract in the solvent in the beaker for 10 minutes.
5. Decant the ternary solvent out of the beaker and into a waste bottle. Use the stirring rod to compress and retain the filters in the beaker as the solvent is slowly decanted off.
6. Refill the beaker with 100 mL of fresh ternary solvent after decanting following step 5. Repeat steps 4 and 5, two times for a total of three solvent washes.
7. After the three rinses are complete, drain off as much solvent as possible. Remove the filters from the beaker using forceps and place them onto a clean stainless steel metal tray that has been covered with a large, lint-free paper towel. Alternatively, place them on a clean stainless steel screen. Place them onto the tray or screen, sampling side up. Allow the filters to dry overnight.
   Warning: Keep the hood sash approximately at or below the sash height level as marked on the hood. If the sash is pushed lower, the higher air flow may blow the filters off the drying tray or screen. Place a sign on the sash indicating that it is to be left at this height overnight and **not to be moved.**
8. Place the dried filters in a clean French square glass bottle or a wide-mouthed Teflon™ capped ointment jar. Label the container "PTFE 2-µm filters rinsed with MWF solution," giving the date, initials, and number of filters. Do not store filters in plastic containers. Filters are now ready to be used for sampling. Since the filters are not separated by spacers, use care to remove them from the storage container for use.

Cleanup Procedure Evaluation

This cleanup procedure has been incorporated into NMAM Method 5524 in order to deal with reported spurious weight gains and losses before and after analysis of the PTFE filters used with this method. It is believed that trace levels of dust or extractable material are entrained in these filters during the manufacturing process. This cleanup procedure has been evaluated using 60 filters from three different batches of PTFE filters (20 filters/batch) [1]. Prior to cleaning, the filters were weighed **(untreated filters)**, then washed with the ternary blend according to the procedure in Appendix 1, dried, and then reweighed **(treated filters)**.

Results: The differences in each of the 3 batches were compared by subtracting the **treated** filter weights from their **untreated** weights. For all 60 samples, the overall mean difference in weights (+/-the standard error of the mean) was 0.2 µg (± 1.4 µg). For each of the 3 batches, the differences in weight were reported as mean (+/-standard error): 5 µg (± 2.5 µg) , -2 µg (± 2.0 µg), and -3 µg(± 2.7 µg) for batches 1, 2 and 3, respectively. The weight differences were not statistically significant from zero overall or by batch using a paired t-test (p = 0.05), and allowing for multiple comparisons.

To determine if the washing procedure affected the filter's performance for analysis of metalworking fluids, each of the filters was analyzed according to the procedure of NMAM Method 5524, which includes extraction with the binary and ternary solvent blends. The following differences were computed: **post-analysis** weights of the filters minus their **treated** or **untreated** weights. The average difference in the weights of the 60 **untreated** filters and their **post-analysis** weights reported as mean (± standard error of the mean) was 34 µg (± 1.9 µg). For each of the 3 batches, the differences in the **untreated** and **post-analysis** weights were: 30 µg (± 3.9 µg), 38 µg (± 2.0 µg) and 34 µg (± 3.3 µg) for batches 1, 2 and 3, respectively. These differences are statistically significantly different from zero, both overall and individually by batch, using a paired t-test (p = 0.05), and allowing for multiple comparisons.

The average differences in the weights of the 60 **treated** filters and their **post-analysis** weights were: 34 µg (± 1.4 µg). Again the differences in weight are reported as mean (± standard error). For each of the 3 batches, the differences, (**post-analysis minus treated**) weights, were: 35 µg (± 3.4 µg), 36 µg (± 2.0 µg), and 31 µg (± 1.8 µg) for batches 1, 2 and 3, respectively. These differences are statistically significantly different from zero, both overall and individually by batch, using a paired t-test (p = 0.05), and allowing for multiple comparisons.

In summary, the weight differences were statistically different from zero by batch and overall using a paired t-test for both the **post-analysis minus treated** weights and for the **post analysis-untreated** weights (p = 0.05). However, the untreated/treated differences were not statistically different using the same tests.

These experiments indicate that cleaning the filters lowered the overall LOQ of the analytical method. The LOQ determined from the differences in weights between the **untreated** and **analyzed** filters was 140 µg and was greater than the LOQ of 110 µg determined from the differences in weights between the **treated** and **analyzed** filters. The extraction procedure produced a more consistent blank and therefore a lower average standard deviation from which lower LOD s and LOQs were determined.

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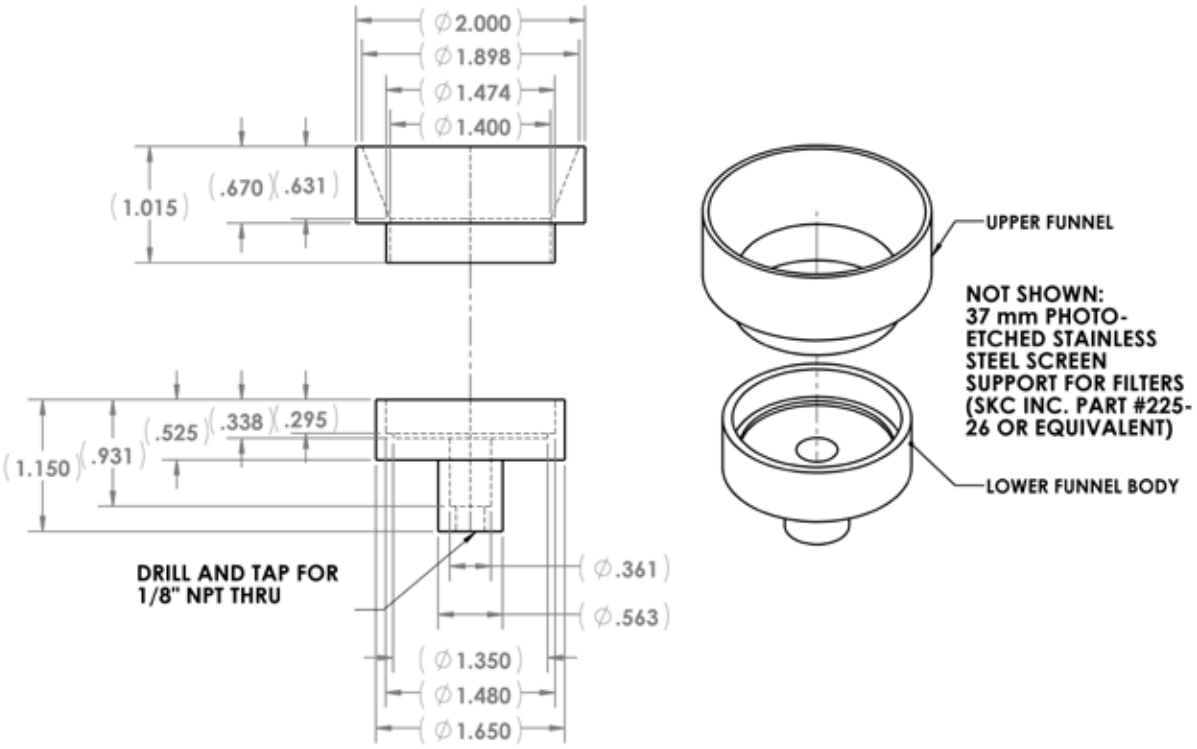
Figure 1. Schematic diagram of funnel. May be ordered from Case Custom Environmental Equipment, Erlanger, Kentucky (859-250-8558); www.casecustomenvironmentalequipment.com) or equivalent source. Dimensions are given in inches.



Formula: Table 1 MW: Table 1 CAS: Table 1 RTECS: Table 1

METHOD: 5526, Issue 2 **EVALUATION: FULL** **Issue 1: 15 March 2003**
Issue 2: 13 January 2016

OSHA: See Table 1
NIOSH: See Table 1

PROPERTIES: See Table 1

SYNONYMS: Methyltin trichloride: monomethyltin trichloride, trichloromethylstannane
Dimethyltin dichloride: dichlorodimethylstannane, dichlorodimethyltin
Trimethyltin chloride: chlorotrimethylstannane, chlorotrimethyltin, trimethylstannyl chloride

SAMPLING

SAMPLER: FILTER + SORBENT TUBE (OVS-2 tube: 13 mm glass fiber filter; XAD-2, 270 mg/140 mg)

FLOW RATE: 0.25 L/min to 1 L/min

VOL-MIN: 15 L
-MAX: 75 L

SHIPMENT: Ship assembled sampler cold

SAMPLE STABILITY: 14 d @ 4 °C

FIELD BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: Table 2

BIAS: Table 2

OVERALL PRECISION ($\hat{S}_{rT}$): Table 2

ACCURACY: Table 2

MEASUREMENT

TECHNIQUE: GAS CHROMATOGRAPHY, FPD (tin-specific filter)

ANALYTE: Sodium tetraethylborate derivatives of the analytes

DESORPTION: 2 mL 0.17 mol/L acetic acid in acetonitrile

INJECTION: 1 µL

TEMPERATURE-INJECTOR: Cool on-column
-DETECTOR: 250 °C
-COLUMN: 50 °C (3 min), 12 °C/min to 200 °C (1 min)

CARRIER GAS: Helium, 6 mL/min

COLUMN: Capillary, fused silica, 30 m × 0.53 mm ID, 1.5 µm film, (5% phenyl)-methylpolysiloxane; US Pharmacopeia (USP) G27

CALIBRATION: Analytes in hexane

RANGE: 0.01 µg to 15 µg per sample (as tin) [2]

ESTIMATED LOD: 0.01 µg [2]

PRECISION ($\bar{S}_r$): 0.065 [2]

APPLICABILITY: This method was developed for air monitoring of methyltin chlorides [2].

INTERFERENCES: None were identified.

OTHER METHODS: NIOSH method 5504 is another method for the measurement of organotin compounds using a filter with a sorbent tube for collection and HPLC/AA for analysis [3].

REAGENTS:

1. Acetic acid, 99+%.*
2. Acetonitrile, HPLC grade.*
3. Diethyl ether, 99+%.*
4. Hexane, HPLC grade*.
5. Methyltin trichloride, 97%.
6. Dimethyltin dichloride, 97%.
7. Trimethyltin chloride.
8. Acetic acid, 0.17 mol/L in acetonitrile. Dilute 1.00 mL of glacial acetic acid to 100 mL with acetonitrile.
9. Sodium tetraethylborate.*
   NOTE: Purity of sodium tetraethylborate is critical. It should appear as a fine white powder. Clumping or yellowing indicates that the compound must be replaced.
10. Sodium acetate-acetic acid buffer, pH 4.0 ± 0.2.
11. Derivatizing solution: Prepare a solution containing 10 g/L of sodium tetraethylborate in diethyl ether. Prepare the solution fresh daily, preferably immediately before use.
12. Calibration stock solution: Prepare a stock calibration solution by accurately weighing (to ± 0.1 mg) about 0.1 g each of methyltin trichloride, dimethyltin dichloride, and trimethyltin chloride into a 50 mL volumetric flask. Dilute to volume with 0.17 mol/L acetic acid in acetonitrile. The stock solution contains about 1000 µg/mL (as tin) of each component. Stored in a freezer, this solution remains stable for several weeks.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: OSHA versatile sampler (OVS-2 tube), 13 mm OD inlet, 6 mm OD outlet. Front section contains 270 mg 20/60 mesh XAD-2 sorbent held in place by an 11 mm diameter glass fiber filter and PTFE ring, separated from the back section of 140 mg XAD-2 sorbent by a short plug of polyurethane foam. The back section is held in place with a long plug of polyurethane foam. The tube is available commercially.
2. Personal sampling pump: 0.1 L/min to 1 L/min with flexible and inert connecting tubing.
3. Gas chromatograph equipped with a cool on-column injection port, automated injector, capillary column, flame-photometric detector (FPD) with a tin-specific filter (610 nm), and data collection system (page 5526-1).
4. Balance capable of weighing to ±0.1 mg.
5. Mechanical shaker.
6. Vials, 10 mL, with PTFE-lined screwcaps.
7. Transfer pipettes or eyedroppers.
8. GC autosampler vials with PTFE-lined caps.
9. Volumetric flasks, 5 mL, 10 mL, and 50 mL.
10. Pipettes capable of accurately delivering 10 µL, 1.0 mL, and 2.0 mL.
11. Refrigerant packs for shipping.

SPECIAL PRECAUTIONS: Concentrated acetic acid is corrosive and an irritant. Sodium tetraethylborate is sensitive to air and moisture. This chemical should be stored and handled under a nitrogen atmosphere. Acetonitrile, diethyl ether, and hexane are all flammable. Wear appropriate protective clothing and work with these compounds in a well-ventilated hood.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Uncap the sorbent tube immediately before sampling and connect to a personal sampling pump with flexible tubing.
3. Sample at an accurately known flow rate between 0.25 L/min for full shift sampling and 1 L/min for 15 min samples (STEL) for a maximum of 75 L.
4. Cap the samplers. Pack securely for shipment with cold refrigerant packs.
   NOTE: After receipt at the laboratory, samples should be stored at 4 °C and analyzed within 14 d of collection.

SAMPLE PREPARATION:

5. Remove the retaining ring from the sorbent tube and discard. Transfer the glass fiber filter and the main resin bed to a 10 mL sample vial.
6. Remove and discard the foam plug that separates the two resin sections in the sorbent tube. Transfer the backup resin bed to a second 10 mL sample vial.
7. Into each vial, add 2 mL of 0.17 mol/L acetic acid in acetonitrile to desorb the methyltin chlorides. Put the vials on a mechanical shaker for 30 min.
8. Into each vial, add 2 mL of pH 4 buffer and 1 mL of derivatizing solution. Place the vials on the mechanical shaker for 15 min.
9. Extract the solution with three 1 mL portions of hexane. Combine the hexane fractions in a 5 mL volumetric flask and dilute to volume with hexane.

CALIBRATION AND QUALITY CONTROL:

10. Calibrate daily with at least six working standards over the range of interest.
    a. Accurately pipette 10 µL of the calibration stock solution into a vial that contains 5 mL of 0.17 mol/L acetic acid in acetonitrile. Derivatize like a sample following steps 7, 8, and 9.
    b. Serially dilute this standard derivatized solution with hexane to produce solutions over the range of 0.2 µg/mL to 0.02 µg/mL (as tin) of each methyltin chloride.
    c. Transfer to autosampler vials with PTFE-lined caps.
    d. Analyze together with samples and blanks (steps 13, 14, and 15).
    e. Prepare calibration graph (peak areas vs. µg tin for each methyltin chloride).
11. Determine desorption efficiency (DE) at least once for each lot of OVS tubes used for sampling in the calibration range (step 10). Prepare three samplers at each of six levels plus three media blanks.
    a. Transfer the front sorbent section of the OVS sampler to a 4 mL vial.
    b. Inject a known volume of calibration stock solution, or serial dilution, directly onto the front sorbent bed of each OVS tube.
    c. Cap vial and allow spiked sorbent bed to stand overnight.
    d. Desorb (steps 7, 8, and 9) and analyze together with standards and blanks (steps 13, 14, and 15).
    e. Prepare a graph of DE vs. µg for each methyltin chloride recovered.
12. Analyze three quality control blind spikes and three analyst spikes to ensure that the calibration graph and DE graphs are in control.

MEASUREMENT:

13. Set gas chromatograph according to manufacturer's recommendations and to conditions given on page 5526-1.
14. Inject a 1 µL sample aliquot manually using solvent flush technique or with an autosampler.
    NOTE: If peak area is above the linear range of the working standards, dilute with hexane, reanalyze, and apply the appropriate dilution factor in the calculations.
15. Measure the areas of the peaks of the methyltin chlorides. A sample chromatogram is shown in Figure 1.

CALCULATIONS:

16. Determine the mass, µg (corrected for DE), for each methyltin chloride found in the sample front (W_f) and back (W_b) sorbent sections, and in the average media blank front (B_f) and back (B_b)sorbent sections.
    NOTE: If $W_b > W_f / 10$, report breakthrough and possible sample loss.
17. Calculate concentration, C, of each methyltin chloride in the air volume sampled, V (L):

$$C = \frac{W_f + W_b - B_f - B_b}{V}, \text{ µg/L or mg/m}^3.$$

EVALUATION OF METHOD:

This method, developed to collect air samples and analyze the methyltin chlorides, was adapted from existing methodology for measuring organotin compounds in air [3,4]. Reference 2 details the validation of this method for sampling and quantifying of trimethyltin chloride, dimethyltin dichloride, and methyltin trichloride in air. The validated method was needed to provide air monitoring capabilities during methyltin chloride and stabilizer production. Table 2 lists the results of the validation experiments, which followed the guidelines established by NIOSH [5]. However, fewer replicates and concentration levels were used than recommended. This method met the NIOSH criteria for accuracy, bias, and sample stability. The recommended sampling conditions are 250 mL/min for 5.5 h maximum for time-weighted average (TWA) sampling and 1000 mL/min for 20 min maximum for short-term exposure limit (STEL) sampling.

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METHOD WRITTEN BY:

R.E. Yoder, C. Boraiko, Atofina Chemicals; P.F. O'Connor, NIOSH/DART.

Table 1. General information [1]

Analyte	Formula	MW	CAS No.	RTECS No.	Properties	OSHA PEL* (mg/m^3)	NIOSH REL* (mg/m^3)
Methyltin trichloride	CH_3Cl_3Sn	240.08	993-16-8	WH8585500	Colorless crystals; MP 43 °C; BP 171 °C	0.1	0.1
Dimethyltin dichloride	$(CH_3)_2Cl_2Sn$	219.67	753-73-1	WH7245000	Colorless crystals; MP 90 °C (107 °C); BP 185 °C to 190 °C	0.1	0.1
Trimethyltin chloride	$(CH_3)_3ClSn$	199.26	1066-45-1	WH6850000	Colorless crystals; MP 37.5 °C; BP 154 °C to 156 °C	0.1	0.1

*Measured as the amount of tin for organotin compounds in air.

Table 2. Method evaluation [2]

Compound	Range Studied (µg tin per sample)	Bias (%)	Precision ($\hat{S}_{rT}$) (%)	Accuracy (%)
Trimethyltin chloride	0.46 to 9.29	0.3	5.2	±11
Dimethyltin dichloride	0.42 to 9.17	−2.5	5.8	±12
Methyltin trichloride	0.07 to 10.48	−5.2	7.6	±16

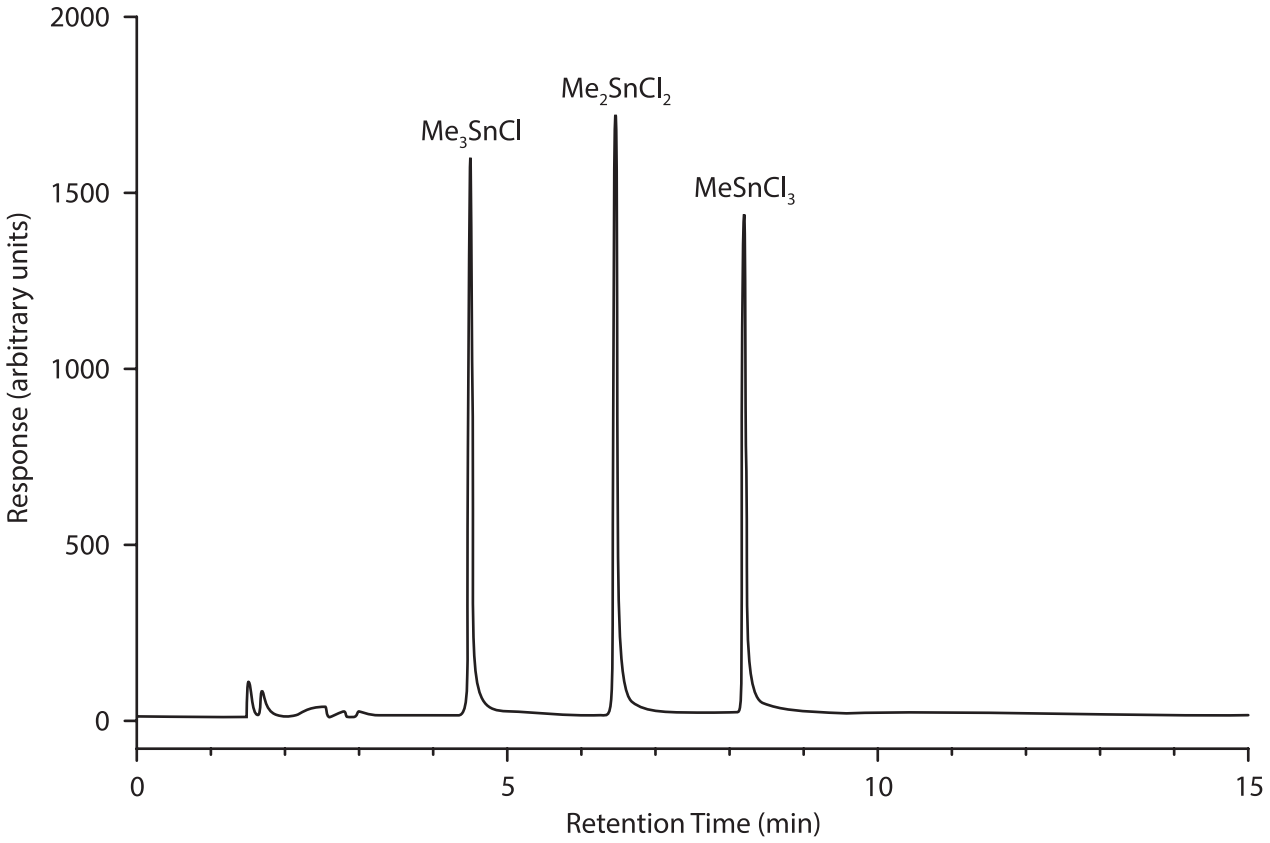

Figure 1. Sample chromatogram.

ORGANOPHOSPHORUS PESTICIDES 5600

Analytes: Table 1 Formula: Table 1 MW: Table 1 CAS: Table 1 RTECS: Table 1

METHOD: 5600, Issue 2 **EVALUATION:** FULL **Issue 1:** 15 August 1993
Issue 2: 2 March 2016

OSHA: Table 2
NIOSH: Table 2

PROPERTIES: Table 3

SYNONYMS: Table 4

SAMPLING

SAMPLER: FILTER + SOLID SORBENT TUBE (OVS-2 tube: 13-mm quartz filter; XAD-2, 270 mg/140 mg)

FLOW RATE: 0.2 to 1 L/min

VOL-MIN: 12 L
-MAX: 480 L; 60 L (Malathion, Ronnel)

SHIPMENT: Routine

SAMPLE STABILITY: at least 10 days @ 25 °C
at least 29 days @ 0 °C

BLANKS: 2 to 10 field blanks per set

ACCURACY [9]

RANGE STUDIED: Table 5

BIAS: Table 5

OVERALL PRECISION ($\hat{S}_{rT}$): Table 5

ACCURACY: Table 5

MEASUREMENT

TECHNIQUE: GC, flame photometric detection (FPD)

ANALYTE: Organophosphorus pesticides, Table 1

EXTRACTION: 2 mL 90% toluene/10% acetone solution

INJECTION VOLUME: 1 to 2 µL

TEMPERATURE
-INJECTION: 240 °C
-DETECTOR: 180 °C to 215 °C (follow manufacturer's recommendations)

CARRIER GAS: Helium @ 15 psi (104 kPa)

COLUMN: Fused silica capillary column; Table 6

DETECTOR: FPD (phosphorous mode)

CALIBRATION: Standard solutions of organophosphorus compounds in toluene

RANGE: Table 8

ESTIMATED LOD: Table 9

PRECISION ($\bar{S}_r$): Table 5

APPLICABILITY: The working ranges are listed in Table 5. They cover a range of 1/10 to 2 times the OSHA PELs. This method also is applicable to STEL measurements using 12-L samples. This method may be applicable to the determination of other organophosphorous compounds after evaluation for desorption efficiency, sample capacity, sample stability, and precision and accuracy.

INTERFERENCES: Several organophosphates may co-elute with either target analyte or internal standard causing integration errors. These include other pesticides (see Table 7), and the following: tributyl phosphate (a plasticizer), tris-(2-butoxy ethyl) phosphate (a plasticizer used in some rubber stoppers), tricresyl phosphate (a petroleum oil additive, hydraulic fluid, plasticizer, flame-retardant, and solvent), and triphenyl phosphate (platicizer and flame-retardant in plastics, laquers, and roofing paper).

OTHER METHODS: This method may be used to replace previous organophosphorous pesticide methods. See Table 11 for partial listing. The sampler recommended here is similar in concept to the device of Hill and Arnold [11], but offers greater convenience and lower flow resistance.

REAGENTS:

1. Organophosphorous analytes listed in Table 1; and triphenyl phosphate, analytical standard grade.*
2. Toluene, pesticide analytical grade.*
3. Acetone, ACS reagent grade or better.*
4. Desorbing solution. Add 50 mL acetone to a 500-mL volumetric flask. Dilute to volume with toluene. (Do not keep longer than 30 days at 0-4 °C).
   NOTE: For optional internal standard, add 1 mL of a 5 mg/mL solution of triphenyl phosphate in toluene to 500 mL desorbing solution.
5. Organophosphorous stock solutions, 10 mg/mL. Prepare individual standard stock solutions of each pesticide of interest in 90/10 toluene/acetone (v/v). All pesticides in Table 1 were found to be soluble to at least 10 mg/mL.
6. Spiking solutions for calibration (step 9) and media fortification (steps 10, 11)
   NOTE: Spiking solutions may contain more than one analyte.
   a. Spiking solution SS-1: Dilute the volume of stock solution indicated in Table 12 to 10 mL with toluene or 90/10 toluene/acetone (v/v).
      NOTE: Spiking solutions may contain more than one analyte.
   b. Spiking solution SS-0.1: Dilute 1 mL of SS-1 solution with toluene to 10 mL.
7. Purified gases: Helium, Hydrogen, Dry air, Nitrogen, and Oxygen (if required by detector)

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: resin filled sampling tube; glass tube, 11-mm i.d. x 13-mm o.d. x 50-mm long, with the outlet end drawn to a 6-mm o.d. x 25-mm long tube. The enlarged part of the tube contains a 270-mg front section of 20/60 mesh XAD-2 sorbent held in place by a 9 to10-mm o.d. quartz fiber filter and polytetrafluoroethylene (PTFE) retaining ring. The front section is separated from the back section of 140 mg XAD-2 sorbent with a short plug of polyurethane foam. The back section is held in place by a long plug of polyurethane foam. The tube is available commercially. See Figure 2.
   NOTE: Some commercially available samplers contain glass fiber filters. These are specified in the OSHA methods (see Table 11). These tubes, however, did not perform as well for the more polar analytes (amides, phosphoramides, and sulfoxides; (see Table 10). Low or erratic recoveries for Malathion may be encountered with glass fiber filters.
2. Personal sampling pump, 0.2 to 1 L/min. with flexible connecting tubing, preferably silicon, polyethylene, or PTFE tubing.
3. Vials, 4-mL with PTFE-lined cap; 2-mL GC autosampler vials with PTFE-lined crimp caps.
4. Gas chromatograph, flame photometric detector with 525-nm bandpass filter for phosphorous mode, integrator, and column (Table 6).
5. Syringes, 5-mL and 100-, 50-, and 10-mL for making standard solutions and GC injections.
6. Volumetric flasks, 500-, 10-, and 2-mL.
7. Tweezers.
8. GC vial crimper.
9. Small ultrasonic cleaning bath.

SPECIAL PRECAUTIONS: Organophosphorous compounds are highly toxic. Special care must be taken to avoid inhalation or skin contact through the wearing of gloves and suitable clothing when handling pure material [13,14,15,16,17]. Toluene is flammable and toxic. Acetone is highly flammable. Prepare all samples in a well ventilated hood.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Connect the sampler to personal sampling pump with flexible tubing. The sampler should be placed vertically with the large end down, in the worker's breathing zone in such a manner that it does not impede work performance [12].
3. Sample at an accurately known flowrate between 0.2 and 1 L/min for a total sample size of 12 to 240 L.
4. Cap both ends of the sampler with plastic caps and pack securely for shipment.

SAMPLE PREPARATION:

5. Remove cap from large end and remove PTFE retainer ring; transfer filter and front XAD-2 section to a 4-mL vial. Transfer the short polyurethane foam plug with back-up XAD-2 section to a second 4-mL vial.
6. Add 2-mL of desorbing solvent with internal standard to each vial using a 5-mL syringe or 2-mL pipette. Cap each vial.
7. Allow to stand 30 minutes, immerse vials approximately 1/2 inch in an ultrasonic bath for 30 minutes. Alternatively, place the vials in a shaker or tumbler for 1 hour.
8. Transfer 1 to 1.5 mL from each 4-mL vial to a clean 2-mL GC vial, cap and label.

CALIBRATION AND QUALITY CONTROL:

9. Calibrate daily with at least six working standards covering the analytical range of the method for individual analytes. See Table 12 for recommended preparation of spiking solutions.
   a. Add known amounts of calibration spiking solution (SS-1 or SS-0.1 according to schedule in Table 12) to desorbing solution in 2-mL volumetric flasks and dilute to the mark.
      NOTE: If an internal standard is included in the desorbing solution, then exactly 2 mL of desorbing solution in a volumetric flask must be concentrated slightly under a gentle stream of nitrogen in order to accommodate the specified volume of the spiking solutions. After adding the spiking solutions to the slightly concentrated desorbing solution, dilute to the 2-mL mark with toluene or 90/10 toluene/acetone.
   b. Include a calibration blank of unspiked desorption solution.
   c. Analyze together with field samples, field (trip) blanks, and laboratory control samples (step 12 and 13).
   d. Prepare calibration graph (peak area vs. µg analyte), or if internal standard (IS) is used (peak area of analyte/peak area of IS vs. µg analyte).
10. Prepare Laboratory Control Samples (LCS) with each sample set, in duplicate.
    a. Remove cap from large end of sampler tube, apply 30 µL of spiking solution SS-1 (refer to Table 13) to face of quartz fiber filter. Cap and allow to stand for a minimum of 1 hour. Preferably, these should be prepared as soon as samples arrive and should be stored with the field samples until analyzed.
    b. Include an unspiked sampler as a media (method) blank.
    c. Analyze along with field samples and blanks, and liquid calibration standards (steps 12 through 16).

11. When extending application of this method to other organophosphorous compounds, the following minimal desorption efficiency (DE) test may be performed as follows:
    a. Determine the NIOSH REL or OSHA PEL, in mg/m^3.
    b. Prepare spiking solution SS-1 (refer to Table 12); or use the following formulae, which are specific for the calculation of the weight of analyte to add to 10 mL 90/10 toluene/acetone).
    For REL > 1 mg/m^3 (assuming 12-L collection vol.), let W = REL x 4 m^3
    For REL ≤ 1 mg/m^3 (assuming 120-L collection vol.), let W = REL x 40 m^3
    Where W = weight (mg) of analyte to dissolve into 10 mL of desorbing solvent.
    Let [SS-1] = W/10 mL where [SS-1] = concentration of spiking solution SS-1 in mg/mL.
    c. Prepare spiking solution SS-0.1 by diluting 1 mL of SS-1 to 10 mL in a volumetric flask. Let [SS-0.1] = [SS-1] x 0.1 where [SS-0.1] = concentration of spiking solution SS-0.1.
    d. Prepare three tubes at each of five levels plus three media blanks. Concentration at each level may be calculated using formulae in last entry of Table 12.
        i. Remove plastic cap from large end of sampler, apply appropriate volume of spiking solution to face of quartz fiber filter following schedule in Table 13.
        ii. Cap and allow sampler to stand overnight.
    e. Prepare tubes for analysis (steps 5 through 8).
    f. Analyze with liquid standards (steps 12 and 13).
    g. Prepare a graph of desorption efficiency (DE) vs. µg of analyte.
    h. Acceptable desorption criteria for 6 replicates is >75% average recovery with a standard deviation of < ±9%.

MEASUREMENT:

12. Set gas chromatograph according to manufacturer's recommendations and to conditions listed in Table 6 and on page 5600-1. Inject sample aliquot manually using solvent flush technique or with autosampler. See Table 7 for retention times of selected analytes.
    NOTE: If peak area is greater than the linear range of the working standards, dilute with desorbing solution containing internal standard and reanalyze. Apply the appropriate dilution factor in calculations.
13. Measure peak area of analyte and of internal standard.

CALCULATIONS:

14. Determine the mass in µg (corrected for DE) of respective analyte found in the sample front (W_f) and back (W_b) sorbent sections, and in the media blank front (B_f) and back (B_b) sorbent sections.
    NOTE: The filter is combined with front section. If $W_b > W_f/10$ report breakthrough and possible sample loss.
15. Calculate concentration, C, of analyte in the air volume sampled, V (L):

$$C = \frac{(W_f + W_b - B_f - B_b)}{V}, \frac{mg}{m^3}$$

CONFIRMATION:

16. Whenever an analyte is detected, and its identity is uncertain, confirmation may be achieved by analysis on a second column of different polarity. If primary analysis was performed using a non-polar or weakly polar column (DB-1 or DB-5), confirmation should be accomplished by reanalysis on a polar column (DB-1701 or DB-210). See Table 7 for approximate retention times for each column type. Fewer analytes co-elute on DB-210 than on DB-1701. Relative retention times are more convenient for the identification of unknown analytes. If triphenyl phosphate is not used as the retention time reference compound, then another related compound such as tributyl phosphate, Ronnel, or Parathion may be substituted.

EVALUATION OF METHOD:

This method was evaluated over the ranges specified in Table 5 at 25 °C using 240-L air samples. Sampler tubes were tested at 15% and 80% relative humidity and at 10 °C and 30 °C. In these tests, test atmospheres were not generated; instead, analytes were fortified on the face of the sampler filters. This was followed by pulling conditioned air at 1 L/min for 4 hours. No difference in sampler performance was noted at any of these temperature/humidity combinations. Evaluations of sampler precision and stability were conducted at 30 °C and 15% relative humidity. Overall sampling and measurement precisions, bias, accuracy, and average percent recovery after long-term storage are presented in Table 5. No breakthrough was detected after 12 hours of sampling at 1 L/min with a sampler fortified with the equivalent of 4x the NIOSH REL. Malathion and Ronnel were tested at 1/40 x REL, Sulprofos at 1/20 x REL (See Table 5, note 4). All criteria [9] were met.

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METHOD WRITTEN BY:

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TABLE 1. Formula and registry numbers

Compound (alphabetically)	MW[(1)] (Daltons)	Empirical Formula	CAS No.[(2,3,4)]	RTECS[(2)]
Azinphos Methyl	317.32	$C_{10}H_{12}N_3O_3PS_2$	86-50-0	TE1925000
Chlorpyrifos	350.58	$C_9H_{11}Cl_3NO_3PS$	2921-88-2	TF6300000
Diazinon	304.34	$C_{12}H_{21}N_2O_3PS$	33-41-5	TF3325000
Dicrotophos	237.19	$C_8H_{16}NO_5P$	141-66-2	TC3850000
Disulfoton	274.39	$C_8H_{19}O_2PS$	298-04-4	TD9275000
Ethion	384.46	$C_9H_{22}O_4P_2S_4$	563-12-2	TE4550000
Ethoprop	242.33	$C_8H_{19}O_2PS_2$	13194-48-4	TE4025000
Fenaminphos	303.36	$C_{13}H_{22}NO_3PS$	22224-92-6	TB3675000
Fonofos	246.32	$C_{10}H_{15}OPS_2$	944-22-9	TA5950000
Malathion	330.35	$C_{10}H_{19}O_6PS_2$	121-75-5	WM8400000
Methamidophos	141.12	$C_2H_8O_2PS$	10265-92-6	TB4970000
Methyl Parathion	263.20	$C_8H_{10}NO_5PS$	298-00-0	TG0175000
Mevinphos	224.15	$C_7H_{13}O_6P$	7786-34-7	GQ5250000
Monocrotophos	223.17	$C_7H_{14}NO_5P$	6923-22-4	TC437500
Parathion	291.26	$C_{10}H_{14}NO_5PS$	56-38-2	TF4550000
Phorate	260.36	$C_7H_{17}O_2PS_3$	298-02-2	TD9450000
Ronnel	321.54	$C_8H_8Cl_3O_3PS$	299-84-3	TG0525000
Sulprofos	322.43	$C_{12}H_{19}O_2PS_3$	35400-43-2	TE4165000
Terbufos	288.42	$C_9H_{21}O_2PS_3$	13071-79-9	TD7740000

(1) Molecular weights are calculated from the empirical formula using 1979 IUPAC Atomic Weights of the Elements

(2) RTECS = NIOSH Registry of Toxic Effects of Chemical Substances [1]

(3) Merck Index [2]

(4) Farm Chemicals Handbook [3]

TABLE 2. Toxicity and maximum exposure limits

Compound (alphabetically)	LD_{50}, mg/kg[1]	OSHA PEL[3] (mg/m^3)	NIOSH REL[4] (mg/m^3)	NIOSH REL[4] (ppm)
Azinphos Methyl	11 f	0.2	0.2	0.015
Chlorpyrifos	145	0.2	0.2	0.014
Diazinon	250 m, 285 f	0.1	0.1	0.008
Dicrotophos	16 f, 21 m	0.25	0.25	0.026
Disulfoton	2.3 f, 6.8 m	0.1	0.1	0.009
Ethion	27 f, 65 m	0.4	0.4	0.025
Ethoprop	61.5[2]			
Fenamiphos	19.4	0.1	0.1	0.008
Fonofos	3-17[2]	0.1	0.1	0.010
Malathion	1000	15	10	0.740
Methamidophos	25 m, 27 f			
Methyl Parathion	14 m, 24 f	0.2	0.2	0.019
Mevinphos	3.7 f, 6.1 m	0.1 skin	0.1	0.01
Monocrotophos	17 m, 20 f	0.25	0.25	0.027
Parathion	3.6 f, 13m	0.1	0.05 skin	0.004
Phorate	1.1 f, 2.3 m	0.05	0.05 skin	0.005
Ronnel	1250 m, 2630 f	15	10	0.760
Sulprofos	227	1	1	0.076
Terbufos	1.6-1.7 m, 1.3-1.57 f			

(1) Rat-oral; from Merck Index, unless otherwise noted, f = female, m = male. [2]
(2) Farm Chemicals Handbook [3]
(3) OSHA Final Rule, 1989 (unenforceable, 1992); only Malathion and Parathion had previous PELs
(4) NIOSH Recommendations for Occupational Safety and Health [5]

TABLE 3. Physical properties [1]

Compound (Alphabetically)	Liquid Density (g/mL)	mp (°C)	bp (°C @ 1 atm)	Vapor Pressure (Pascal)	Vapor Pressure (mm Hg)	Solubility in Water [2,3], % by weight (g/100mL @ 20 °C)
Azinphos Methyl	1.44	73-74	decomposes	0.024	$8x10^{-9}$	0.003%
Chlorpyrifos	1.40	41-42	160 (decomposes)	0.0027	$2x10^{-5}$	0.0002%
Diazinon	1.116-1.118	liquid	>120 (decomposes)	0.019	$1.4x10^{-4}$	0.004%
Dicrotophos	1.216	liquid	400	0.013	0.0001	miscible
Disulfoton	1.144	oil	>180 °C flash pt.	0.0267	0.0002	0.003% (22.7 °C)
Ethion	1.220	-12 to -13	>150 (decomposes)	0.0002	$1.5x10^{-6}$	0.0001%
Ethoprop	1.094	oil	86-91	0.047	$3.5x10^{-4}$	0.075%
Fenaminphos	1.15	49	decomposes	0.00012	$5x10^{-5}$	0.03%
Fonofos	1.16	30	130	0.03 (25 °C)	-	0.001%
Malathion	1.23	2.9	60 (decomposes)[4]	0.005	$4x10^{-5}$	0.02%
Methamidophos	1.31	44	-	0.002	$3x10^{-4}$	-
Methyl Parathion	1.358	37-38	<120 (decomposes)	0.0002	$7.5x10^{-6}$	0.006% (25 °C)
Mevinphos	1.25[5]	20.6[5]	300[5] (decomposes)	0.4	$3x10^{-3}$	miscible
Monocrotophos	1.3	53-54[6]	125	0.0003	$7x10^{-6}$	miscible
Parathion	1.26	6	375	0.005	$3.78x10^{-5}$	0.001%
Phorate	1.156	liquid	118-120	0.11	$8.4x10^{-4}$	0.005%
Ronnel	1.49[7]	41	decomposes	0.1	$8x10^{-4}$	0.004% (25 °C)
Sulprofos	1.20	liquid	210	<0.0001	$<10^{-6}$	low
Terbufos	1.105	-29.2	88 °C flash pt.	0.0346	$2.6x10^{-4}$	0.0005

(1) From Merck Index, unless otherwise noted [2].
(2) Farm Chemicals Handbook [3].
(3) NIOSH Pocket Guide [6].
(4) NIOSH 4th Edition Method 5012 (EPN, Malathion, Parathion) [8].
(5) NIOSH 4th Edition Method 2503 for Mevinphos [8].
(6) 54-55 °C for pure material, 25-30 °C for commercial mixture.
(7) NIOSH 2nd Edition Method for Ronnel, S299 [7]

TABLE 4. Synonyms

Compound[1] (alphabetically)	Other name[2]	CAS name[3,4]
Azinphos Methyl	Guthion*	O,O-dimethyl S-[(4-oxo-1,2,3-benzotriazin-3(4H)-yl)methyl] phosphorodithioate
Chlorpyrifos	Dursban*	O,O-diethyl 0-(3,5,6-trichloro-2-pyridinyl) ester
Diazinon	Spectracide*	O,O-diethyl 0-[6-methyl-2-(1-methylethyl)-4-pyrimidinyl] phosphorodithioate
Dicrotophos	Bidrin*	2-dimethyl-cis-2-dimethylcarbamoyl-1-methylvinyl phosphate
Disulfoton	Di-Syston*	O,O-diethyl S-[2-(ethylthio)ethyl] phosphorodithioate
Ethion		S,S'-methylene, O,O,O,'O'-tetraethyl ester, O,O,O'-O'-Tetra ethyl S,S'-methylene di-phosphorodithioate [4]
Ethoprop	Prophos*	Phosphorodithioic acid, 0-ethyl S,S-dipropyl ester
Fenaminphos	Nemacur*,Phenamiphos [1]	Ethyl-3-methyl-4-(methylthio) phenyl (1-methylethyl) phosphoramidate
Fonofos	Dyfonate*	O-ethyl, S phenyl ethyl phosphorodithioate
Malathion	Cythion*	S-[1,2 bis(ethoxycarbony1)ethyl] O,O-dimethyl-phosphorodithioate; Diethyl(dimethoxyphosphinothioylthio) succinate
Methamidophos	Monitor*	Phosphoramidothioic acid, O,S-dimethyl ester
Methyl Parathion	Parathion Methyl [1]	Phosphorothioic acid, O,O-dimethyl 0-[4-nitrophenyl] ester
Mevinphos	Phosdrin*	Methyl-3(dimethyoxyphosphinyloxy)but-2-enoate 2-methyoxy carbonyl-1-methylvinyl dimethyl phosphate
Moncrotophos	Azodrin* Monocron	Dimethyl [1-methyl-3-(methylamino)-3-oxo-1-propenyl] ester[4]
Parathion	Ethyl Parathion [1]	O,O-diethyl 0-(4-nitrophenyl) phosphorodithioate
Phorate	Thimet*	Phosphorodithioic acid, O,O-diethyl S-[(ethylthio) methyl] phosphorodithioate
Ronnel	Fenchlorphos [1]	O,O-dimethyl O-(2,4,5-trichlorophenyl) ester
Sulprofos	Bolstar*	O-ethyl 0-[4-(methylthio) phenyl] S-propyl phosphorodithioate[4]
Terbufos	Counter*	O,O-diethyl S-[[(1,1-dimethylethyl) thio] methyl] ester[4]

(1) Common name as given in Farm Chemicals Handbook [3].
(2) *=Trade name (Trademark or Registered Name) as given in Farm Chemicals Handbook [3].
(3) Source, Merck Index [2].
(4) NIOSH RTECS [1] or alternate CAS name in Merck Index [2].

TABLE 5. Method Evaluation [1]

Compound (alphabetically)	Range Studied[2] (mg/m³)	Range Studied[2] (mg/sample)	Accuracy	Bias Average	Overall Precision $\hat{S}_{rT}$	Measurement Precision $\bar{S}_r$	% Recovery at 30 days @ 25 °C (0 °C)
Azinphos Methyl	0.02-0.4	0.0048-0.096	±0.178	-0.038	0.070	0.030	97 (105)
Chlorpyrifos	0.02-0.4	0.0048-0.096	±0.163	-0.027	0.068	0.018	92 (90)
Diazinon	0.01-0.2	0.0024-0.048	±0.162	-0.032	0.065	0.020	94 (93)
Dicrotophos	0.025-0.5	0.006-0.120	±0.169	-0.037	0.66	0.025	89 (92)
Disulfoton	0.01-0.2	0.0024-0.048	±0.196	-0.064	0.066	0.024	87 (89)
Ethion	0.04-0.8	0.0096-0.192	±0.165	-0.29	0.068	0.18	96 (95)
Ethoprop[3]	0.01-0.2	0.0024-0.048	±0.157	-0.025	0.066	0.024	97 (93)
Fenaminphos	0.01-0.2	0.0024-0.048	±0.155	-0.029	0.063	0.022	94 (96)
Fonofos	0.01-0.2	0.0024-0.048	±0.168	-0.036	0.66	0.023	95 (92)
Malathion[4]	0.025-0.5	0.006-0.120	±0.172	-0.038	0.067	0.019	93 (93)
Methamidophos[5]	0.02-0.4	0.0048-0.096	±0.156	-0.018	0.069	0.026	88 (95)
Methyl Parathion	0.02-0.4	0.0048-0.096	±0.160	-0.034	0.063	0.018	95 (95)
Mevinphos	0.01-0.2	0.0024-0.048	±0.176	-0.42	0.067	0.028	89 (91)
Moncrotophos	0.025-0.5	0.006-0.12	±0.185	-0.043	0.071	0.026	88 (92)
Parathion	0.005-0.1	0.0012-0.024	±0.163	-0.012	0.071	0.019	92 (92)
Phorate	0.005-0.1	0.0112-0.024	±0.202	-0.070	0.066	0.025	91 (91)
Ronnel[4]	0.025-0.5	0.006-0.120	±0.172	-0.040	0.066	0.018	95 (94)
Sulprofos[4]	0.01-0.2	0.0024-0.048	±0.181	-0.047	0.067	0.017	94 (94)
Terbufos[3]	0.01-0.2	0.0024-0.048	±0.188	-0.054	0.067	0.022	92 (91)

(1) Back-up Data Report [9]

(2) The ranges studied were 1/10 to 2x the NIOSH REL (except as noted) using a flowrate of 1 L/min. over 4 hours sampling time.

(3) No NIOSH REL or OSHA PEL available; used 0.1 mg/m³.

(4) Malathion and Ronnel were studied at 1/400 to 1/20 the NIOSH REL, Sulprofos at 1/200 to 1/10 the NIOSH REL.

(5) No NIOSH REL or OSHA PEL available; used 0.2 mg/m³.

(6) Data in parentheses are for % recovery at 30 days at 0 °C

TABLE 6. Recommended gas chromatographic columns and conditions [1]

	DB-1[2]	DB-5[2]	DB-1701[2]	DB-210[2]
Stationary Phase[3] Polarity	Non-	Weakly	Moderately	Moderately
Length (meters)	30	30	30	30
I.D. (millimeters)	0.32	0.32	0.32	0.32
Film thickness (mm)[4]	0.25	1.0	1.0	0.25
Injection volume (µL) [5]	1	1	1	1
Injection mode[6]	SPL	DIR	DIR	SPL
Initial oven temp (°C)	100	125	125	100
Final oven temp (°C) [6]	275	275	275	250
Recommended max oven temp (°C)[7]	325	325	280	240/260
Oven temp program (°C/min)	3.0	4.0	4.0	3.0
He Carrier gas head pressure (psi)	15	15	15	15

(1) Actual conditions may vary depending on column and analytical objectives.

(2) Wide Bore Fused Silica Capillary Column

(3) DB-1, 100% methyl silicone; DB-5, 5% phenyl, methyl silicone; DB-1701, 14% cyanopropylphenyl, methyl silicone; DB-210, 50% trifluoropropyl, methyl silicone. DB-1 is non-polar, DB-5 is weakly polar, and DB-1701 and DB-210 are moderately strong polar phases. Equivalent phases are acceptable. Other phase types may also work well.

(4) Film thickness: Thinner films give faster separations at lower temperatures promoting analyte stability.

(5) Injection (Vol.): Use 2 mm i.d. injection port liners for 0.5 mL injection and 4 mm i.d. injection port liners for 1 to 2 mL injections with 0.32 mm i.d. capillary columns.

(6) Injection (mode): SPL = splitless mode, initial oven temp. 5 to 10 °C less than b.p. of desorption solvent; DIR = direct mode, initial oven temperature > b.p. of desorption solvent; OC = on-column, sample injected within the lumen of the column rather than within the injection port liner. In the splitless and direct injection modes, split-vent off time should be 60 seconds for 1 to 2 µL injections with 4 mm i.d. injection port liners, and 20 to 30 seconds for 0.5 µL injections with 2 mm i.d. injection port liners.

(7) J & W Scientific Catalog of High Resolution Chromatography Products, p. 21. [10]

TABLE 7. Approximate retention times (RT) of selected organophosphorous compounds on capillary columns [1,2]

Compound (by RT on DB-1)	DB-1 RT (min)	DB-1 RRT[3]	DB-1 Elution T, °C[4]	DB-5 RT (min)	DB-1701 RT (min)	DB-210 RT (min)
TEPP	3.71	0.128	111	5.47	7.18[B]	7.88
Triethylphosphorothioate	4.37	0.107	113	6.34	7.14[B]	4.93
Methamidophos	5.12	0.125	115	7.64	13.61	12.03
Dichlorvos	5.81	0.142	117	8.24	10.67	10.54
Mevinphos	10.45	0.256	131	12.92	16.69	19.20
Ethoprop	17.15	0.420	151	19.09	21.52	20.10
Naled	17.61	0.431	153	(6)	23.17[C]	21.46[H]
Dicrotophos	18.00	0.440	154	19.94	25.84[E]	31.43
Monocrotophos	18.27	0.447	155	20.12	28.11	31.60
Sulfotepp	19.06	0.466	157	(6)	23.09[C]	21.11
Phorate	19.18	0.469	158	20.94	23.10[C]	18.92
Dimethoate	19.44	0.476	158	21.84	(6)	29.33[I]
Demeton-S	20.15	0.493	160	21.70	25.06[D]	24.97
Dioxathion	21.30	0.521	164	23.04	26.33[F]	23.46
Fonofos	22.04	0.539	166	23.57	25.87[E]	22.20
Terbufos	22.22	0.544	168	23.80	25.02[D]	21.52[H]
Disulfoton	23.09	0.565	169	24.19	26.43[F]	22.78
Diazinon	23.37	0.572	170	23.75	25.00[D]	20.99
Methyl Parathion	25.37	0.621	176	26.48	31.37	33.21
Oxydemeton Methyl	26[5]	0.63[5]	179	(6)	(6)	(6)
Ronnel	26.86	0.657	181	27.39	29.30	26.27
Pirimiphos Methyl	28.13	0.688	184	27.90	29.72	26.77
Malathion	28.53	0.698	186	28.33	31.78[G]	33.08[J]
Fenthion	28.74	0.703	186	28.93	31.78[G]	29.35[I]
Parathion	28.98	0.709	187	29.10[A]	33.28	35.60
Chlorpyrifos	29.11	0.712	187	29.10[A]	30.79	27.72
Crufomate	29.64	0.725	189	29.54	34.00	35.34
Isofenphos	31.91	0.780	196	31.17	33.81	33.02[J]
Tetrachlorvinphos	33.26	0.814	200	32.60	35.96	37.01
Fenamiphos	34.09	0.834	202	33.03	37.14	38.95
Merphos	35.19	0.861	206	(6)	30.57	23.89
Fensulfothion	36.61	0.896	210	35.78	42.41	46.98
Ethion	37.88	0.927	214	36.30	39.30	37.96
Sulprofos	38.49	0.942	216	36.96	39.54	37.11
Triphenyl Phosphate	40.88	1.000	223	39.06	(6)	(6)
EPN	42.64	1.043	228	41.06	47.83	47.13
Azinphos Methyl	44.16	1.080	232	43.67	(7)	49.24
Leptophos	45.12	1.104	235	43.91	47.38	41.68
Azinphos Ethyl	46.55	1.139	240	46.50	47.43	50.40
Coumaphos	49.31	1.206	248	50.10	67.86	60.88

(1) Actual retention times (RT) will vary with individual columns and chromatographic conditions. See Table 10 for chromatographic performance notes. Data from Backup Data Report [9].
(2) Capillary Column conditions given in Table 6. Sets of co-eluting or nearly co-eluting peaks are identified by letters: (A), (B), (C), (D), (E), (F), (G), (H), (I), and (J)
(3) Relative Retention Times, relative to Triphenyl Phosphate.
(4) Elution temperature (°C) for DB-1 column (see Table 6 for column conditions.)
(5) Broad, tailing peak.
(6) No data.
(7) Did not elute.

TABLE 8. Applicable working range

Compound	Atmospheric working range (mg/m3)[1]	Atmospheric working range (ppm)[2]	Sample working range (µg/sample)[3]	Instrument working range (ng on column)[4]
Azinphos Methyl	0.02-0.6	0.0015-0.046	2.4 to 72	1.2-36
Chlorpyrifos	0.02-0.6	0.0014-0.042	2.4 to 72	1.2-36
Diazinon	0.01-0.3	0.0008-0.024	1.2 to 36	0.6-18
Dicrotophos	0.025-0.75	0.0026-0.077	3.0 to 90	1.5-45
Disulfoton	0.01-0.3	0.0009-0.027	1.2 to 36	0.6-18
Ethion	0.04-1.2	0.0025-0.076	4.8 to 144	2.4-72
Ethoprop	0.01-0.3	0.0010-0.030	1.2 to 36	0.6-18
Fenamiphos	0.01-0.3	0.0008-0.024	1.2 to 36	0.6-18
Fonofos	0.01-0.3	0.0010-0.030	1.2 to 36	0.6-18
Malathion	1.0-30	0.074-2.2	12. to 360(5)	6.-180(5)
Methamidophos	0.02-0.6	0.0035-0.10	2.4 to 72	1.2-36
Methyl Parathion	0.02-0.6	0.0019-0.056	2.4 to 72	1.2-36
Mevinphos	0.01-0.3	0.0011-0.033	1.2 to 36	0.6-18
Monocrotophos	0.025-0.75	0.0027-0.082	3.0 to 90	1.5-45
Parathion	0.005-0.15	0.0004-0.013	0.6 to 18	0.3-9
Phorate	0.005-0.15	0.0005-0.014	0.6 to 18	0.3-9
Ronnel	1.0-30	0.076-2.3	12. to 360(5)	6.-180(5)
Sulprofos	0.1-3.0	0.0076-0.23	12. to 360	6.-180
Terbufos	0.01-0.3	0.0008-0.026	1.2 to 36	0.6-18

(1) To cover range of 1/10 to 3x NIOSH REL.
(2) Calculated for 25 °C and 760 mm Hg (NTP).
(3) Calculated for a collection volume of 120 L (2 hrs @ 1 L/min., 4 hrs @ 0.5 L/min., or 10 hrs @ 0.2 L/min.).
(4) Desorbing sample in 2.0 mL solvent and injecting 1 µL into gas chromatograph.
(5) Calculated for a collection volume of 12 L (12 min. @ 1 L/min., 24 min. @ 0.5 L/min., or 1 hour @ 0.2 L/min.).

TABLE 9. Limits of detection and margin of sensitivity

Compound	Instrument Estimated LOD (ng on colum)	Sample estimated LOD (µg/sample)[1]	Atmospheric estimated LOD (mg/m³)[1]	Margin of sensitivity (REL/LOD)[2]
Azinphos Methyl	0.06	0.12	0.0012	167
Chlorpyrifos	0.02	0.04	0.0004	500
Diazinon	0.02	0.04	0.0004	250
Dicrotophos	0.1	0.2	0.002	125
Disulfoton	0.02	0.04	0.0004	250
Ethion	0.02	0.04	0.0004	1000
Ethoprop	0.02	0.04	0.0004	(3)
Fenamiphos	0.07	0.14	0.0014	71
Fonofos	0.02	0.04	0.0004	250
Malathion	0.05	0.1	0.001	10000
Methamidophos	0.3	0.6	0.005	(3)
Methyl Parathion	0.02	0.04	0.0004	500
Mevinphos	0.06	0.12	0.0012	83
Monocrotophos	0.2	0.4	0.004	63
Parathion	0.02	0.04	0.0004	125
Phorate	0.02	0.04	0.0004	125
Ronnel	0.02	0.04	0.0004	25000
Sulprofos	0.03	0.06	0.0005	2000
Terbufos	0.02	0.04	0.0004	(3)

(1) Calculated for a collection volume of 120 L (2 hrs @ 1 L/min., 4 hrs @ 0.5 L/min., or 10 hrs @ 0.2 L/min.).
(2) REL in mg/m^3 (Table 2) ÷ Atmospheric LOD (Table 9).
(3) No REL

TABLE 10. Notes on analytical characteristics of organophosphorous compounds[1,2]

Compound (alphabetically)	A. Chemical and Physical	B. Desorption and Dissolution	C. Gas Chromatography
Azinphos Methyl (Guthion*)	-	-	3,5,6
Azinphos Ethyl (Guthion Ethyl)	-	-	5
Chlorpyrifos (Dursban*)	-	-	-
Coumaphos (Co-Ral*)	-	-	5
Crufomate (Ruelene*)	1	1,4	1
Demeton (Systox*)	2,6	5	3
Diazinon (Spectracide*)	-	-	-
Dichlorvos (DDVP, Vapona*)	7	-	4
Dicrotophos (Bidrin*)	-	-	-
Dimethoate (Cygon*)	1	1,4	1
Dioxathion (Delnav*)	-	-	-
Disulfoton (Di-Syston*)	2	-	2
EPN (Santox*)	-	-	5
Ethion	-	-	-
Ethoprop (Prophos*)	-	-	-
Fenamiphos (Nemacur*)	1	1,4	1
Fensulfothion (Dasanit*)	3	4	-
Fenthion (Baytex*)	-	5	-
Fonofos (Dyfonate*)	-	-	-
Isofenphos (Oftanol*)	1	1	1
Leptophos (Phosvel*)	-	5	5
Malathion (Cythion*)	-	1,3,4	-
Merphos (Folex*)	4		2
Methamidophos (Monitor*)	1	1,2,4	1,4
Methyl Parathion (Parathion Methyl)	-	5	-
Mevinphos (Phosdrin*)	6,7	1,5	3,4
Monocrotophos (Azodrin*)	1	-	1
Naled (Dibrom*)	5	-	2
Oxydemeton Methyl (Metasystox-R)	3	-	1,2
Parathion (Ethyl Parathion)	-	-	-
Phorate (Thimet*)	2,7	-	2
Pirimiphos Methyl (Actellic*)	-	-	4
Ronnel (Fenchlorphos)	-	-	-
Sulfotepp (TEDP)	-	-	-
Sulprofos (Bolstar*)	-	-	-
TEPP	7	5	4
Terbufos (Counter*)	2	-	2
Tetrachlorvinphos (Gardona*)	-	-	-
Tributyl Phosphate	-	-	7
Triphenyl Phosphate	-	-	7

* = Trade name, Registered name, or Trademark (Farm Chemicals Handbook [3]).

(1) Observations made during selection and validation of selected analytes. [9]

(2) Refer to notes on the following pages.

Table 10 continued. Notes on Analytical Characteristics

A. Chemical and Physical

1. Amide or phosphoramide, slightly acidic, very polar chemically.
2. Alkyl thio-ether, easily oxidized to sulfone and sulfoxide.
3. Sulfoxides, easily oxidized to sulfone. Also very polar chemically.
4. Phosphite, easily air oxidized to phosphate (Merphos to DEF).
5. Vicinal dibromide, easily debrominated (Naled to Dichlorvos).
6. Two or more isomers commonly exist (e.g. Demeton-O and Demeton-S; cis- and trans-mevinphos).
7. Relatively volatile, can be lost if media or vials are left uncapped for even a short period of time.

   General: Organophosphorous compounds are easily destroyed at mildly alkaline conditions (pH ≥8). Loses can occur for trace levels of compounds on alkaline glass surfaces. Glassware should be neutralized after washing, if alkaline detergent is used.

B. Desorption and Dissolution

1. Solubility of concentrated solutions in toluene enhanced by the addition of 1% Methanol or 10% acetone. Solubility in hexane very unfavorable even for dilute solutions.
2. Changing from 100% toluene to 90/10 toluene/acetone, desorption from glass fiber filters improved from 62% to 98%, desorption from quartz fiber filters improved from 30% to 101%.
3. Changing from glass fiber filters to quartz fiber filters, desorption in toluene improved from 16% to 88% and desorption in 90/10 toluene/acetone improved from 70% to 99%.
4. These compounds are more chemically polar than the other listed organophosphorous compounds; desorption from XAD-2 or from glass or quartz fiber filters in hexane was incomplete or non-existent. Desorption in toluene was adequate except as noted in 2 and 3 above. The use of toluene containing 10% acetone improved recoveries for all analytes to satisfactory levels.
5. The desorption characteristics of these compounds were not evaluated.

   General:
   1. The presence of acidic hydrogen or double bonded oxygen anywhere in the molecular structure greatly decreases solubility in non-polar solvents and increases the difficulty of desorption from polar surfaces and sorbents.
   2. While glass fiber filters and toluene desorbant were adequate for most compounds in preliminary tests, the method was given wider application for the more polar compounds by the use of quartz fiber filters and 90/10 toluene/acetone desorbant.
   3. Greater flame photometric detector response was observed for organophosphorous compounds when injections were made in toluene or 90/10 toluene/acetone. Solvents with lower boiling points (e.g. methylene chloride, chloroform, methyl-t-butyl ether, and ethyl acetate) possessed fair to good desorption power, but rendered less satisfactory gas chromatographic responses for the analytes. This effect may be due to better analyte mass-transfer from the injection port to the capillary column with higher boiling solvents using splitless or direct injection techniques.

C. Gas Chromatography

1. Poor chromatography may be encountered with dirty or undeactivated columns or injection ports. Clean quartz wool plugs stuffed in the injection port liner are better than silanized glass wool at reducing losses within the injection port.
2. Multiple, shifted, irregular, or severely tailing peaks may be observed in the chromatogram if degradation or oxidation of the analytes occur prior to injection, within the injection port, or during chromatographic separation on-column.
3. Multiple peaks may be observed due to presence of isomers.
4. Short elution time, compound may co-elute with solvent if oven temperature is too high.
5. Long elution time, compound may be lost if run time is too short, column or injection port is too cool, or split-vent-valve opens too soon when injected in splitless or direct injection mode.
6. Azinphos Methyl did not elute from DB-1701 even though Azinphos ethyl did elute.
7. Potential internal standards: Triphenyl phosphate is more favorable if multiple analytes are expected because it is less volatile and elutes in an area of the chromatogram having fewer competing analytes.

TABLE 11. Other methods of analysis for organophosphorous compounds in air

Document	Method Number	Organophosphorous Compound(s)
AEC&T[1]		Chlorpyrifos, Demeton-O, Demeton-S, Diazinon, Dimethoate, Malathion, Paraoxon, and Parathion
NMAM, 2nd ed [2]	v. 1 P&CAM 158 v. 5 P&CAM 295 v. 6 P&CAM 336 v. 3 S 208 v. 3 S 209 v. 3 S 210 v. 6 S 280 v. 3 S 285 v. 3 S 295 v. 6 S 296 v. 6 S 299 v. 3 S 370	Parathion Dichlorvos (DDVP) TEPP Tributyl phosphate Triorthocresyl phosphate Triphenyl phosphate Demeton EPN Parathion Mevinphos Ronnel Malathion
NMAM, 4th ed. [3]	2503 2504 5012 5514	Mevinphos TEPP EPN, Malathion, and Parathion Demeton
OSHA A.M.M. [4]	62	Chlorpyrifos, Diazinon, Parathion, DDVP, and Malathion
OSHA Partially Validated Methods[5]	PV2087 PV2045 PV2134 PV2015 PV2027 PV2071 PV2099 PV2037 PV2105 PV2112	Azinphos methyl Monocrotophos Coumaphos Crufomate Fonofos Pirimiphos Methyl Dicrotophos Sulprofos Disulfoton Methyl Parathion

(1) Hill and Arnold in Arch. Environ. Contam. & Toxicol . [11]

(2) NIOSH Manual of Analytical Methods, 2nd ed., Volumes 1-7 [7]

(3) NIOSH Manual of Analytical Methods, 4th ed. [8]

(4) OSHA Analytical Methods Manual [12]

(5) OSHA Partially Validated Methods (refer to by name) [4]

TABLE 12. Spiking concentrations for organophosphorous compounds

Compound	Total µg spiked[1] at 1/30 x REL	Total µg spiked[1] at 1/10 x REL	Total µg spiked[1] at 1/3 x REL	Total µg spiked[1] at 1 x REL	Total µg spiked[1] at 3 x REL	Volume (mL) of 10 mg/mL stock solution needed to prepare 10 mL of SS-1
Azinphos Methyl	0.8	2.4	8	24	72	0.8
Chlorpyrifos	0.8	2.4	8	24	72	0.8
Diazinon	0.4	1.2	4	12	36	0.4
Dicrotophos	1.0	3	10	30	90	1.0
Disulfoton	0.4	1.2	4	12	36	0.4
Ethion	1.6	4.8	16	48	144	1.6
Ethoprop	0.4	1.2	4	12	36	0.4
Fenamiphos	0.4	1.2	4	12	36	0.4
Fonofos	0.4	1.2	4	12	36	0.4
Malathion[3]	4	12	40	120	360	4.0
Methamidophos	0.8	2.4	8	24	72	0.8
Methyl Parathion	0.8	2.4	8	24	72	0.8
Mevinphos	0.4	1.2	4	12	36	0.4
Monocrotophos	1.0	3	10	30	90	1.0
Parathion	0.2	0.6	2	6	18	0.2
Phorate	0.2	0.6	2	6	18	0.2
Ronnel[3]	4	12	40	120	360	4.0
Sulprofos	4	12	40	120	360	4.0
Terbufos	0.4	1.2	4	12	36	0.4
General (for 120L)[2,3]	x/30	x/10	x/3	x	3x	4y

(1) Total µg per sample, for spiked media, or per 2 mL desorption solution for liquid calibration standards.
(2) Where x, µg/sample = REL, µg/L x 120 L/sample; and y, mg/mL = REL, mg/m^3 x 4 m^3/mL.
(3) For all REL > 1 mg/m^3, use 1/10 x REL in the calculations (assumes that collection volume in these cases would be 12 L instead of 120 L).

TABLE 13. Spiking of media

Spiking Levels[1] (fraction of REL)	Spiking Solution	Preferred Syringe Size	Spiking Volume[2]
1/30x REL	SS-0.1	50 µL	10 µL
1/10x REL	SS-0.1	50 µL	30 µL
1/3x REL	SS-1	50 µL	10 µL
1x REL	SS-1	50 µL	30 µL
3x REL	SS-1	100 µL	90 µL

(1) For a collection volume of 120 L. Range corresponds to values within "Working Range" column, Table 8.
(2) For liquid calibration standard preparations, add specified volume to 2 mL desorption solution in 2-mL volumetric flask. For laboratory control samples spiked at the REL, apply volume specified in "Spiking Volume" column to front section of sampler; do in duplicate. For Desorption Efficiency determination, apply specified volume to front section of sampler; do each of five levels in triplicate.

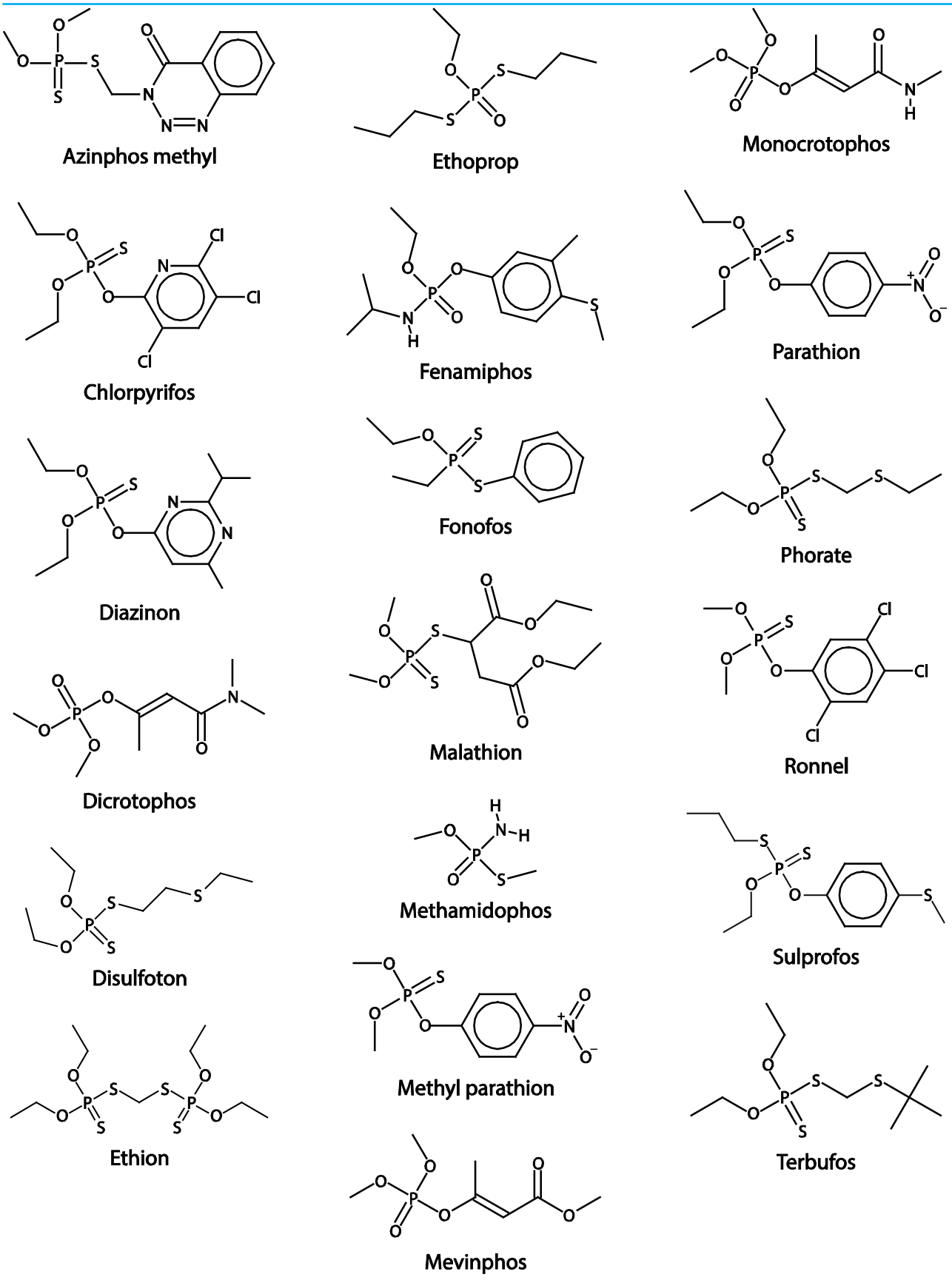

Figure 1. Structures of organophosphorus compounds

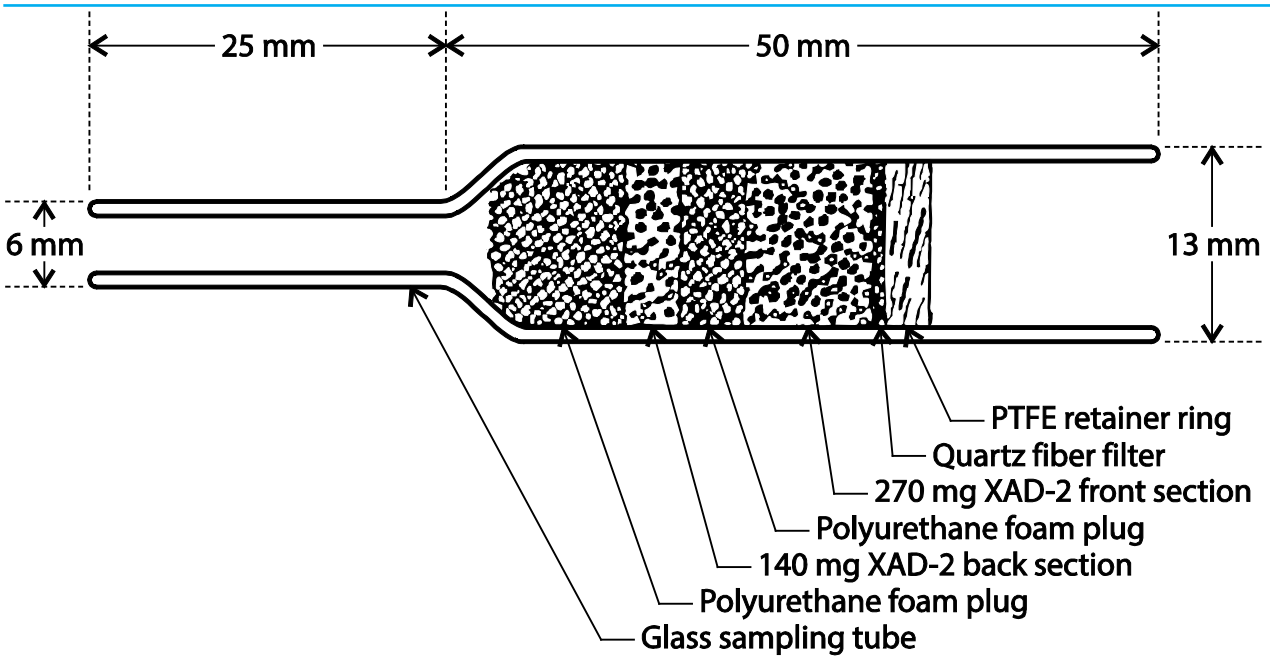

Figure 2. OVS-2 Sampler

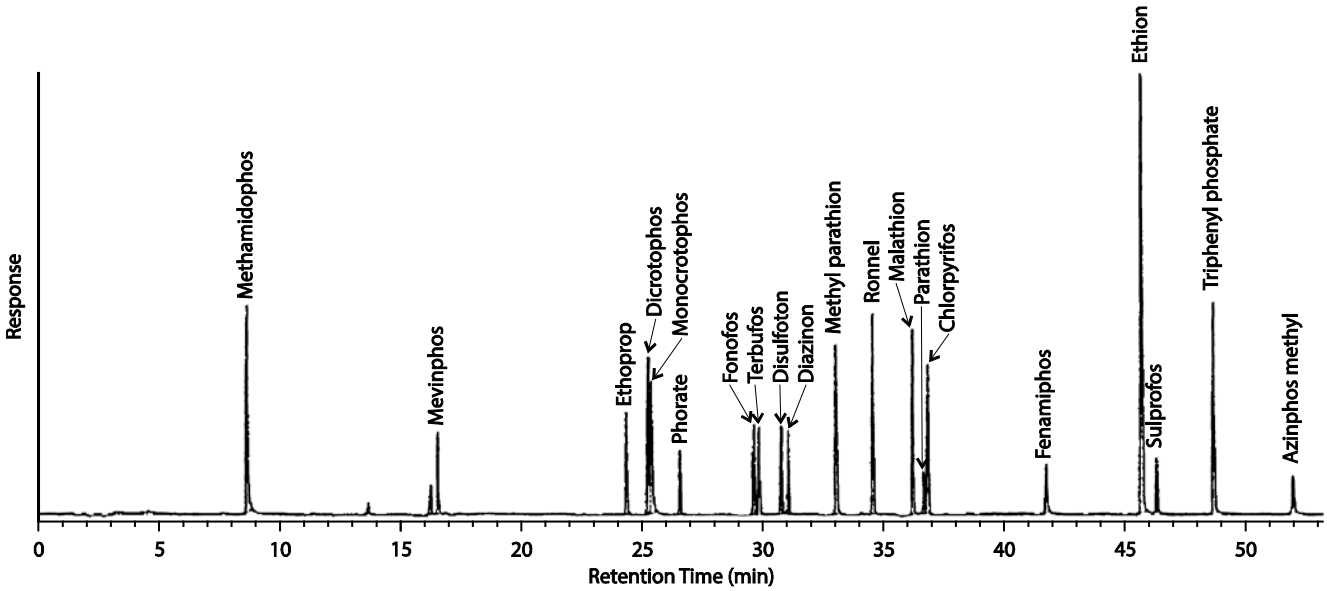

Figure 3. Typical chromatogram of organophosphorus compounds

Column: DB-1 fused silica capillary column, 30 meters x 0.32 mm I.D. x 0.25 µm film thickness
Temperature program: 80 to 275 °C at 3.0 °C per minute.
Concentration of analytes: 0.6 x NIOSH REL, except Sulprofos (0.06x REL), and Malathion and Ronnel (both at 0.006x)

- 1.8 µg/mL Parathion and Phorate
- 3.6 µg/mL All other compounds
- 7.2 µg/mL Azinphos methyl, Chlorpyrifos, Methamidophos, and Methyl parathion
- 9.0 µg/mL Dicrotophos and Monocrotophos
- 14 µg/mL Triphenyl phosphate
- 14.4 µg/mL Ethion

ORGANONITROGEN PESTICIDES 5601

Formula: Figure 1 MW: Table 1 CAS: Table 1 RTECS: Table 1

METHOD: 5601, Issue 2 **EVALUATION:** FULL **Issue 1:** 15 January 1998
Issue 2: 25 February 2016

OSHA: Table 1
NIOSH: Table 1

PROPERTIES: Table 1

SYNONYMS: Aldicarb, Benomyl, Captan, Carbaryl, Carbendazim, Carbofuran, Chlorprophan, Diuron, Formetanate, Methiocarb, Methomyl, Oxamyl, Propham, Propoxur, Thiobencarb (Table 1)

SAMPLING

SAMPLER: FILTER/SOLID SORBENT TUBE (OVS-2 Tube: 13-mm quartz fiber filter; XAD-2, 270 mg/140 mg)

FLOW RATE: 0.1 - 1 L/min [1]

VOL-MIN: variable (see Table 2)
-MAX: 480 L

SHIPMENT: routine

SAMPLE STABILITY: at least 30 days @ -12 °C [1]
at least 7 days @ 24 °C [1]

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: Table 2

BIAS: Table 2

OVERALL PRECISION ($\hat{S}_{rT}$): Table 2

ACCURACY: Table 2

MEASUREMENT

TECHNIQUE: HPLC, UV DETECTION

ANALYTE: organonitrogen pesticides (Table 1)

EXTRACTION: 2 mL extraction solution (0.2% V/V 0.1 M aqueous triethylamine phosphate buffer in acetonitrile, pH 6.9 to 7.1)

INJECTION VOLUME: 5 µL

MOBILE PHASE A: 2% 1-propanol in aqueous 0.02 M triethylamine phosphate (pH 6.9 to 7.1)

MOBILE PHASE B: 2% 1-propanol in acetonitrile

PROGRAM: mobile phase B, 3 to 95% in 30 min, hold 95% 5 min

COLUMN: C18, 30 cm x 3.9-mm ID; ambient temperature (Table 3)

DETECTOR: UV absorption at 200 and 225 nm

CALIBRATION: solutions of analytes in extraction fluid

RANGE: Table 2

ESTIMATED LOD: Table 2

PRECISION ($\bar{S}_r$): Table 2

APPLICABILITY: The working ranges (Table 2) for aldicarb, carbofuran, and oxamyl range from 0.5 to 10 times the OSHA PEL. Others cover 0.1 to 2 times the OSHA PELs with appropriate dilutions [1].This method may be applicable to the determination of other organonitrogen compounds after evaluation, and to a broad range of pesticides having UV chromophores, e.g., acetanilides, acid herbicides, organophosphates, phenols, pyrethroids, sulfonyl ureas, sulfonamides, triazines, and uracil pesticides.

INTERFERENCES: Because of the broad response of the UV detector at shorter wavelengths, there are many potential interferences. Those tested include solvents (chloroform and toluene), antioxidants (BHT), plasticizers (dialkylphthalates), nitrogen compounds (nicotine and caffeine), impurities in HPLC reagents (e.g., in triethylamine), other pesticides (2,4-D, atrazine, parathion, etc.), and pesticide hydrolysis products (1-naphthol). Retention times are given in Table 4. Confirmation techniques are recommended when analyte identity is uncertain.

OTHER METHODS: This method may be used to replace previous related pesticide methods: S273 Carbaryl [2]; 5006 Carbaryl [3]; OSHA 63 Carbaryl and 74 Aldicarb [4]; OSHA Stopgap methods for several pesticides [5]; and EPA TO-10 for Captan, Folpet, and Mexacarbate [6]. The OVS-2 Tube is similar in concept to the device of Hill and Arnold [7], but offers convenience and lower flow resistance.

REAGENTS:

1. Carbamate, urea, and sulfenimide analytes listed in Table 1; internal standards acetanilide and acetophenone, analytical grade.*
2. Acetonitrile, UV grade.*
3. Methanol, HPLC grade.*
4. Deionized water, ASTM Type II.
5. 1-Propanol, UV grade.*
6. n-Butyl isocyanate.*
7. Triethylamine (TEA), HPLC grade.* Keep refrigerated (0 to 4 °C) and store under nitrogen for longer shelf life [1, 8].
8. Ortho-phosphoric acid, >85% by weight, ACS grade or better.*
9. Extraction solution. Prepare separate trimethylamine phosphate (TEA-PO_4) preservative and internal standard solutions.
   a. TEA-PO_4 preservative, 0.1 *M*. Dissolve1.4 mL of TEA in 90 mL of deionized water. Add phosphoric acid to lower pH to 7.0 (± 0.1) as indicated by a calibrated pH meter. Bring volume to 100 mL. Keep tightly capped and refrigerated.
      NOTE: Do not use chloroacetic acid as a preservative [9]. Formetanate, at least, is unstable with chloroacetic acid.
   b. Internal standard stock solution, 5 mg/mL. Add 100 mg of each internal standard of choice for each 20 mL of solution required. Dissolve in acetonitrile. Store capped at –12 ± 1 °C.
   c. Final extraction solution. Add 1 mL of the TEA-PO_4 solution and 12 mL of the internal standard stock solution to a 500-mL volumetric flask. Dilute to volume with acetonitrile. Concentration of TEA = 0.2 mM, water = 0.2%, and internal standards = 120 µg/mL. Stable up to 30 days at 0 to 4 °C.
10. Individual analyte stock solutions, 5 mg/mL. Add each analyte to acetonitrile in separate volumetric flasks. Use methylene chloride for benomyl and carbendazim. Use 50/50 v/v methanol/acetonitrile or formetanate. Store at –12 ± 1 °C. (Solutions are stable up to 30 days.)

EQUIPMENT

1. Sampler: OSHA Versatile Sampler (OVS-2 tube), resin filled sampling tube; glass tube, 11-mm i.d. x 13-mm o.d. x 50-mm long, with the outlet end drawn to a 6-mm o.d. x 25-mm long tube. The enlarged part of the tube contains a 270-mg front section of 20/60 mesh XAD-2 sorbent held in place by a 9-10-mm o.d. quartz fiber filter and polytetrafluoroethylene (PTFE) retaining ring. The front section is separated from the back section of 140 mg XAD-2 sorbent with a short plug of polyurethane foam. The back section is held in place by a long plug of polyurethane foam. The tube is available commercially. OVS-2 tubes with glass fiber filters have equivalent desorption efficiencies and are commercially available.
2. Personal sampling pump: 0.1 to 1 L/min with flexible and inert connecting tubing.
3. High Performance Liquid Chromatograph capable of mixing two mobile phases in a linear gradient. Must be capable of pumping up to 4000 psi, to accommodate 300 mm long columns.
4. Autosampler, low dead-volume, capable of 5-µL injections. Preservative (TEA-PO_4) in the desorbing solution may be eliminated if a refrigerated autosampler tray is available**
5. Analytical columns.
   a. Primary column: Base-deactivated octadecylsilyl (C18) column, 3.9-mm ID X 300 mm, 5-µm particle size.
   b. Secondary column: Cyanopropyl silica column, 4.6 X 250-mm, 5-µm particle size.
6. Guard column, low dead-volume, containing analytical column packing material**
7. Ultraviolet detector, low dead-volume, with 1-cm path length cell capable of monitoring two wavelengths (200- and 225-nm) simultaneously.
8. Vials: 4-mL with PTFE-lined caps; 2-mL HPLC autosampler vials with PTFE- or polyethylene-lined snap caps.
9. Syringes: 0.01-, 0.05-, 0.1-, 1.0- and 2.5-mL; luer lock style, 1- or 2.5-mL for sample filtering.
10. Volumetric flasks: 2-, 5-, 10-, 25-, 50-, 100-, 500-, and 1000-mL.
11. PTFE syringe filter: 0.45-µm.

REAGENTS: (continued)

11. Calibration stock solution. Combine stock solutions of analytes of interest in a volumetric flask to produce the highest concentration standard (suggest 120 to 480 µg/mL).
    NOTE: Do not combine benomyl and carbendazim in the same standard solution. [10-12]. See APPENDIX.
12. Quality control spiking solutions: Add analyte stock solutions to acetonitrile at concentrations in the analytical range of the samples. Store in the freezer at –12 ± 1 °C until immediately before spiking.
    NOTE: Spiking solutions must not contain internal standard.
13. Mobile phase A. Combine 20 mL of 1-propanol and 2.8 mL of TEA in a 1-L volumetric flask and bring to volume with deionized water. Adjust pH to 7.0 (± 0.1) with phosphoric acid using a pH meter. Final concentrations: 2% 1-Propanol, 0.02 M TEA-PO_4. Degas prior to use.
14. Mobile phase B. Add 20 mL of 1-propanol to acetonitrile in a 1-L volumetric flask and bring to volume. Degas prior to use.

EQUIPMENT: (continued)

12. Forceps.
13. Small vial/tube tumbler capable of 5 to 10 RPM.
14. pH meter.
15. Graduated cylinders, 10-mL, 25-mL.
16. Pippettes, glass, disposable.

*See SPECIAL PRECAUTIONS.

**Low dead volumes will give lower dwell volumes [13, 14] and better resolution [15]

SPECIAL PRECAUTIONS: Pesticides: Avoid inhaling vapors or dust; avoid skin contact. Wear gloves and suitable clothing when handling pure material. Solvents: Avoid skin contact and open flame. Use in a hood. Phosphoric acid: Avoid skin contact. n-Butyl isocyanate may act as a sensitizer. Avoid skin contact.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Connect the sampler to the personal sampling pump with flexible tubing. Place sampler vertically, with the large end down, in the worker's breathing zone.
3. Sample at an accurately known flow rate between 0.1 and 1 L/min for a total sampling volume up to 480 L. Record volume, and document presence of any known or potential interferences.
4. Cap both ends of the sampler with plastic caps and pack securely for shipment.

CALIBRATION AND QUALITY CONTROL

5. Remove cap from large end. Transfer filter, PTFE retainer ring, and front resin section to a 4-mL vial. Transfer the polyurethane foam divider plug along with the back-up resin bed to a second 4-mL vial.
6. Add 2.0 mL of desorbing solvent with internal standards to each vial using a 2.5- or 5-mL syringe or 2-mL pipette; cap each vial.

7. Mix by rotating the vials end-over-end at 5 to 10 RPM for approximately 45 minutes.
8. Filter an aliquot into a 2-mL autosampler vial through a 0.45-µm PTFE filter.

CALIBRATION AND QUALITY CONTROL

9. Determine retention times for the analytes of interest using the column and chromatographic conditions of choice for the analysis.
10. Calibrate daily with at least six working standards covering the analytical range for individual analytes.
    a. Prepare working standards by diluting aliquots of the high-level calibration standard with desorbing solution containing internal standard in a volumetric flask. Include an unspiked desorption solution calibration blank.
    b. Filter aliquots of standards and blanks for analysis (See Step 8).
    c. Analyze together with samples, blanks, and laboratory control samples (Steps 12 through 14).
    d. Prepare a calibration graph (ratio of peak area of analyte over peak area of internal standard vs. µg analyte).
    NOTE: Use of an internal standard is recommended [1, 6], but optional if the precision of the injection device and HPLC system are known to be adequate.
11. Prepare desorption efficiency (DE) samples and Laboratory Control Samples (LCS) with each sample set at a rate of 10% of samples.
    a. Remove cap and the PTFE retainer ring from large end of sampler tube (to prevent wicking behind the ring). Apply known volume of calibration solution to face of quartz fiber filter.
    NOTE: Spike no more than 15 to 30 µL at a time. If more needs to be applied, connect the sampler to a vacuum pump with a flow ≤1 L/min, then apply spiking solution in 15- to 30-µL aliquots. Allow several minutes for the solvent to evaporate between each aliquot, to prevent wicking along the sides of the tube into the back-up section (5% or more may deposit on the walls of the tube).
    b. Cap and allow to stand a minimum of one hour.
    NOTE: Prepare LCS when samples arrive and store with field samples until analyzed.
    c. Include an unspiked sampler as a media (method) blank.
    d. Analyze with the field samples, blanks, and the liquid standards (Steps 12 through 14).

MEASUREMENT:

12. Set liquid chromatograph according to manufacturer's recommendations and to conditions listed in Table 3. Select two wavelengths for detection with 200 and 225 nm for general-purpose screens. For selected analytes, chose a more specific wavelength UV spectra where available.
13. Inject sample aliquot with autosampler. See Table 4 for approximate retention times of selected analytes.
    NOTE: If peak area is greater than the area of the highest standard, dilute with desorbing solution containing internal standards and reanalyze. Apply the appropriate dilution factor in calculations.
14. Measure peak area of analyte(s) and internal standard(s). Divide peak area of analyte by peak area of internal standard on same chromatogram.

CALCULATIONS:

15. Determine the mass, µg, (corrected for DE) of analyte found in the sample filter and front sorbent section (W_f), back sorbent section (W_b), and the media blank front (B_f) and back (B_b) sorbent sections from a standard curve.

16. Calculate concentration, C (mg/m^3), of each analyte in the air volume sampled, V (L)

$$C = \frac{W_f + W_b - B_f - B_b}{V}, mg/m^3$$

NOTE: µg/mL ≅ mg/m^3

CONFIRMATION:

Retention Times with Alternate Conditions. Whenever the identity of an analyte is uncertain, confirmation may be achieved by analysis on an alternate column. If primary analysis was performed on a base-deactivated octadecylsilyl (C18) column, identity may confirmed by reanalysis on a cyanopropyl silica column, or by changing to a water/methanol mobile phase (see Table 9 for recommended alternative conditions). See Table 4 for approximate retention times for each column type and condition. Relative retention times (retention indices for a particular set of conditions) are more convenient for the identification of unknown analytes.

UV or Mass Spectra. Confirmation may be achieved through comparison of unknown spectra with reference spectra where available. Relative response ratios will give a moderate level of confirmation. Some analytes (O-aryl carbamates especially) can be confirmed by GC/MS using highly deactivated injection ports and analytical GC columns, or by HPLC/MS.

EVALUATION OF METHOD:

This method was evaluated over the ranges specified in Table 2 at 25 °C with 240-L air samples. Samplers were tested at 15 and 80% relative humidity and 10 and 30 °C. In these experiments, test atmospheres were not generated; instead, analytes were fortified on the face of the sampler filters. The conditioned air was pulled through the samplers at 1 L/min for four hours. No significant difference in sampler performance was noted at any of these temperature/humidity combinations. Evaluation of sampler precision and stability was conducted at ambient conditions of temperature and relative humidity. Overall sampling and measurement precision, bias, accuracy, and average percent recovery after long-term storage are presented in Table 2. No breakthrough was detected with samplers fortified with 480 µg per analyte per tube after sampling eight hours at 1 L/min. For the estimation of LOD/LOQ, a series of media-spiked standards were prepared in triplicate, analyzed, and responses fitted to a quadratic curve. The Limit of Detection (LOD) and Limit of Quantitation (LOQ), given in Table 2, were estimated according to NIOSH SOP 018 [1,17]. Criteria established by NIOSH were met [1].

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TABLE 1. General Information

Name/Synonym	Formula	MW	Properties	Solubility in H_2O (g/L)	Exposure Limit (mg/m^3)
Aldicarb CAS# 116-06-3 RTECS UE2275000	$C_7H_{14}N_2O_2S$	190.3	MP 99-100 °C; vp 3.9 mPa ($2.9x10^{-5}$ mm Hg) @ 25 °C; LD_{50} 1 mg/kg	6 @ 25 °C	
Benomyl CAS# 17804-35-2 RTECS DD6475000	$C_{14}H_{18}N_4O_3$	290.36	MP decomposes; vp <1.3 mPa (<$1x10^{-5}$ mm Hg) @ 20 °C; LD_{50} >9590 mg/kg	0.002 @ 25 °C	OSHA 5.0 (resp)
Captan CAS# 133-06-2 RTECS GW5075000	$C_9H_8Cl_3NO_2S$	300.6	MP 178 °C; vp <1.3 mPa (<1x10-5 mm Hg) @ 20 °C; LD_{50} 9000 mg/kg	<0.005 @ ~25 °C	NIOSH 5
Carbaryl CAS# 63-25-2 RTECS FC5950000	$C_{12}H_{11}NO_2$	201.24	MP 142 °C; vp <5.3 mPa (<4x10-5 mm Hg) @ 25 °C; LD_{50} 250 mg/kg	0.12 @ 30 °C	OSHA 5 NIOSH 5
Carbendazim CAS# 10605-21-7 RTECS DD6500000	$C_9H_9N_3O_2$	191.21	MP 302-307 °C (decomposes); LD_{50} 6400 mg/kg	0.008/pH 7 @ 24 °C	
Carbofuran CAS# 1563-66-2 RTECS FB9450000	$C_{12}H_{15}NO_3$	221.28	MP 150-153 °C; vp 0.031 mPa ($2.3x10^{-7}$ mm Hg) @ 20 °C; LD_{50} 5.3 mg/kg	0.70 @ 25 °C	NIOSH 0.1
Chlorpropham CAS# 101-21-3 RTECS FD8050000	$C_{10}H_{12}ClNO_2$	213.68	MP 40.7-41.1 °C; vp 2.7 mPa ($2x10^{-5}$ mm Hg) @ 33 °C; LD_{50} 1200 mg/kg	slightly soluble	
Diuron CAS# 330-54-1 RTECS YS8925000	$C_9H_{10}Cl_2N_2O$	233.11	MP 158-159 °C; vp 0.41 mPa ($3.1x10^{-6}$ mm Hg) @ 50 °C; LD_{50} 437 mg/kg	0.042 @ 25 °C	NIOSH 10
Formetanate.HCl CAS# 23422-53-9 RTECS FC2800000	$C_{11}H_{16}ClN_3O_2$	257.75	MP 200-202 °C (decomposes); LD_{50} 20 mg/kg	>50% as hydrochloride	
Methiocarb CAS# 2032-65-7 RTECS FC5775000	$C_{11}H_{15}NO_2S$	225.34	MP 121.5 °C; vp 0.036 mPa (2.7x10-7 mm Hg) @ 25 °C; LD_{50} 60 mg/kg	insoluble	
Methomyl CAS# 16752-77-5 RTECS AK2975000	$C_5H_{10}N_2O_2S$	162.24	MP 78-79 °C; vp 6.7mPa ($5x10^{-5}$ mm Hg) @ 25 °C; LD_{50} 17 mg/kg	58 @ 25 °C	NIOSH 2.5
Oxamyl CAS# 23135-22-0 RTECS RP2300000	$C_7H_{13}N_3O_3S$	219.3	MP 100-102 °C; vp 31 mPa ($2.4x10^{-4}$ mm Hg) @ 20 C; LD_{50} 5 mg/kg	280 @ 25 °C	
Propham CAS# 122-42-9 RTECS FD9100000	$C_{10}H_{13}NO_2$	179.24	MP 90 °C; vp 18 mPa ($1.35x10^{-4}$ mm Hg); LD_{50} 50 mg/kg	0.25 @ 25 °C	
Propoxur CAS# 114-26-1 RTECS FC3150000	$C_{11}H_{15}NO_3$	209.27	MP 91.5 °C; vp 1.3 mPa (9.75 mm Hg) @ 20 C; LD_{50} 83 mg/kg	2 @ 20 °C	NIOSH 0.5
Thiobencarb CAS# 28249-77-6 RTECS EZ7260000	$C_{12}H_{16}ClNOS$	257.81	Not available; LD_{50} 1130 mg/kg	~0.03 @20 °C	

Abbreviations: MW=molecular weight (Daltons); RTECS=Registry of Toxic Effects of Chemical Substances [18]; LD_{50}=lethal dose 50% [19,20]; mPa=milliPascals

TABLE 2. Method Evaluation

Compound	Min. Sample Vol (L)	Range Studied (µg/samp)	LOD (µg/ samp)	Mean Bias	Overall Precision ($\hat{s}_{rT}$)	Accuracy	Storage Stability 31-Day % recovery 24 °C	Storage Stability 31 day % recovery -12 ℃
Aldicarb	240	12.0-240	1.2	-0.009	0.066	± 0.131	93.2	95.6
Benomyl	6	12.0-120	0.6	[A]	[A]	[A]	[A]	[A]
Captan	30	48.0-960	4.8	-0.036	0.061	±0.142	98.7	102.2
Carbaryl	6	12.0-240	0.06	+0.012	0.061	±0.123	88.2	91.8
Carbendazim	6	[B]	0.6	+0.006	0.061	±0.121	92.1	89.3
Carbofuran	240	12.0-240	0.6	-0.020	0.060	±0.126	89.1	92.4
Chlorpropham	6	12.0-240	0.6	-0.017	0.068	±0.140	84.3	85.9
Diuron	3	12.0-240	0.6	-0.062	0.060	±0.167	86.0	87.1
Formetanate.	60	12.0-240	0.6	+0.032	0.056	±0.129	89.8	93.0
Methiocarb	60	12.0-240	0.6	+0.009	0.061	±0.122	85.1	89.1
Methomyl	12	12.0-120	0.6	-0.002	0.063	±0.124	90.5	95.2
Oxamyl	240	12.0-240	0.6	+0.037	0.055	±0.132	94.8	95.9
Propham	3	12.0-240	0.8	-0.053	0.066	±0.168	88.5	92.5
Propoxur	60	12.0-240	0.6	+0.007	0.079	±0.156	91.4	95.4
Thiobencarb	6	12.0-240	0.6	-0.068	0.073	±0.197	75.0	79.8

[A] Results calculated as carbendazim, the primary breakdown product of benomyl.
[B] See range for benomyl, a precursor for carbendazim.

TABLE 3. Recommended liquid chromatographic columns and conditions

	C18 Column	C18 Column	Cyano Column	Cyano Column
Solvent	Acetonitrile	Methanol	Acetonitrile	Methanol
Application	Primary Analysis	Confirmation	Confirmation	Confirmation
Stationary phase	Octadecyl	Octadecyl	Cyanopropyl	Cyanopropyl
Length (mm)	300	150	250	250
ID (mm)	3.9	3.9	4.6	4.6
Particle size (µm)	4	4	5	5
Ligand density[A]	2.7	2.7	5.2	5.2
Mobile phase A Solvent	Water	Water	Water	Water
Mobile phase A organic modifier[B]	2% 1-propanol	None	None	None
Mobile phase A buffer[C]	TEA-PO_4	None	TEA-PO_4	TEA-PO_4
Mobile phase A concentration (M)	0.02 *M*	None	0.02 *M*	0.02 *M*
Mobile phase B solvent[D]	Acetonitrile	Methanol	Acetonitrile	Methanol
Mobile phase B organic modifier	2% 1-propanol	None	None	None
Initial hold time	0	0	0	0
Program rate	3-95% B	10-80% B	3-60% B	3-95% B
Program time (min)	30	30	30	30
Program type	Linear	Linear	Linear	Linear
Final hold time (min)	5	5	5	5
Flow rate (mL/min)	1.00	1.00	1.00	1.00
Column temperature (°C)	Ambient (~24)	Ambient (~24)	Ambient (~24)	Ambient (~24)
Dwell volume (mL)	0.6-0.8	3.5-3.8	0.6-0.8	0.6-0.8
Injection volume (µL)	5	30	5	5
Injection solvent	Acetonitrile	1:3 acetonitrile:H_2O	Acetonitrile	Acetonitrile

[A] Ligand density (micromole/m^2) is a better description of surface coverage than % carbon loading [22, 23].

[B] Choice of alcohol modifier is not critical. Percentages may be varied to adjust retention times and peak shapes for early eluting analytes. Reequilibration time may be shorter with 1-propanol [24-26].

[C] Buffer is very essential for basic analytes such as Formetanate, Carbendazim, and Benomyl [12,27,28]. Formentate is cationic at about pH 7, and its actual elution time is sensitive to small changes in pH and ionic strength of the buffer in mobile phase A.

[D] Acetonitrile is the better choice when monitoring compounds at UV absorptions below 210 nm [20,29].

TABLE 4. Approximate retention times and indices for organonitrogen pesticides and potentially interfering compounds

Compound[A] (by retention time)	C18 Column Retention index[B]	C18 Column (MeCN solvent) retention time (min)	C18 Column (MeOH solvent) retention time (min)	Cyano Column retention index	Cyano column (MeCN solvent) retention time (min)	Cyano column (MeOH solvent) retention time (min)
Solvent void volume	0.000	2.3	1.4	0.000	3.0	3.2
Asulam	0.004	2.3				
Imazapyr	0.372	3.2				
Acetaminophen/*IS*	1.000	4.7		1.000		
Oxamyl	1.269	6.1	9.9	1.865	7.0	6.4
Caffeine	1.397	6.8				
Methomyl	1.445	7.0	10.7	1.915	7.4	6.6
Formetanate	1.573	7.7	[C]	2.574	12.8	11.3
Sulfometuron methyl	1.868	9.3				
Acetanilide/*IS*	2.000	9.9		2.00	8.1	7.7
Fenuron	2.053	10.2				
2,4-D acid	2.064	10.2				
Nicotine	2.179	10.8				
Carbendazim	2.192	10.8	[C]	4.274	13.6	12.9
Chlorimuron ethyl	2.422	11.9				
Aldicarb	2.755	13.5	19.9	3.00	10.5	10.1
Tebuthiuron	2.817	13.8	23.9			
m-Cresol	2.866	14.0				
Bromacil	2.902	14.2				
Hexazinone	2.921	14.3				
Dinoseb	2.928	14.3				
Simazine	2.938	14.3				
Monuron	2.981	14.5				
Acetophenone/*IS*	3.00	14.6		3.00	10.5	9.9
Cyanazine	3.003	14.6				
Metribuzin	3.115	15.0				
Thiodicarb	3.247	15.5				
Aminocarb	3.301	15.7				
Propoxur	3.317	15.8	22.9	3.675	13.1	11.9
Bendiocarb	3.376	16.0	23.3			
Carbofuran	3.399	16.1	23.2	4.018	14.4	14.1
Fluometuron	3.551	16.6	25.2			
Chloroform	3.601	16.8				
Carbaryl	3.654	17.0	24.5	5.236	19.1	18.2
Atrazine	3.668	17.1				
Metalaxyl	3.837	17.6				
Diuron	3.843	17.6	27.0	5.751	21.1	19.9
DEET	3.851	17.7				
Alpha-Naphthol	3.893	17.8				
Propiophenone/*IS*	4.000	18.2		4.00	14.4	
Propachlor	4.241	18.8				
Thiophanate	4.241	18.8	27.6			
Propham	4.267	18.9	25.9	5.092	17.7	17.3
Diethyl phthalate	4.367	19.2				
Clomazone	4.459	19.4				
Siduron	4.615	19.9				
Desmedipham	4.696	20.1				
Phenmedipham	4.700	20.1	>33			
Methiocarb	4.744	20.2	29.3	6.680	22.5	21.8

TABLE 4. Continued

Compound[A] (by retention time)	C18 Column Retention index[B]	C18 Column (MeCN solvent) retention time (min)	C18 Column (MeOH solvent) retention time (min)	Cyano Column retention index	Cyano column (MeCN solvent) retention time (min)	Cyano column (MeOH solvent) retention time (min)
Linuron	4.848	20.5	28.9			
BDMC/IS	4.904	20.6				
SWEP	4.919	20.7				
Captan	4.926	20.7	27.7	6.172	20.9	21.6
Promecarb	4.981	20.8	20.4			
Butyrophenone/*IS*	5.000	20.9		5.000	17.4	
Mexacarbate	5.186	21.3				
Toluene	5.269	21.5				
Chlorpropham	5.504	22.1	30.1	6.700	23.4	23.3
Folpet	5.537	22.2	>33			
Barban	5.566	22.3	>33			
Malathion	5.731	22.7				
Fenitrothion	5.802	22.8				
Benomyl	5.822	22.9	[C]	7.391	25.8	23.9
Oryzalin	5.860	23.0				
Metolachlor	5.876	23.0				
Alachlor	5.979	23.3				
Acetochlor	5.983	23.3				
Valerophenone/*IS*	6.000	23.3		6.000	20.9	
Captafol	6.018	23.4	30.1			
Neburon	6.045	23.4				
Parathion	6.640	24.7				
Hexanophenone/*IS*	7.000	25.5		7.000	24.0	
Thiobencarb	7.148	25.8	33.4	7.916	26.2	26.8
Heptanophenone/*IS*	8.000	27.6		8.000	26.4	
Di-n-butyl phthalate	8.016	27.6				
Chlorpyrifos	8.701	28.9				
Pendimethalin	8.724	28.9				
2,4-D butoxyethyl ester	8.892	29.2				
Octanophenone/*IS*	9.000	29.4		9.000	29.0	
BHT	9.488	30.2				
Amitraz	9.886	30.9				
Nonanophenone/*IS*	10.000	31.1				
2,4-D ethylhexyl ester	10.545	31.9				
Decanophenone/*IS*	11.000	32.5				

[A] Organonitrogen pesticides are in bold letters.

[B] Estimated (~) retention times are extrapolated from shorter columns using relative retention times.

[C] Without TEA-PO_4 buffer, basic compounds had irregular peak shapes and retention times, or were not detected. Abbreviations: MeCN=acetonitrile; MeOH=methanol; IS=internal standard.

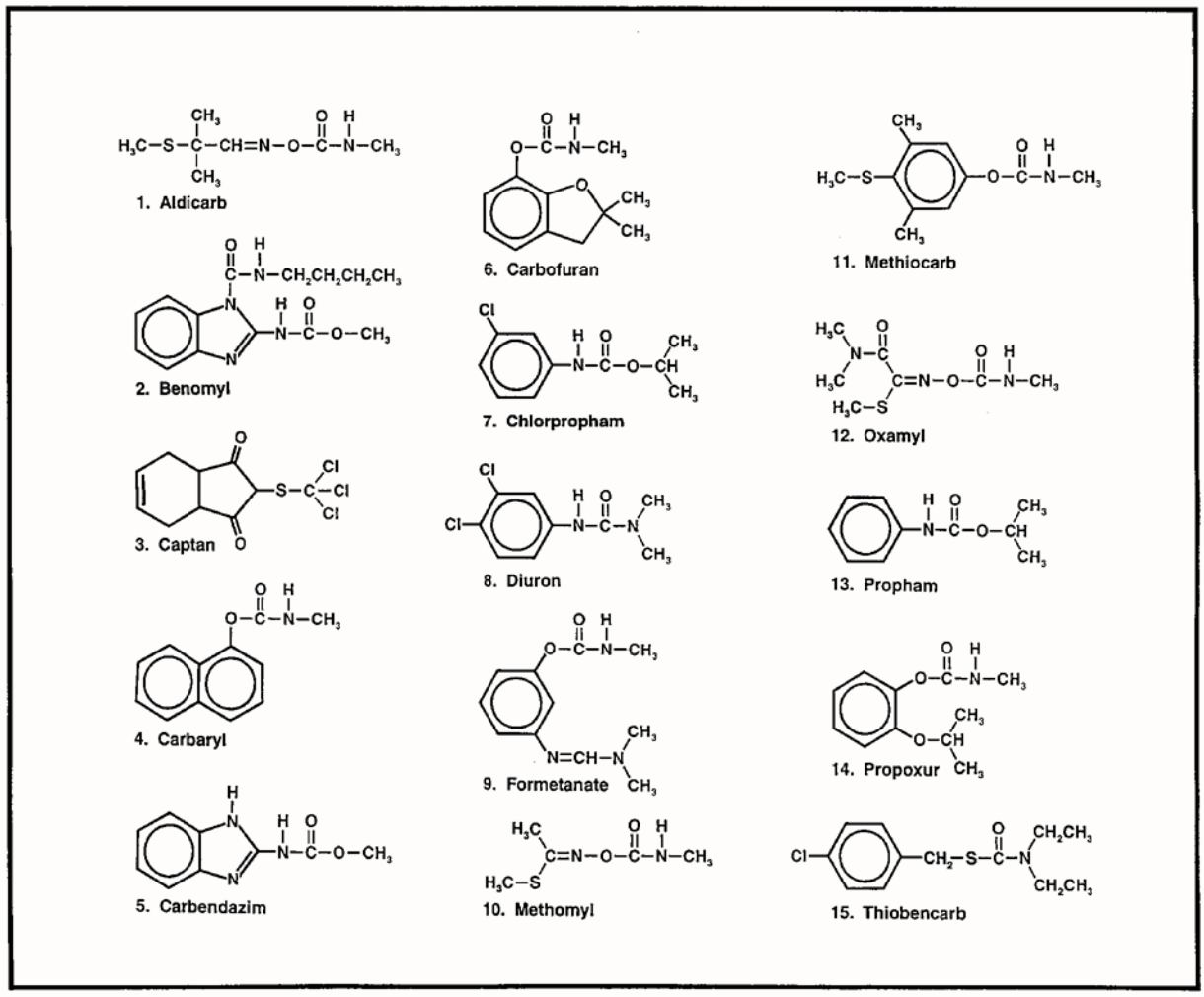

Figure 1. STRUCTURE OF CARBAMATE, UREA, AND SULFENIMIDE PESTICIDES

APPENDIX A. NOTES ON HPLC ANALYS IS OF CARBAMATE, UREA, AND SULFEN IMIDE PESTICIDES

A. ANALYTES

1. Aldicarb
   a. UV response for aldicarb passes through a minimum at approximately 225 nm. If only two wavelength channels are used (225 nm and 200 nm), the response for aldicarb at 200 nm should be monitored. At 205 nm the signal will be smaller, but the signal-to- noise ratio may be better on particular instruments. An alternative but lesser maximum is at approximately 245 to 246 nm. This latter maximum, though small, may have less background noise and interferences from coelutants.
   b. Aldicarb is a highly toxic pesticide. Care should be exercised in handling pure stock material.
2. Benomyl (see also Carbendazim)
   a. Benomyl breaks down rapidly by either hydrolysis in protic solvents (e.g., water or methanol) or solvolysis in nonproticsolvents (e.g., methylene chloride or acetonitrile) to carbendazim. The breakdown of benomyl can be so rapid that no benomyl will be detected at all after approximately 4 to 24 hours at room temperature.The rate of solvolysis is slower in the less polar methylene chloride andvery rapid in acetonitrile, even exceeding the rate of hydrolysis [10-12]. Benomyl standards in these nonprotic solvents can be stabilized with the addition of 1% n-butyl isocyanate [30]. The preservative effect is lost as soon as the solution is diluted in solvents that contain or consist of protic solvents, since protic solvents also react with the isocyanates. It is generally unnecessary to add any preservative to the benomyl standard solution (it breaks down anyway). The carbendazim produced can precipitate out, if the solutions are too concentrated. In such an event, the addition of 1% n-butyl isocyanate is essential.
   b. Since benomyl breaks down to carbendazim, do not include both benomyl and carbendazim in the same standard mixture.
   c. When analyzing for benomyl, both benomyl and carbendazim must be determined. The results can be reported as either benomyl or carbendazim by converting the response of one to the equivalent response for the other at any particular wavelength. The relative response of benomyl to carbendazim at 225 nm has been determined to be approximately 1.0738, (adsorption-benomyl/ adsorption-carbendazim). This ratio should be determined for individual instruments with equimolar solutions analyzed separately, and with the benomyl injection solution being preserved with 1% n-butyl isocyanate. To convert carbendazim response to the equivalent benomyl response so that the values can be summed, multiply the carbendazim response by 1.0738 and add this to the benomyl response. Report results as benomyl. Alternately, to report results as carbendazim, divide benomyl response by 1.0738 and then add this to the carbendazim response. Report as total carbendazim.
   d. See notes for carbendazim.
3. Captan
   a. Captan is not stable in methanol or in aqueous mixtures of methanol or acetonitrile at temperatures greater than –12 °C. Therefore, do not dilute desorbing solutions with water or methanol to weaken the injection solvent. Instead, use small injection volumes of acetonitrile solutions.
   b. Use methylene chloride for making stock standard solutions. See Note 16 of this Appendix.
   c. Captan has low absorption at 225 nm (see UV spectrum for captan). If only two wavelength channels are used (225 and 200 nm), the response for captan at 200 nm should be monitored. Although a lesser response may be obtained at approximately 205 or 210 nm, this can be accompanied by a proportionately better signal-to-noise response and may be an optional choice of wavelength if it is compatible with other analytical objectives.
4. Carbaryl (see also Diuron): Carbaryl tends to break down to 1-naphthol. Chloroacetic acid in methanol will inhibit this reaction [9], but this reagent is deleterious to other analytes. Carbaryl is

stabilized in acetonitrile desorbing solutions containing the TEA- PO_4 preservative for at least 24 hours at room temperature, long enough to permit HPLC analysis. Any 1-naphthol that is detected may represent breakdown of carbaryl prior to desorption or may come from another source. Carbaryl has been stabilized with the TEA-PO_4 buffer/preservative for up to three weeks at room temperature.

5. Carbendazim
   a. See notes for benomyl.
   b. Carbendazimcan break down to 4-aminobenzimidazole and other compounds. In acetonitrile containing TEA-PO_4 preservative, this breakdown appears to be inhibited for up to 24 hours at room temperature, long enough to permit analysis of desorbates.
   c. Carbendazim is itself used as a pesticide. There are also other analytes such as thiophanate methyl that can break down to carbendazim. Therefore, any carbendazim should not automatically be assumed to represent benomyl.
6. Carbofuran
   a. In most instances carbofuran and bendiocarb coeluted under all conditions tested. Their UV spectra are so nearly alike as to be practically indistinguishable. Any positive identification for carbofuran must be tempered by this knowledge and would require an alternate confirmation such as by mass spectrometry or a knowledge of the history of the sample.
   b. Propoxur and carbofuran elute very close together. The separation of the two compounds with nearly baseline resolution is a good test of resolving power of the HPLC system for neutral compounds on a C18 HPLC column. If they cannot be resolved, there may be problems with large dead volumes in the system, analytical column quality, or injection quality.
7. Chlorpropham: No serious problems are expected to be encountered.
8. Diuron: The breakdown product of carbaryl, 1-naphthol, elutes immediately after diuron under the conditions given. On certain columns, it may coelute with diuron, giving false positive responses. The retention time of 1-naphthol relative to diuron must be determined for any particular column if carbaryl is anticipated to have been present in the sample.
9. Formetanate
   a. At analytical concentrations formetanate is not stable either in methanol or in aqueous mixtures of methanol or acetonitrile with or without chloroacetic acid. Therefore, do not dilute desorbing solutions with methanol or water to weaken the injection solvent. Do not use chloroacetic acid as a preservative. Use only small injection volumes of acetonitrile solutions.
   b. The breakdown of formetanate in analytical solutions is inhibited in acetonitrile containing TEA-PO_4 preservative at room temperature for up to 24 hours, long enough to permit analysis.
   c. At stock standard concentrations, formetanate dissolves better in 50:50 mixtures of methanol: acetonitrile and is stable if kept in freezer at -12 ± 1 °C.
   d. Formetanate is basic and possesses a single positive charge in solution at neutral pH (6.9 – 7.1). The use of TEA-PO_4 buffer and/or base-deactivated HPLC columns is essential for the analysis for this compound.
   e. The exact retention time of formetanate is more affected by exact pH and ionic strength of the buffer (or any other electrolytes) than are the noncharged analytes. Day-to-day inconsistencies in the preparation of mobile phases will cause differences in retention time. If the analyte is eluting too close to methomyl (which just precedes it under the specified conditions), its retention time may be delayed by either raising the pH slightly (by 0.1 to 0.2 units), or by lowering the ionic strength of mobile phase A.
10. Methiocarb: Methiocarb has the same problems as carbaryl, only to a lesser extent. As methiocarb breaksdown, there are several other peaks that arise. These have been shown to be alkylthiophenol and/or oxidation products.
11. Methomyl: Attention should be placed on the problem of methomyl as it relates to its early elution time. Refer to Notes B1a and B4 of this Appendix.

12. Oxamyl: Attention should be placed on the problem of oxamyl as it relates to its early elution time. Refer to Notes B1a and B4 of this Appendix.
13. Propham: No problems are expected with propham.
14. Propoxur
    a. With prolonged standing in desorbing solutions at room temperature without preservative, propoxur has been observed to break down to some degree, although much less than carbaryl.
    b. Propoxur elutes very close to carbofuran. See comments under carbofuran.
15. Thiobencarb: Thiobencarb is relatively nonpolar and has lower (but acceptable) recoveries from the XAD-2 resin than the other analytes.
16. Solvent for Analyte Standard Solutions: Most of the analytes (Table 1) are soluble in acetonitrile at stock standard concentrations. The exceptions are benomyl captan and formetanate. Appropriate solvents are described under headings for these compounds. In each of the solvents mentioned, analytes are stable at –12 ± 1 °C for at least 30 days.
17. Desorption Solvent and Preservative for Analytes: All analytes (except benomyl) were stable in acetonitrile at –12 °C for at least 48 hours. If refrigerated HPLC autosampler trays are available and all desorbing and tumbling operations are carried out in subambient conditions, no preservative should be needed. At room temperature, several analytes (e.g., carbaryl, methiocarb, and oxamyl especially) degraded unpredictably over 24 to 48 hours. The addition of as little as 0.2% v/v of aqueous 0.1 M triethylamine phosphate (TEA-PO_4) buffer, pH 6.9 to 7.1, to the acetonitrile desorptionsolvent stabilizes all analytes (except benomyl) from hydrolysis or solvolysis for at least 48 hours at room temperature. Methanol, isopropanol, aqueous methanol, and acetonitrile containing any of these alcohols promote degradation of several analytes (especially captan and formetanate) and poor desorption efficiencies. The use of chloroacetic acid, as is required for aqueous samples in EPA Method 531.1 [9], is destructive to at least formetanate. Since the desorption solvent is also the HPLC injection solvent, refer to note on Injection Solvent (B1) for additional comments.

B. HPLC CONDITIONS

1. Injection Solvent
    a. Normally a solvent producing equal or lower capacity factors than the mobile phase is desirable as an injection solvent in order to produce sharp peaks for early eluting analytes (e.g., oxamyl and methomyl) [31,32]. Since the initial mobile phase mixture of this method is mostly water, the only way to achieve this would be to dilute the samples with water. Water, however, is deleterious to several of the analytes specified in this method (see note A17 above). Therefore, an acceptable alternative is to inject very small volumes, not greater than 5 µL [31], of the desorption solvent (acetonitrile in this method) on a high-resolution HPLC column. If it is known that only analytes that are stable in aqueous solutions are to be determined (e.g., oxamyl and methomyl, but not formetanate or captan), the desorbates may be diluted with water and larger volumes injected. By diluting with water, sharper peaks may be obtained for early eluting compounds with accelerated elution conditions such as the use of shorter HPLC columns, higher percentages of organic modifier, or higher percentages of mobile phase B in the initial conditions.
    b. All sample extracts must be filtered through individual 0.45-micron PTFE filters in order to prolong guard column lifetimes and to protect the injection system valving.
    c. The accidental or intentional inclusion of significant amounts of solvents less polar than acetonitrile in the injection solvent, such as tetrahydrofuran or acetone, may shorten retention times and adversely affect the peak shapes of early eluites (e.g., oxamyl and methomyl) [31].
2. Guard Columns: Guard columns are essential to the long life and reproducibility of results on the main analytical column. There are several on the market. Those giving the lowest possible dead volume preserve good peak shapes and resolution of quality analytical columns and are preferred.

3. Analytical Columns
   a. General: The main analytical column specified in this method is a C18 reverse-phase column. Other columns known to perform well also may be used, following manufacturer recommendations. There are many good columns available [28, 33].
   b. Base Deactivation: The basic compounds (benomyl, carbendazim, and formetanate) present special challenges that are easily overcome with highly inert or base-deactivated columns [26]. The addition of TEA-PO_4 buffer to mobile phase A also greatly improves performance for these compounds [16, 26, 27].
   c. Dimensions: A longer column (300 mm) was used in this method in order to improve resolution for a large number of analytes and interferences, expected and unexpected. Long columns have higher operating pressures; therefore, necessary steps should be taken to provide for them, such as thicker-walled (narrower-bore) transfer lines (if polymer tubing is used, etc.) Shorter columns may work well if a limited number of analytes or interferences are expected. The diameter (3.9-mm) is not necessarily critical and should be governed by user preference and equipment, adjusting flow rates and other parameters as necessary. Diameters from 2.0 to 4.6 mm should be expected to perform similarly, as long as the columns are stable and rugged.
   d. Packing Density: Packing (or ligand) density is a better parameter than carbon loading for comparing columns [21,22]. A column with a ligand density near that of the one used in this method should be expected to perform similarly.
4. Mobile Phase Composition
   a. Modifier: Because of the high percentage of water in the initial mobile phase, a condition referred to as hydrophobic collapse of the C18 phase occurs [23,24], which results in poor reequilibration and irreproducible retention times and peak shapes for early eluting analytes such as oxamyl and methomyl. The addition of a constant amount of an alcohol to both mobile phases A and B has been reported and found to improve column performance under these conditions. The method specifies 2% 1-propanol to be added to both mobile phases A and B. A concentration of 1-propanol between 3% and 4% has been reported as optimum [24, 25]; 2% is a compromise made in order to generate retention (capacity) factors for the earliest eluites, oxamyl and methomyl, of greater than 5,as suggested in the literature [26]. Also, 1-propanol has been reported (and found) to reduce the time required for reequilibration at the end of the run [24]. Other alcohols may be used at higher concentrations (except for reducing reequilibration times) [1]. These are isopropanol (at 3% to 5%) and methanol (at 5% to 10%). If early-eluting analytes are to be determined, or if a column is found that gives sufficiently long retention times for the earliest expected eluite with an initial mobile phase composition as high as 5% to 10% acetonitrile in water, the alcohol could be eliminated (from both phases). Table 4 would not apply if such changes are made.
   b. Mobile Phase B: Pure methanol as mobile phase B results in a steep rise in the baseline UV response, making automatic integrations difficult and UV scanning for confirmation spectra nearly impossible. For this reason acetonitrile has been chosen [28, 29]. Methanol is acceptable if these conditions are tolerable and is recommended as an alternate solvent system on a C18 column for confirmation (Section F3); however, precision and LOD values reported in Table 2 would not be applicable.
   c. Solvent Programming: One of the most serious concerns that may be encountered in trying to make adaptations of this method is an attempt to shorten retention times by using higher concentrations of organic modifier in mobile phase A, higher percentages of mobile phase B in the initial solvent program condition, or faster solvent programming. In any case, these changes will seriously affect the peak shape, sensitivity, and retention time reproducibility of early eluting analytes. There is also a greater possibility of false positives from potential interferences because of poor resolution in the early region of the chromatogram. Retention times for the earliest eluting analyte should be kept at 3 to 6 times the retention time of the

solvent from an unretained analyte, which is equivalent to a capacity factor of 2 to 5 [5]. The retention or capacity factor for any analyte can be calculated as follows:

$$\text{Retention or Capacity factor} = (t_r - t_0)/t_0$$

Where t_r = the retention time of the compound
And t_0 = the retention time of an unretained analyte (the mobile phase holdup time)
The value of keeping anaylytes from eluting too close to the solvent front cannot be overemphasized.

d. Buffer: For the compounds evaluated, formetanate, carbendazim, and benomyl required a buffer in order to obtain good peak shapes. Of several pHs tested, pH 6.8 to 7.1 gave the best results. Buffer concentration should be 0.01 to 0.05M. The concentration and pH of the buffer had a great effect on exact retention time of formetanate.

5. Dwell Volumes: Dwell volumes can affect the retention times and peak shapes of analytes. This is internal volume of the system from the point of mixture of the mobile phases A and B to the head of the column. It includes the volume of the transfer lines; any in-line filters (which should be between the pump and the sample injector if at all, and definitely not after the sample injector); the sample injector; the guard column; and the head of the analytical column. This volume can range from approximately 0.6 to 3.8 mL. At a flow rate of 1 mL/minute, each mL dwell volume represents a minute delay between the time that the pump produces a given change in a mixture of solvent and the time when the analytical column experiences that change. In effect, it is equivalent to a solvent program delay [13,14]. For this method, lower dwell volumes and no program delays gave better peak shapes for the early eluites.
6. Dead Volumes: Dead volumes can cause the method to fail seriously. Important areas to look for are larger bore and longer-than-necessary transfer lines between the sample injector and the analytical column [15]. Another area of potential large dead volumes are poorly designed or connected guard columns and sample injectors.
7. UV Wavelength Selection
   a. The wavelengths specified in this method are a best compromise for all of the analytes listed in Table 1. There are maxima for each of the pesticides that would give greater sensitivity and/or signal-to-noise ratio. If only a selected few of the pesticides in Table 1 are to be determined, other wavelengths may be considered. For example, if only ureas are to be determined, the selection of an absorbance band of 240 to 250 nm would give greater sensitivity for these compounds and less interference from others.
   b. Spectra are also provided in the Backup Data Report [1] for many analytes and potential interferences. These were obtained under actual operating conditions. Because of unavoidable errors in background subtractions, the profiles of these spectra are subject to errors at the low wavelength ends of the spectra (190 nm to 210 nm). This could be attributed to the absorbance from the alcohol modifier to the mobile phases, which, in spite of efforts to add an equal amount to both phases, produces a slight baseline rise near the end of the chromatograms.
   c. Many of the O-aryl carbamates and the sulfenimides absorb well only in the low UV range (<215 nm). This is generally an area of great background noise. Many contaminants (plasticizers and solvents) also absorb in this range better than at higher wavelengths. Selecting a longer wavelength that is not at the absorption maximum may give a better signal-to-noise ratio and thus actually increase sensitivity. This should be determined by experimentation for selected analytes.
   d. Bandwidth: A bandwidth of 15 nm was used for evaluation of this method.

C. INTERNAL STANDARDS

1. Calibration Internal Standards: Internal standards are essential for obtaining the precisions listed in Table 2 [1, 16]. Acetanilide was found to be unretained by the media during desorption, and

therefore, could be added to the extraction fluid. It was also found to be relatively stable and not to interfere with the retention times of other analytes. A second compound, acetophenone, may be added as a back-up internal standard. It is also unretained by all media except XAD-2, on which it has about a 95% recovery. It may be used whenever the acetanilide is interfered with by coeluting analytes or contaminants. It alsoserves to indicate, by monitoring relative response between the two internal standards, when the first internal standard has a coeluting interference.

2. Alternate Calibration Internal Standards: It may be wise, especially under isocratic conditions, to select other internal standards having capacity factors closer to particular analytes of interest. There is a wide range of alkyl phenones available for late-eluting analytes, and 4-hydroxy-acetanilide (acetaminophen) for earlier eluting analytes. Their retention times are listed in Table 4. Since these longer alkyl chain phenones have increasingly lower recoveries from the XAD-2 resin, they should not be added to the extraction solutions until after the resin is removed.
3. Retention Index Reference Standards: These are optional standards and are used to establish relative retention times for qualitative purposes. These are highlighted in Table 4 and include a homologous series of alkyl phenones and acetanilides. Establishing retention times between two nearest-eluting reference standards gives a more consistent retention value than retention time alone or relative retention time using a single internal standard alone. This value, the Retention Index, varies according to column and analytical conditions, but should be relatively consistent for any one set of conditions and more reliable as a qualitative tool over a long period of time. This value is calculated as follow:

RI(A) = Retention Index of Analyte "A"

$$\frac{Tr_{(A)} - Tr_{(RS-P)}}{Tr_{(RS-F)} - Tr_{(RS-P)}} + N_{(RS-P)}$$

Where: $Tr_{(A)}$ = retention time of analyte A
$Tr_{(RS-P)}$ = retention time of preceding reference standard
$Tr_{(RS-F)}$ = retention time of following reference standard
$N_{(RS-P)}$ = a number assigned to preceding reference standard, with zero assigned to the first peak in the series.
(Numerical assignments for the acetanilide and phenone series are suggested in Table 4.

In order to avoid confusion in the chromatograms, the retention index reference standards are analyzed periodically as external standards and not added to the analytical samples themselves. The use of these reference standards is optional but is suggested where application of this method is expected to encounter consistently a broad range of unknown analytes and to augment other confirmatory techniques.

D. INTERFERENCES:

The UV detector responds to many compounds. Retention times of some common potential interferences are provided in Table 4. Interfering compounds that may be encountered are discussed below.

1. DF Impurities in Mobile Phases and Additives: Only HPLC-grade solvents should be used. Triethylamine (TEA) was found to develop unidentified impurities over time which contributed to significant irregularities in the baseline. This degradation was reduced or eliminated by storing the TEA under nitrogen in a small desiccator at 0 to 4 °C [8].
2. Organic Solvents or Fuels
   a. Chloroform showed a response that nearly coelutes with carbaryl (Table 4). Benomyl and captan, therefore, are made up in methylene chloride, which is more UV transparent than chloroform.
   b. Toluene (Table 4).

c. Blends of solvents having ketones, ester, or any of the above compounds, such as lacquer solvents, gasoline, paint stripper, and cleaning solvents, are to be avoided or documented during sample collection and handling.

3. Industrial Chemicals (Plastic and Rubber Additives)
   a. Several plasticizers might elute in the window of interest depending upon the selection of column and conditions. These include diethyl and dibutyl phthalates. Dibutyl phthalate is typically found in polyvinyl gloves, flexible tubing, and in coatings on bottles and tool handles. Contact with these materials should be avoided or documented. Other plasticizers, such as dioctyl phthalate and bis-ethylhexyl adipate, have late elution times and will elute after about 30 minutes under the conditions specified. However, if the run times are shortened, these may be carried over on-column to subsequent analyses, causing interferences.
   b. Common antioxidants such as BHT (2,6-di-tert-butyl-4-methyl phenol) also elute late and may be carried over on-column, creating interferences in subsequent analyses.
4. Other Pesticides: Spray mixtures very often contain a mixture of pesticides. It is not uncommon to find chlorpyrifos, an organophosphate, or a pyrethroid pesticide in combination with propoxur, for example. Both of these noncarbamate pesticides can be detected under the conditions of the method. The retention time and spectra of chlorpyrifos is included for qualitative purposes. Most pyrethroids elute later than most of the carbamates; if present, they may elute in a subsequent run if run times are too short. It is also not uncommon to mix herbicides of different classes such as diuron with bromacil, atrazine, or 2,4-D. Because of this possibility, retention times and spectra of other common herbicides are also provided in Table 4 for qualitative purposes.
5. Miscellaneous Chemicals: There are a number of chemicals which elute in the retention time window of interest for carbamates and urea pesticides and may, with particular columns or conditions, interfere with analytes of interest. The presence or the known use of these compounds or their sources should be documented as part of the sample history. Table 4 lists a few of the compounds, which include the following.
   a. The common insect repellent, DEET (N,N-diethyl-meta-toluamide). Since DEET may be heavily used by outdoor workers, its presence on exposed areas of the skin or clothing may contribute to sampler contamination either through direct contact with the face of the sampler or through collection of vapors if the sampler is in close proximity to areas of application or is exposed to overspray during application from a spray can or bottle.
   b. Inadvertent collection of tobacco side-stream smoke may introduce potentially interfering compounds, one of which is nicotine.
   c. Compounds in beverages used during work periods, which include at least caffeine.

E. SAMPLER

1. The OVS-2 Sampler. The OVS-2 (OSHA Versatile Sampler with XAD-2) combines both filter and XAD-2 sorbent in one unit. The filter is necessary to trap submicron aerosols that would pass through the XAD-2 bed. Substitutions should not be made.
2. Quartz Fiber and Glass Fiber Filters (GFF). The OVS-2 tubes are available with either glass or quartz fiber filters. OSHA Methods specify GFF. This method specifies a quartz fiber filter. For analytes being desorbed with acetonitrile, no difference in desorption efficiency was observed between glass fiber and quartz fiber filters. Therefore, the tubes may be interchanged for the analytes specified in this method.
3. Flow Rates. The OVS-2 sampler is designed for a flow rate of 1 L/min. At slower flow rates, 0.1 to 0.2 L/min, there may not be enough capture velocity for aerosols.
4. Applying Liquid Spikes. The Teflon® retainer ring should be removed when spiking the face of the OVS-2 tubes with more than approximately 10 µL, in order to prevent wicking of the carrier solvent behind the ring and consequent loss of standard. Volumes of spiking fluid greater than 15 to 30 µL will flood the XAD-2 section and possibly wick into the back-up section. Whenever more than 15 to 30 µL is to be applied to the tubes, air must be drawn through the tubes at approximately 1

L/min during the spiking procedure and the solvent added in 15- to 30-µL increments with a few minutes between each addition allowed for drying of the solvent. SD

F. CONFIRMATION

1. By Relative Retention Times (Retention Index).The Retention Index (RI) may vary considerably from column to column and from one set of conditions to another. But it will be reasonably consistent once a set of conditions has been chosen and will be much more reliable for day-to-day comparisons than will absolute retention times. Actual RIs need to be established for each set of conditions. Compounds that are ionic under elution conditions or that interact strongly with polar sites on the column will have the most variable retention times and retention indices.
2. By Second Column. The cyanopropyl stationary phase strongly induces some exchanges in elution orders and alters relative spacings between adjacent analytes in the chromatogram that may be useful in confirmations.
3. By Alternate Solvent. As mentioned earlier (Section B1), methanol as the mobile phase B solvent on a C18 column can be used just as effectively to establish confirmations because methanol interacts differently with the stationary phase than acetonitrile, and so different molecular forces come into play. Significant alterations in retention order are thus obtained; for some analytes this is more dramatic than with a cyanopropyl column.
4. By Ratio of Two UV Absorption Bands. As long as the UV absorption channels are not saturated, there should be a consistent ratio between the background-corrected absorption bands that is characteristic of each analyte and should reflect the ratio of relative heights of the absorption spectra at their respective UV bands in the UV spectra. This ratio is dependent, however, on the bandwidth of the adsorption bands employed, and consistent bandwidths must be used. The consistency of the ratio of absorption across the HPLC peak is also indicative of the purity of the peak. A constantly changing ratio indicates that the peak may have multiple components.
5. By Matching to Reference UV Spectra. Unknown spectra should not be oversaturated in any portion. They need to be background-corrected properly. If the baseline is rising, a background selected from the backside of the peak may induce losses of absorption in the region below 210 nm. Conversely, one selected from in front of the unknown HPLC peak may add to this region of the spectra. It is better to get an averaged background first. Spectra maxima should match within a few nanometers. Relative absorbance at each maxima may vary even after background subtraction, depending upon the concentration of the analytes and the characteristics of different scanning UV detectors.

FORMALDEHYDE ON DUST (TEXTILE OR WOOD) 5700

$H_2C=O$ MW: 30.03 CAS: 50-00-0 RTECS: LP8925000

METHOD: 5700, Issue 2 **EVALUATION:** FULL **Issue 1:** 15 August 1994
Issue 2: 29 February 2016

OSHA: 0.75 ppm; 2 ppm STEL
NIOSH: 0.016 ppm; C 0.1 ppm (15 min); carcinogen

PROPERTIES: gas; BP -19.5 °C; vapor density 1.067 (air = 1); explosive range 7 to 73 % in air

SYNONYMS: methanal; formalin (aqueous 30 to 60% w/v formaldehyde); methylene oxide

SAMPLING

SAMPLER: Institute of Occupational Medicine (IOM) inhalable dust sampler or equivalent containing a 25-mm PVC filter, 5 µm pore size

FLOW RATE: 2.0 L/min

VOL-MIN: 240 L @ 0.002 mg/m^3
-MAX: 1050 L

SHIPMENT: Place cassette with filter in 30-mL screw-cap low density polyethylene (LDPE) bottle; keep upright. Ship cold.

SAMPLE STABILITY: 21 days (matrix dependent) (cold storage advised)

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 0.007 to 0.16 mg/m^3 [1] (1050-L samples)

BIAS: -4%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.093 [1]

ACCURACY: ± 22%

MEASUREMENT

TECHNIQUE: HPLC, UV DETECTION

ANALYTE: 2,4-dinitrophenylhydrazone derivative of formaldehyde

EXTRACTION: 10 mL distilled water @ 37 °C, 4 h; 1 mL to 3 mL 2,4-dinitrophenyl - hydrazine/acetonitrile (1.3 mg/mL DNPH/ACN)

INJECTION VOLUME: 15 µL

MOBILE PHASE: 30% acetonitrile/66% methanol/water (1:1v/v), 1 mL/min

COLUMN: C18, 5-µm particle size, 10-cm x 8-mm ID (with a C18 guard column)

DETECTOR: UV @ 365 nm

CALIBRATION: standard solutions of formaldehyde in 1.3 mg/mL DNPH/ACN

RANGE: 0.4 to 4000 µg/sample [1]

ESTIMATED LOD: 0.8 µg/sample [1]

PRECISION ($\bar{S}_r$): 0.078 @ 7 to 174 µg per sample [1].

APPLICABILITY: The working range is 0.0004 to 3.8 mg/m^3 for a 1050-L air sample. This method has been used for the determination of formaldehyde in both textile dusts and wood dusts [1]. Caution should be exercised in the way that data collected with this method are interpreted. These results should be reported separately from vapor-phase formaldehyde exposure data until sufficient data has been collected to allow appropriate epidemiological interpretation of formaldehyde-containing particulate exposures.

INTERFERENCES: None identified

OTHER METHODS: In the absence of phenol or other substances known to interfere with the chromotropic acid analysis of formaldehyde, the analysis procedure described in NIOSH method 3500 [2] can also be used with this extraction technique (See Appendix). The analysis procedure used in this method has also been used for the determination of formaldehyde in automobile exhaust [3]. An alternate analysis [4] may be used in conjunction with this method to determine the amount of "released" formaldehyde from the collected particulate material. NIOSH method 5700 determines both "released" formaldehyde and formaldehyde equivalents (e.g., small oligomeric pieces of formaldehyde-containing resin) present in the hydrolysis solutions. The use of these two analytical approaches may differentiate between the two forms of formaldehyde present in the sample by the difference in results.

REAGENTS:

1. 2,4-dinitrophenylhydrazine (2,4-DNP) (1.3 g) in 1 L acetonitrile; 1.3 mg/mL solution.
2. Formaldehyde stock solution, 1 mg/mL (see Appendix).
3. Methanol, distilled in glass.
4. Acetonitrile, distilled in glass.
5. Water, deionized and distilled.
6. Perchloric acid solution, 1 N. *

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: 25-mm PVC filter (5.0-µm pore size) in a 25-mm Institute of Occupational Medicine Inhalable (IOM) dust sampler. The sampler should meet the American Conference of Governmental Industrial Hygienists (ACGIH) definition for collection of the inhalable fraction of particulate mass [5].
2. Personal sampling pump, 2.0 L/min, with flexible polyethylene or polytetrafluoroethylene (PTFE) tubing.
3. Bottles, screw-cap, low-density polyethylene (LDPE), 30-mL.
   Note: Do NOT use bottles with 'polycone' liners (source of high formaldehyde blank).
4. Liquid chromatograph with a UV detector, recorder, integrator and column (page 5700-1).
5. Tweezers.
6. Syringes, 10-, 25-, 50-, and 100-µL.
7. Volumetric flasks, 10-, 100-mL and 1 L.
8. Pipets, 0.1-, 0.5-, 1.0-, and 3-mL glass, delivery, with pipet bulb.
9. Graduated cylinders, glass, 25-mL.
10. Cotton gloves.
11. Equipment for standardizing formaldehyde stock solution, Burets, 50-mL.
12. pH meter.
13. Magnetic stirrer.
14. Beaker, 50-mL.
15. Vials, 5-mL.
16. Filters, 0.45 µm.
17. Scintillation vials, 20-mL.

SPECIAL PRECAUTIONS: Perchloric acid is a strong oxidizing agent, toxic by ingestion and inhalation and is a strong irritant. Use only in a well-ventilated fume hood. Formaldehyde is a suspect carcinogen [1,6] and should be handled in a hood.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. If gravimetric measurements are needed, handle the IOM cassettes only while wearing cotton gloves. Follow NIOSH method 0500 [7] for pre- and post-collection weighing procedure. Place the cassette containing a 25-mm PVC 5-µm pore filter in the filter holder.
3. Attach outlet of filter holder to the sampling pump.
4. Sample 240 to 1050 L of air at 2.0 L/min flow rate.
5. Transfer cassette from filter holder carefully to a 30-mL LDPE screw-cap bottle while wearing cotton gloves and seal the bottle. Ship in a suitable container in order to prevent damage during transit and keep bottles upright.

6. Collect a bulk sample (ca. 1 g) of the dust/fiber in a glass vial and ship separately.

SAMPLE PREPARATION:

7. If gravimetric weighing is done, post-weigh the entire cassette (see NIOSH method 0500 [7]) then return the cassette to the screw-cap bottle.
8. Transfer 8-mL distilled water to the LDPE screw-cap bottle containing the cassette. Use tweezers (two) to disassemble cassette which is immersed in water, remove all cassette pieces (shake off excess water) leaving the filter and dust in the bottle. Transfer the resulting solution to a 20-mL scintillation vial and rinse the screw-cap bottle with an additional 2 mL of distilled water. Replace the cap on the vial and then place the vial in a 37 °C water bath for four hours. Remove from the bath and allow to cool 1/2 hour. Filter through a 0.45 µm pore size filter into another bottle.

CALIBRATION AND QUALITY CONTROL:

9. Prepare a calibration stock solution by dilution of 1-mL of 1 mg/mL formaldehyde stock solution to 100 mL with distilled water.
10. Pipet aliquots of calibration stock solution (e.g., 40, 200, 750, 2000, 5000, and 10000 µL) into 10-mL volumetric flasks to prepare working standards. Higher level standards, if needed, can be prepared by using different dilutions of the formaldehyde stock solution.
11. Add distilled water to bring the volume of each working standard to 10 mL.
12. Analyze working standards together with samples and blanks (steps 14 through 17).
13. Prepare calibration graph of area vs. amount (µg) of formaldehyde per sample (10-mL total volume).

MEASUREMENT:

14. Transfer a 1-mL aliquot of the solution from step 8 (or step 11) to a 5-mL vial containing 3-mL of an 2,4-dinitrophenylhydrazine/acetonitrile solution (1.3 mg/mL). Add one drop 1 N perchloric acid (to catalyze the reaction to form the corresponding hydrazone), cap the vial and shake it gently for several seconds.
15. Set liquid chromatograph to conditions given on page 5700-1.
16. Inject 15-µL sample aliquot.
17. Measure peak area.

    NOTE 1: If peak area is greater than the highest standard, take a smaller aliquot of the remaining unreacted sample solution, dilute to 1 mL with distilled water and analyze (steps 14 through 17) and apply appropriate dilution factor in the calculations.
    NOTE 2: For optimum results, all samples containing over 400 µg/mL should be diluted and reanalyzed, since the maximum amount of formaldehyde that can react with 3.9 mg of 2,4-dinitrophenylhydrazine is 590 µg.

CALCULATIONS:

18. Determine mass, µg, of formaldehyde (W) found in the sample and the average media blank (B) from the calibration graph. Use the appropriate aliquot factor (e. g., 1 mL aliquot/original volume from step 14) and the total sample volume (10-mL) unless corrected for in calibration plot (step 13).
    NOTE: Include dilution factor for any sample which exceeded the highest calibration standard.
19. Calculate concentration, C, of formaldehyde from dust in the air volume, V (L).

$$C = \frac{W - B}{V}, mg/m^3$$

EVALUATION OF METHOD:

This method was evaluated over the range of 7 to 174 µg/sample at 24 °C and pressure of 761 mm Hg [1] using the chromotropic analysis procedure. Overall measurement precision, $\hat{S}_{rT}$, was 0.093 including a 5% pump error factor. Similar precision was observed with the 2,4-dinitrophenylhydrazine analysis procedure. Sample stability during storage was evaluated at 7 µg formaldehyde/2 mg of wood dust treated with a urea/formaldehyde resin. Samples showed 101% recovery after 21 days of storage at ambient conditions compared to one-day old samples. However, studies with a different matrix (urea- formaldehyde treated wood fibers) indicated that samples may be unstable when stored at room temperature.

Comparison of results from 2,4-DNP analyses with those from acetylacetone analyses [4] indicated that there was a significant difference between the two methods. The acetylacetone analyses used much milder conditions and appears to be reacting only with released formaldehyde, whereas the 2,4-DNP analysis required the addition of perchloric acid and may be breaking up oligomeric pieces of the partially hydrolyzed resin in the sample. By analyzing samples with the two methods, a further characterization of the sample matrix and potential exposure may be obtained. In matrices where materials that can form complexes with formaldehyde are present, such as sulfites, the acetylacetone analysis may be biased low, since it is unable to break up these complexes [8].

Two comparisons of the IOM samplers with closed-face cassette samplers were conducted in field situations [1]. The IOM samplers, on average, collected more dust/fibers measured gravimetrically than the closed-face cassette samplers in both studies. Formaldehyde levels in the dust/fibers on a µg/mg basis measured with the extraction procedure used in this method were comparable for both the IOM and closed-face cassette samplers. On the average, the IOM sampler tended to collect more dust than the closed-face cassette sampler.

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METHOD WRITTEN BY:

Y.T. Gagnon and E.R. Kennedy, NIOSH

APPENDIX: Preparation and Standardization of Formaldehyde Stock Solution (ca. 1 mg/mL)

Dilute 2.7 mL 37% aqueous formalin solution to 1 L with distilled, deionized water. This solution is stable for at least three months. Standardize by placing 5.0 mL of freshly prepared 1.13 M sodium sulfite solution in a 50-mL beaker and stir magnetically. Adjust pH to between 8.5 and 10 with base or acid. Record the pH. Add 10.0 mL formaldehyde stock solution. The pH should now be greater than 11. Titrate the solution back to its original pH with 0.02 N sulfuric acid (1 mL acid = 0.600 mg formaldehyde; about 17 mL acid needed). If the endpoint pH is overrun, back-titrate to the endpoint with 0.01 N sodium hydroxide. Calculate the concentration, Cs (mg/mL), of the formaldehyde stock solution:

$$C_s = \frac{30.0(N_a V_a - N_b V_b)}{V_s}$$

where: 30.0 = 30.0 g/equivalent of formaldehyde
Na = normality of sulfuric acid (0.02 N)
Va = volume of sulfuric acid (mL) used for titration
Nb = normality of NaOH (0.01 N)
Vb = volume of NaOH (mL) used for back-titration
Vs = volume of formaldehyde stock solution (10.0 mL)

Alternate Analysis Procedure for the Determination of Formaldehyde Liberated from Dust/Fiber Samples

NOTE: This analysis procedure should only be used where interferences to the chromotropic acid analysis are not present. These interferences include phenol, oxidizable organic material, other aldehydes and alcohols.

For formaldehyde determination by the chromotropic acid method, a 4-mL aliquot of the solution resulting from the desorption and incubation of the filter (step 8.) was analyzed by the procedure described in NIOSH Method 3500 [2]. The amount of chromotropic acid added to the sample could react with a maximum of 42 µg of formaldehyde per sample aliquot. (Whenever the amount of formaldehyde approached 30 µg per aliquot, the sample was diluted and reanalyzed.) The absorbance of samples at 580 nm was then compared to a calibration curve constructed from results obtained from analysis of calibration standards containing known amounts of formaldehyde. The amount of formaldehyde present in each sample was determined based on the calibration curve.

Calibration standards were prepared by dilution of a standard solution of formalin in distilled water (1 mg/mL) and analyzed in the same manner as the samples. The calibration range usually covered 1 to 25 µg of formaldehyde/4-mL aliquot. A limit of detection of 0.44 µg formaldehyde/filter sampler was determined in laboratory evaluation of this analysis procedure.

ARSINE 6001

AsH_3 MW: 77.95 CAS: 7784-42-1 RTECS: CG6475000

METHOD: 6001, Issue 3 **EVALUATION: FULL** **Issue 1: 15 May 1985**
Issue 3: 20 October 2015

OSHA: 0.05 ppm (0.2 mg/m³)
NIOSH: C 0.002 mg/m³ (15 min); carcinogen

PROPERTIES: Gas; d 3.484 g/L @ 20 °C; BP –62.5 °C; MP –116.3 °C

SYNONYMS: Hydrogen arsenide; arsenic trihydride

SAMPLING

SAMPLER: SOLID SORBENT TUBE (coconut shell charcoal, 100 mg/50 mg)

FLOW RATE: 0.01 L/min to 0.2 L/min

VOL-MIN: 0.1 L @ 0.05 ppm
-MAX: 10 L

SHIPMENT: Routine

SAMPLE STABILITY: At least 6 d @ 25 °C [1]

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 0.09 mg/m³ to 0.4 mg/m³ [1] (10 L samples); 0.001 mg/m³ to 0.01 mg/m³ [2]

BIAS: –6.13% at 0.01 L/min to 0.2 L/min flow rates [1]; –11% @ 0.876 L/min [2]

OVERALL PRECISION ($\hat{S}_{rt}$): 0.087 [2]

ACCURACY: ±23.2%

MEASUREMENT

TECHNIQUE: ATOMIC ABSORPTION, GRAPHITE FURNACE

ANALYTE: Arsenic

DESORPTION: 1 mL 0.01 mol/L nitric acid; 30 min in ultrasonic bath

MATRIX MODIFIER: Nickel, 1000 µg/mL

WAVELENGTH: 193.7 nm; deuterium or hydrogen correction

GRAPHITE FURNACE: DRY: 40 s @ 110 °C; CHAR: 15 s @ 1200 °C; ATOMIZE: 7 s @ 2540 °C

INJECTION: 50 µL

CALIBRATION: Arsenic in 0.01 mol/L nitric acid with 100 mg charcoal present

RANGE: 0.01 µg to 0.3 µg per sample [2]

ESTIMATED LOD: 0.004 µg per sample

PRECISION ($\bar{S}_r$): 0.060 @ 0.012 µg to 0.11 µg per sample [2]

APPLICABILITY: The working range is 0.0003 ppm to 0.06 ppm (0.001 mg/m³ to 0.2 mg/m³) for a 10 L air sample. This is an elemental analysis and is not compound-specific.

INTERFERENCES: Use background correction to control molecular absorption. Other arsenic compounds (gases or aerosols) may be collected on the sampler and would be erroneously reported as arsine. A cellulose ester filter in front of the charcoal tube may be used to remove aerosols [3,4]. The effect of relative humidity on the capacity of charcoal for arsine has not been studied.

OTHER METHODS: This method combines and replaces NIOSH methods P&CAM 265 [5] and S229 [6] for arsine.

REAGENTS:

1. Water, distilled or deionized.
2. Nitric acid, concentrated.*
3. Nitric acid, 0.01 mol/L. Dilute 0.4 mL concentrated nitric acid to 1 L with water.
4. Nitric acid, 0.1 mol/L. Dilute 4 mL concentrated nitric acid to 1 L with water.
5. Arsenic stock solution, 1000 µg/mL arsenic.* Commercial standard or dissolve 1.322 g dried, certified reagent arsenic trioxide in 100 mL of 0.1 mol/L nitric acid; dilute to 1 L with 0.1 mol/L nitric acid.
6. Calibration stock solution, 1.0 µg/mL arsenic.* Dilute 0.1 mL arsenic stock solution (1000 µg/mL arsenic) to 100 mL with 0.01 mol/L nitric acid. Prepare fresh daily.
7. Nickel nitrate solution, 1000 µg/mL nickel. Commercial nickel atomic absorption standard or dissolve 3.112 g dried reagent nickel nitrate in 100 mL of 0.1 mol/L nitric acid; dilute to 1 L with water.
8. Argon, compressed.*
9. Arsine,* 99%, or certified mixture in nitrogen.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: Activated coconut shell charcoal (100 mg/50 mg sections, 20/40 mesh), in a glass tube, 7 cm long, 6 mm OD, 4 mm ID, with flame-sealed ends. A silylated glass wool plug precedes the front section and urethane foam plugs separate the sorbent sections and follow the back section.
   NOTE: Use a cellulose ester membrane filter in front of the sampler if particulate arsenic is present [3,4].
2. Personal sampling pump, 0.01 L/min to 0.2 L/min, with flexible connecting tubing.
3. Graphite furnace atomic absorption spectrophotometer with non-pyrolytic tubes, background correction, and electrodeless discharge (and power supply) or hollow cathode lamp for arsenic.
4. Volumetric flasks, 1 L and 100 mL.†
5. Micropipets, 5 µL to 500 µL.†
6. Centrifuge tubes, 10 mL or 15 mL.†
7. Ultrasonic bath.
8. Centrifuge.
9. Syringe, gas, 0.1 mL, readable to 1 µL.

†Clean all glassware with concentrated nitric acid and rinse thoroughly with distilled or deionized water before use.

SPECIAL PRECAUTIONS: Arsenic is a human carcinogen [7]. Wear gloves, lab coat, and safety glasses while handling acids. Perform all concentrated acid handling in a fume hood. Arsine is extremely poisonous by inhalation. Handle in well-ventilated hood and wear appropriate protective clothing and gloves. Users must be familiar with the proper use of flammable and nonflammable gases, cylinders, and regulators.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Break the ends of the sampler immediately before sampling. Attach sampler to personal sampling pump with flexible tubing.
   NOTE: Use a cellulose ester membrane prefilter if particulate arsenic compounds may be present [3,4].
3. Sample at an accurately known flow rate between 0.01 L/min and 0.2 L/min for a total sample size of 0.1 L to 10 L.
4. Cap the sampler with plastic (not rubber) caps and pack securely for shipment.

SAMPLE PREPARATION:

5. Place the front and back sorbent sections of the sampler tube in separate centrifuge tubes. Discard the glass wool and foam plugs.
6. Add 1.0 mL of 0.01 mol/L nitric acid to each tube. Cap each tube.

7. Agitate for 30 min in an ultrasonic bath.
8. Centrifuge each tube.

CALIBRATION AND QUALITY CONTROL:

9. Calibrate daily with at least six working standards over the range 0.004 µg to 0.3 µg arsenic per sample.
   a. Add known amounts of calibration stock solution and 0.01 mol/L nitric acid for a 1.0 mL final solution volume to centrifuge tubes containing 100 mg activated charcoal from a media blank sampler.
   b. Analyze standards together with samples and blanks (steps 12 and 13). Analyze a working standard for every five samples to check for instrument drift.
   c. Prepare a calibration graph (absorbance vs. µg arsenic).
10. Determine desorption efficiency (DE) at least once for each batch of charcoal used for sampling in the range 0.004 µg to 2 µg arsenic per sample. Prepare three tubes at each of five levels plus three media blanks.
   a. Remove and discard back sorbent section of a media blank sampler.
   b. Inject a known amount of pure arsine gas (or a certified gas mixture containing arsine) directly onto front sorbent section with a microliter syringe.
   c. Cap the tube. Allow to stand overnight.
   d. Desorb (steps 5, 6, 7, and 8) and analyze together with working standards (steps 12 and 13).
   e. Prepare a graph of DE vs. µg arsenic recovered.
11. Analyze three quality control spikes to ensure that the calibration graph is in control.

MEASUREMENT:

12. Set the spectrophotometer and furnace to manufacturer's recommendations and to conditions given on page 6001-1.
13. Inject a 50 µL aliquot of sample or standard followed by a 50 µL aliquot of nickel nitrate solution prior to initiating the analysis program. Measure peak area.
   NOTE 1: If sample absorbance is above the linear range of the standards, dilute with 0.01 mol/L nitric acid, reanalyze and apply the appropriate dilution factor in calculations.
   NOTE 2: Monitor the reproducibility of peak area for a working standard throughout the measurements. If erratic results occur, reoptimize instrumental parameters and replace the graphite tube.

CALCULATIONS:

14. Determine the mass, µg, of arsine found in the sample front (W_f) and back (W_b) sorbent sections, and in the average media blank front (B_f) and back (B_b) sorbent sections by multiplying the mass of arsenic found for each of these sections by 1.040 (MW of arsine/MW of arsenic).
   NOTE: If $W_b > W_f / 10$, report breakthrough and possible sample loss.
15. Calculate concentration, C, of arsine in the air volume sampled, V (L):

$$C = \frac{W_f + W_b - B_f - B_b}{V}, \text{ µg/L or mg/m}^3.$$

EVALUATION OF METHOD:

NIOSH method S229 [6] was evaluated over the range 0.094 mg/m^3 to 0.404 mg/m^3 using 10 L air samples collected on SKC Lot 105 activated coconut charcoal [1]. Breakthrough (onto the backup section) did not occur after 240 min of sampling at 0.227 L/min from an arsine concentration of 0.405

mg/m^3 (0.022 mg loading). The recovery was found to be 93.7%. Desorption efficiency was 0.90 at 1 µg arsine per sample and 1.00 at 2 µg and 4 µg arsine per sample.

NIOSH method P&CAM 265 [5] was evaluated over the range 0.001 mg/m^3 to 0.01 mg/m^3 using 15 L air samples [2]. These samples were collected on SKC Lot 106 activated coconut charcoal at a sampling flow rate of 0.875 L/min for 15 min. At this flow rate, a collection efficiency of 89.1% was found [3]. The effect of high humidity on the sampler capacity was not studied. Desorption efficiency was 0.90 in the range 0.015 µg to 0.2 µg arsine per sample.

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METHOD REVISED BY:

R. D. Hull, Ph.D., NIOSH/DBBS.

PHOSPHINE 6002

PH_3 MW: 34.00 CAS: 7803-51-2 RTECS: SY7525000

METHOD: 6002, Issue 3 **EVALUATION: FULL** **Issue 1: 15 August 1994**
Issue 3: 20 October 2015

OSHA: 0.3 ppm (0.4 mg/m^3)
NIOSH: 0.3 ppm (0.4 mg/m^3); 1 ppm (1 mg/m^3) STEL

PROPERTIES: Gas, BP 87.8 °C; vapor density 1.17 (air = 1); spontaneously flammable in air if diphosphane is present

SYNONYMS: Hydrogen phosphide; phosphorus hydride; phosphorated hydrogen; phosphorus trihydride

SAMPLING

SAMPLER: SORBENT TUBE
(mercuric cyanide-coated silica gel, 300 mg/150 mg)

FLOW RATE: 0.01 L/min to 0.2 L/min

VOL-MIN: 1 L @ 0.3 ppm
-MAX: 16 L

SHIPMENT: Routine

SAMPLE STABILITY: 7 d @ 25 °C

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 0.195 mg/m^3 to 0.877 mg/m^3 [1] (16 L samples)

BIAS: 0.4%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.091 @ 2.64 µg to 17.41 µg per sample [2]

ACCURACY: ±17.6%

MEASUREMENT

TECHNIQUE: UV-VIS SPECTROMETER

ANALYTE: Phosphate

EXTRACTION: 10 mL hot (65 °C to 70 °C) acidic permanganate reagent solution

DETECTOR: UV @ 625 nm

CALIBRATION: Standard solutions of potassium dihydrogen phosphate (1.00 mL contains phosphorus equivalent to 49.94 µg of phosphine)

RANGE: 0.3 µg to 10 µg per sample [2]

ESTIMATED LOD: 0.1 µg per sample [1]

PRECISION ($\bar{S}_r$): 0.074 @ 2.6 µg to 17.4 µg per sample [2]

APPLICABILITY: The working range is 0.013 ppm to 0.6 ppm (0.02 mg/m^3 to 0.9 mg/m^3) for a 16 L air sample.

INTERFERENCES: The colorimetric determination of phosphate is subject to interference by any species that also forms a molybdate complex under these conditions; possible interfering species include phosphorus trichloride and phosphorus pentachloride vapors and organic phosphorus compounds.

OTHER METHODS: This revises NIOSH method S332 [2]. OSHA method 1003, "Phosphine" [3], employing a mercuric chloride-treated polyester filter used to capture phosphine and ICP-AES to analyze for the total phosphorus, may be used as an alternative method.

REAGENTS:

1. Potassium dihydrogen phosphate, anhydrous, ACS reagent grade.
2. Sulfuric acid,* concentrated, ACS reagent grade.
3. Ammonium molybdate tetrahydrate.
4. Ferrous ammonium sulfate, anhydrous.
5. Potassium permanganate.*
6. Stannous chloride.
7. Glycerol.
8. Toluene.*
9. Isobutanol.*
10. Methanol.*
11. Water, deionized or distilled.
12. Mercuric cyanide.*
13. Standard phosphate solution. Dissolve 200 mg anhydrous potassium dihydrogen phosphate in distilled water and dilute to 1 L (1.00 mL contains phosphorus equivalent to 49.94 µg of phosphine).
14. Molybdate solution. Dissolve 49.4 g of ammonium molybdate tetrahydrate and 112 mL concentrated sulfuric acid in distilled water and dilute to 1 L.
15. Alcoholic sulfuric acid solution. Add 50 mL of concentrated sulfuric acid to 950 mL methanol.
16. Toluene-isobutanol solvent. Mix equal volumes of toluene and isobutanol.
17. Ferrous solution. Dissolve 7.9 g anhydrous ferrous ammonium sulfate and 1 mL concentrated sulfuric acid in distilled water and dilute to 100 mL.
18. Stannous chloride solution. Dissolve 0.4 g stannous chloride in 50 mL glycerol (heat to dissolve).
19. Acidic permanganate solution. Dissolve 0.316 g potassium permanganate and 6 mL concentrated sulfuric acid in distilled water and dilute to 1 L.
20. Mercuric cyanide solution.* Dissolve 2 g mercuric cyanide in 100 mL water.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: Sorbent tube, silica gel (mercuric cyanide), 300 mg/150 mg sorbent, 40/60 mesh; or, glass tube 12 cm long, 6 mm O.D., 4 mm I.D., flame-sealed ends with plastic caps, with two sections of mercuric cyanide-treated silica gel (45/60 mesh), (front = 300 mg, back = 150 mg), separated and retained by silylated glass wool plugs. (See APPENDIX.)
2. Personal sampling pump, 0.01 L/min to 0.2 L/min, with flexible polyethylene or PTFE tubing.
3. Spectrometer capable of measuring absorbance or transmittance at 625 nm.
4. Two matched 5 cm absorbance cells, silica, with tight fitting caps.
5. Separatory funnel, 125 mL.
6. Beakers, 50 mL.
7. Pipets, 0.2 mL, 10 mL, and 25 mL, and other convenient sizes to make standard dilutions.
8. Volumetric flasks, 10 mL, 25 mL, 100 mL, and 1000 mL.
9. Water bath (maintained at 65 °C to 70 °C).
10. Graduated cylinders, glass, 10 mL.
11. Syringes, 0.5 mL and 1.0 mL.
12. Balance.
13. Thermometer.
14. Stopwatch.
15. Barometer.

SPECIAL PRECAUTIONS: Caution should be exercised when preparing the sampling media because mercuric cyanide is toxic by inhalation, ingestion, and skin contact. Contact of mercuric cyanide with acid will produce hydrogen cyanide gas. Concentrated sulfuric acid is highly corrosive. All work with these compounds should be performed in a hood. Use proper protective clothing including gloves, safety glasses, and laboratory coat. Potassium permanganate is a strong oxidizer with risk of fire and explosion upon contact with combustible substances and reducing agents. Toluene, isobutanol, and methanol are flammable.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Immediately before sampling, break the ends of the silica gel tubes to provide an opening of at least one half the internal diameter of the tube. Attach the silica gel tube to the sampling pump with flexible tubing.
3. Sample at an accurately known flow rate between 0.01 L/min and 0.2 L/min for a total sample size of 1 L to 16 L.
4. Seal tubes with plastic (not rubber) caps.

SAMPLE PREPARATION:

5. Place front and back sorbent sections in separate 50 mL beakers.
6. Add 10 mL of acidic permanganate solution to each beaker. Place in a water bath maintained at 65 °C to 70 °C for 90 min.
7. Decant the acidic permanganate solution into a 10 mL volumetric flask, and dilute to volume with distilled water.
8. Wash the silica gel twice with 3 mL portions of distilled water and decant the contents into another 10 mL volumetric flask containing 1 mL of ferrous solution. Dilute to volume with distilled water.
9. Add the contents of both 10 mL volumetric flasks (extract and washings) to a 125 mL separatory funnel.
10. Add 7.5 mL of molybdate reagent and 25 mL of toluene-isobutanol solvent to the funnel. Shake funnel for 60 s. Let the separatory funnel stand for 60 s to allow the aqueous and nonaqueous layers to separate. Discard the lower (aqueous) layer.
11. Pipet 10 mL of the nonaqueous layer into a 25 mL volumetric flask containing 10 mL of the alcoholic sulfuric acid solution.

CALIBRATION AND QUALITY CONTROL:

12. Calibrate daily with at least six working standards.
    a. Add 10 mL of acidic permanganate solution and 1 mL of ferrous reagent to a 125 mL separatory funnel.
    b. Add 2 µL to 400 µL of the standard phosphate solution to cover the range 0.1 µg to 10 µg of phosphine. Add 8 mL to 9 mL of water to make the total volume of the solution (permanganate solution, ferrous solution, phosphate solution and water) equal to 20 mL. Prepare at least six calibration standards and a blank containing no phosphate.
    c. Add 7.5 mL of molybdate reagent and 25 mL of toluene-isobutanol solvent to the funnel. Shake funnel for 60 s. Let the separatory funnel stand for 60 s to allow the aqueous and nonaqueous layers to separate. Discard the lower (aqueous) layer. (step 10)
    d. Pipet 10 mL of the nonaqueous layer into a 25 mL volumetric flask containing 10 mL of the alcoholic sulfuric acid solution. (step 11)
    e. Analyze with samples and blanks (steps 15, 16, 17, and 18).
    f. Prepare a calibration graph (absorbance versus µg of phosphine added).
13. Determine desorption efficiency (DE) at least once for each lot of sorbent used for sampling in the range of interest. Prepare three tubes at each of five levels plus three media blanks.
    a. Remove and discard back sorbent section of a media blank sampler.
    b. Inject a known amount (20 µL to 400 µL) of standard phosphate solution directly onto front sorbent section with a microliter syringe.
    c. Cap the tube. Allow to stand overnight.
    d. Desorb (steps 6, 7, and 8) and analyze with working standards (steps 15, 16, 17, and 18).
    e. Prepare a graph of DE vs. µg recovered.

14. Analyze three quality control blind spikes and three analyst spikes to ensure that the calibration graph and DE graph are in control.

MEASUREMENTS

15. Turn on the spectrophotometer and allow sufficient time for warmup. Adjust the wavelength to 625 nm and set the zero and 100% transmittance scale using 5 cm cells filled with distilled water. Check these settings prior to making any measurement to check on instrument drift.
    NOTE: Steps 16, 17, and 18 must be performed within 1 min.
16. Add 0.5 mL (25 drops) of stannous chloride reagent and dilute to volume using alcoholic sulfuric acid solution. Mix thoroughly.
17. Transfer the sample into a 5 cm cell and stopper immediately.
18. Measure the absorbance or transmittance using water as a blank.

CALCULATIONS:

19. Determine mass, µg (corrected for DE), of phosphine found in the sample front (W_f) and back (W_b) sorbent sections, and in the average media blank front (B_f) and back (B_b) sorbent sections.
    NOTE: If $W_b > W_f / 10$, report breakthrough and possible sample loss.
20. Calculate concentration, C, of phosphine in the air volume sampled, V (L).

$$C = \frac{W_f + W_b - B_f - B_b}{V}, \text{ µg/L or mg/m}^3.$$

EVALUATION OF METHOD:

This method was validated over the range 0.195 mg/m^3 to 0.877 mg/m^3 at 19 °C and 102.0 kPa (765.3 mmHg) using 16 L samples [1]. Desorption efficiency must be determined over the range used. The upper range of the method depends on the adsorptive capacity of the mercuric cyanide-treated gel. This capacity may vary with the concentration of phosphine and other substances in the air. When an atmosphere at 90% relative humidity containing 0.957 mg/m^3 of phosphine was sampled at a flow rate of 0.2 L/min, breakthrough was determined to occur at a sample volume of 20.75 liter (capacity = 19.86 µg phosphine).

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METHOD REVISED BY:

Charles Lorberau, NIOSH/DPSE.

APPENDIX: PREPARATION OF SAMPLING MEDIA

Coating of Silica Gel

1. Dry 100 g of silica gel (45/60 mesh) at 90 °C for 2 h.
2. Prepare a mercuric cyanide solution in distilled water (2 g mercuric cyanide in 100 mL water).
3. Add the dried silica gel to the mercuric cyanide solution and let set for 15 min with occasional stirring.
4. Drain the excess mercuric cyanide solution and dry the remaining silica gel at 90 °C for 3 h.
5. Cool the silica gel to room temperature in a covered beaker.
6. Expose the silica gel to a humid atmosphere (>80% RH) for 24 h.

Preparing the Sampling Tubes

7. Place a plug of silylated glass wool at the end of a glass tube (6 mm OD and 4 mm ID) about 12 cm long. Pour 300 mg of the treated silica gel into the tube. Place another plug of silylated glass wool behind this front section. Add another 150 mg of the treated silica gel into the tube. Place a final plug of silylated glass wool behind this backup section.
8. Check the pressure drop of a representative sampler. The pressure drop across the tube must be less than 6.7 kPa (50 mmHg) at a flow rate of 0.2 L/min.
9. Flame seal both ends of the sampling tubes.

SULFURYL FLUORIDE 6012

SO_2F_2 MW: 102.06 CAS: 2699-79-8 RTECS: WT5075000

METHOD: 6012, Issue 2 **EVALUATION: FULL** **Issue 1: 15 August 1994**
Issue 2: 12 January 2016

OSHA: 5 ppm
NIOSH: 5 ppm; STEL 10 ppm
(1 ppm = 4.17 mg/m^3 @ NTP)

PROPERTIES: Gas; BP −55 °C; vapor density (air = 1) 3.5; VP 1.7 × 10^3 kPa; nonflammable, colorless, odorless [1]

SYNONYMS: Sulfonyl difluoride, sulfur difluoride dioxide, sulfuric oxyfluoride

SAMPLING

SAMPLER: SOLID SORBENT TUBE
(coconut shell charcoal, 800 mg/200 mg)

FLOW RATE: 0.05 L/min to 0.1 L/min

VOL-MIN: 1.3 L @ 5 ppm
-MAX: 10 L

SHIPMENT: Ship at 0 °C

SAMPLE STABILITY: At least 12 d @ 0 °C

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 20 mg/m^3 to 420 mg/m^3 (0.2 L to 6 L samples)

BIAS: −3.0%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.070 [2]

ACCURACY: ±16.7%

MEASUREMENT

TECHNIQUE: ION CHROMATOGRAPHY
CONDUCTIVITY DETECTION

ANALYTE: Fluoride ion

EXTRACTION: 20 mL 40 mmol/L sodium hydroxide; sonicate 60 min

INJECTION: 50 µL

ELUENT: 40 mmol/L sodium hydroxide, 1.0 mL/min

COLUMN: US Pharmacopeia (USP) L12 separator column, manufacturer's compatible anion guard column, and micromembrane suppressor as recommended by the manufacturer. See OTHER METHODS.

DETECTOR: Conductivity, 30 µS full scale

CALIBRATION: Standard solutions of fluoride ion spiked onto sample media

RANGE: 10 µg to 80 µg fluoride per sample [3]

ESTIMATED LOD: 7 µg sulfuryl fluoride per sample [3]

PRECISION ($\bar{S}_r$): 0.052 (27 µg to 420 µg sulfuryl fluoride per sample) [2]

APPLICABILITY: The working range is 2.2 ppm to 17 ppm (9 mg/m^3 to 75 mg/m^3) for a 3 L air sample. This method is applicable to STEL measurements using a 1.5 L sample. The method has been used to sample for sulfuryl fluoride at dwelling fumigation sites [3,4].

INTERFERENCES: Other fluoride compounds may interfere.

OTHER METHODS: This method is based on the method of Bouyoucos, et al. [5]. NIOSH method S245 uses gas bag samples, gas chromatography-flame photometric detector (GC-FPD) [6].

REAGENTS:

1. Sodium hydroxide,* ACS reagent grade.
2. Sulfuric acid,* concentrated, ACS reagent grade.
3. Water, high-purity.
4. Desorbing/extracting solution and eluent: 40 mmol/L sodium hydroxide. Dissolve 3.2 g sodium hydroxide in 2 L of degassed high-purity water.
5. Suppressor regenerant, 12.5 mmol/L sulfuric acid. Add 0.70 mL concentrated sulfuric acid to 1 L of high-purity water.
6. Calibration stock solution, 1 mg/mL fluoride anion. Dissolve 0.2210 g sodium fluoride in high-purity water and dilute to the mark in a 100 mL volumetric flask.
7. Sulfuryl fluoride* calibration gas standard(s) (optional).

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: Activated coconut shell charcoal sampling tube; glass tube, 11 cm long, 10 mm OD, 7 mm ID, flame-sealed ends, containing two sections of activated (600 °C) coconut shell charcoal (front = 800 mg, back = 200 mg), separated by a 2 mm urethane foam plug. A silylated glass wool plug precedes the front section and a 3 mm urethane foam plug follows the back section. Pressure drop across the tube at 1 L/min airflow must be less than 3.4 kPa.
2. Personal sampling pump, 0.05 L/min to 0.10 L/min, with flexible polyethylene or PTFE tubing.
3. Refrigerant, water solution, sealed, refreezable, reusable.
4. Filter, membrane, 0.45 µm pore size, 13 mm, with Luer fitting.
5. Ion chromatograph, with a conductivity detector, chart recorder, integrator, and columns (page 6012-1).
6. Vials, glass, 20 mL, with plastic caps.
7. Vials, polyethylene, 20 mL, with plastic caps.
8. Micropipettes, with disposable plastic tips.
9. Volumetric flasks, 100 mL.
10. Pipet, 10 mL, graduated in 0.1 mL intervals.
11. Pipet, volumetric, 20 mL.
12. Syringes, 10 mL, plastic, with Luer tip.
13. Sonicator.
14. Analytical balance, to ±0.0001 g.

SPECIAL PRECAUTIONS: Sulfuryl fluoride is a restricted use pesticide owing to its inhalation toxicity. It is extremely hazardous as vapor or liquid. Inhalation of vapors may be fatal. Read and follow all label precautions [7]. Sulfuric acid and sodium hydroxide are corrosive to skin, eyes, and mucous membranes. Use proper protective clothing including gloves, safety glasses, and laboratory coat. Handle all hazardous chemicals in a fume hood.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Break the ends of the sampler immediately before sampling. Attach a sampler to personal sampling pump with flexible tubing.
3. Sample at an accurately known flow rate between 0.05 L/min and 0.1 L/min for a total sample volume of 1.3 L to 10 L.
4. Cap the samplers with plastic (not rubber) caps and pack securely for shipment at 0 °C.

SAMPLE PREPARATION:

5. Place the front and back sorbent sections of the sampler tube in separate 20 mL plastic vials. Discard the glass wool and foam plugs.

6. Add 20 mL 40 mmol/L sodium hydroxide eluent to each plastic vial. Cap. Sonicate for 60 min.
7. Transfer a 5 mL to 7 mL aliquot to a tare weighted 20 mL glass vial using a plastic syringe fitted with a 0.45 µm membrane filter.
8. Reweigh each glass vial and contents so that the net weight of the aliquot can be calculated.
9. Take each sample to complete dryness in an uncapped glass vial on a hot plate. Cool, then reconstitute to the original net weight with high-purity water.

CALIBRATION AND QUALITY CONTROL:

10. Calibrate daily with at least six working standards.
    NOTE: Standards should be spiked onto charcoal tubes as follows to avoid high recoveries seen with liquid standards [4].
    a. Add known amounts of calibration stock solution onto charcoal tubes (5.0 µg to 80 µg fluoride) and desorb in the same manner as field samples (steps 5, 6, 7, 8, and 9).
    b. Analyze working standards together with samples and blanks (steps 12, 13, and 14).
    c. Prepare a calibration graph of peak height vs. amount (µg) of fluoride per 20 mL of sample.
11. (Optional). Determine recovery (*R*) for each lot of tubes used for sampling in the concentration range of interest. Prepare four tubes at each of five levels plus three media blanks.
    a. Collect a known amount of sulfuryl fluoride gas onto each charcoal tube (steps 1, 2, 3, 4, 5, 6, 7, 8, and 9).
    b. Analyze samples in the same manner as field samples (steps 12, 13, and 14).
    c. Prepare graph of recovery vs. µg sulfuryl fluoride.

MEASUREMENT:

12. Set ion chromatograph to conditions given on page 6012-1.
13. Refilter sample if necessary, then inject a sample aliquot into the ion chromatograph.
14. Measure peak height.

CALCULATIONS:

15. Determine mass (µg) of fluoride found on the front (W_f) and back (W_b) sections, and in the average media blank front (B_f) and back (B_b) sorbent section.
    NOTE: If $W_b > W_f / 10$, report breakthrough and possible sample loss.
16. Calculate concentration, *C*, of sulfuryl fluoride in the actual air volume, *V* (L), applying the conversion factor 2.686 (molecular weight of sulfuryl fluoride divided by the atomic weight of 2 fluoride anions; the reaction is $SO_2F_2 + 4\ NaOH \rightarrow 2\ NaF + Na_2SO_4 + 2\ H_2O$):

$$C = \frac{(W_f + W_b - B_f - B_b) \times 2.686}{V}, \text{ µg/L or mg/m}^3.$$

EVALUATION OF METHOD:

This method was evaluated over the range 20 mg/m³ to 420 mg/m³. Overall sampling and measurement precision, $\hat{S}_{rT}$, was 0.070 [2]. The average recovery of sulfuryl fluoride from charcoal was 99% when sampling atmospheres prepared in aluminized gas bags (Calibrated Instruments, Inc., Hawthorne, NY 10532). Recovery of fluoride from sampling media was 97% in the range 10 µg to 160 µg fluoride per sample. Sample stability during storage was evaluated at an air concentration of 417 mg/m³ sulfuryl fluoride. Samples showed 101% recovery after 12 d of storage at 0 °C to 5 °C compared to one-day-old samples.

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METHOD WRITTEN BY:

George Y. Williamson, MRSB, DPSE.

AMMONIA by IC

6016

NH_3 MW: 17.03 CAS: 7664-41-7 RTECS: BO0875000

METHOD: 6016, Issue 2 **EVALUATION:** FULL **Issue 1:** 15 May 1996
Issue 2: 3 March 2016

OSHA: 50 ppm
NIOSH: 25 ppm; STEL 35 ppm

PROPERTIES: gas; MP -77.7 C; BP -33.4 C; VP 888 kPa (8.76 atm) @ 21.1 C; vapor density 0.6 (air = 1); explosive range 16 to 25% v/v in air

SYNONYMS: none

SAMPLING

SAMPLER: SOLID SORBENT TUBE (sulfuric acid-treated silica gel); a 0.8-µm MCE prefilter may be used to remove particulate interferences.

FLOW RATE: 0.1 - 0.5 L/min

VOL-MIN: 0.1 L @ 50 ppm
-MAX: 96 L @ 50 ppm {1}

SHIPMENT: routine

SAMPLE STABILITY: at least 35 days @ 5 °C [2]

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 17 to 68 mg/m^3 [1] (30-L samples)

BIAS: -2.4%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.071 [1]

ACCURACY: ± 14.5%

MEASUREMENT

TECHNIQUE: ION CHROMATOGRAPHY, CONDUCTIVITY DETECTION

ANALYTE: ammonium ion (NH_4^+)

EXTRACTION ION: 10 mL deionized water

INJECTION VOLUME: 50 µL

ELUENT: 48 mM HCl/4 mM DAP-HCl/4 mM L-histidine-HCl; 1 mL/min
alternate: 12 mM HCl/0.25 mM DAP-HCl/0.25 mM L-histidine-HCl; 1 mL/min

COLUMNS: cation separator; cation guard; cation micromembrane suppressor

CONDUCTIVITY SETTING: 30 µS full scale

CALIBRATION: standard solutions of NH_4^+ in deionized water

RANGE: 8 to 100 µg/sample [3]

ESTIMATED LOD: 2 µg/sample [3]

PRECISION ($\bar{S}_r$): 0.038 [2]

APPLICABILITY: The working range is 24 to 98 ppm (17 to 68 mg/m^3) for a 30-L sample [1]. This method is applicable to STEL measurements when sampled at 0.2 L/min.

INTERFERENCES: Ethanolamines (monoethanolamine, isopropanolamine, and propanolamine) have retention times similar to NH_4^+. The use of the alternate (weak) eluent will aid in separating these peaks.

OTHER METHODS: This method combines the sampling procedure of methods S347 [4] and 6015 [5] with an ion chromatographic analytical procedure similar to Method 6701 [6] and OSHA Method ID-188 [3].

REAGENTS:

1. Water, deionized, filtered.
2. Sulfuric acid (H_2SO_4), 0.01 N:* Add 0.28 mL conc. H_2SO_4 to 500 mL deionized water in 1-L volumetric flask. Dilute to 1 L with deionized water.
3. Hydrochloric acid (HCl), 1 N:* Add 82.5 mL conc. HCl to 500 mL deionized water in 1-L volumetric flask. Dilute to 1 L with deionized water.
4. 2,3-diaminopropionic acid monohydrochloride (DAP-HCl)
5. L-histidine monohydrochloride monohydrate (L-histidine-HCl)
6. Eluent (48 mM HCl/4 mM DAP-HCl/4 mM L-histidine-HCl): Place 0.560 g DAP-HCl and 0.840 g L-histidine-HCl in a 1-L volumetric flask. Add 48 mL of 1 N HCl, dilute to volume with deionized water. Prepare monthly.
7. Alternate eluent (12 mM HCl/0.25 mM DAP-HCl/0.25 mM L-histidine-HCl): Dilute 252 mL strong eluent and 36 mL 1 N HCl to 4 L with deionized water. Prepare fresh for each use.
8. Tetramethylammonium hydroxide (TMAOH), 25% in water.
9. Regenerant solution: Dilute 57.4 mL of 25% TMAOH to 4 L with deionized water.
10. Ammonia stock solution, 1000 µg/mL as NH_3 (1059 µg/mL as NH_4^+): Dissolve 3.1409 g ammonium chloride in deionized water. Dilute to 1 L.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler:
   a. Prefilter: 37-mm mixed cellulose ester membrane filter, 0.8-µm pore size, stainless steel or porous plastic screen in two piece cassette filter holder.
   b. Sulfuric acid-treated silica gel, glass tube, unsealed and fire-polished, 6.0 cm long, 6-mm OD, 4-mm ID, containing two sections of 20/40 mesh sulfuric acid-treated silica gel (200 mg front/100 mg back) separated and held in place with plugs of silylated glass wool, and capped with plastic caps.
2. Personal sampling pump, 0.1 to 0.5 L/min, with flexible tubing.
3. Ion Chromatograph with conductivity detector, cation column and guard, and cation micromembrane suppressor (see Evaluation).
4. Syringes, 10-mL, polyethylene, Luer tip.
5. Centrifuge tubes, 15-mL, graduated, plastic with screw caps.
6. Volumetric flasks, 10-, 50-, 100-mL, and 1-L.
7. Syringe filters, 13-mm, 0.8-µm, membrane filter.
8. Micropipets, disposable tips.
9. Analytical balance (sensitivity to 0.01 mg).

SPECIAL PRECAUTIONS: Concentrated acids are corrosive to skin. Handle acid in a fume hood. Wear protective gloves.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Sample at an accurately known flow rate between 0.1 and 0.5 L/min for a total sample size of 0.1 to 96 L.
3. Cap the sampling tubes with plastic (not rubber) caps immediately after sampling.
4. Pack securely for shipment.

SAMPLE PREPARATION:

5. Remove caps from sampling tubes. Transfer the front and back sections of sulfuric acid-treated silica gel to separate 15-mL graduated centrifuge tubes.
   NOTE: Firm tapping of the tube may be necessary to effect complete transfer of the sulfuric acid-treated silica gel.
6. Add 10 mL of deionized water to each centrifuge tube. Cap and shake vigorously. Allow to stand 45 minutes with occasional shaking. (Desorption is complete in 45 minutes.)
   NOTE: Analyses should be completed within one day after the ammonia is desorbed.
7. Transfer samples to 10-mL syringes fitted with inline syringe filters for manual injection or transfer to autosampler vials.

CALIBRATION AND QUALITY CONTROL:

8. Calibrate daily with at least six working standards over the range of 1 to 110 µg NH_3 per sample (about 0.11 to 12 µg/mL NH_4^+).
9. Add known aliquots of ammonia stock solution to 0.01 N H_2SO_4 in 10-mL volumetric flasks.
   NOTE: Prepare standards just before use.
10. Analyze working standards together with samples and blanks (steps 9 through 11).
11. Prepare calibration graph (peak height vs. µg NH_3).

MEASUREMENT:

12. Set ion chromatograph to conditions given on page 6016-1, according to manufacturer's instructions.
13. Inject 50-µL sample aliquot manually or with autosampler. For manual operation, inject 2 to 3 mL of sample from filter/syringe to ensure complete rinse of sample loop.
14. Measure peak height.
    NOTE: If peak height exceeds linear calibration range, dilute with 0.01 N H_2SO_4, reanalyze and apply the appropriate dilution factor in calculations.

CALCULATIONS:

15. Determine the mass, µg, of ammonia found in the sample front (W_f) and back (W_b) sorbent sections, and in the average media blank front (B_f) and back (B_b) sorbent sections.
16. Calculate concentration, C, of NH_3 in the air volume sampled, V (L):

$$C = \frac{W_f + W_b - B_f - B_b}{V}, mg/m^3$$

EVALUATION OF METHOD:

This method combines the sampling procedure of NIOSH Methods S347 [4] and 6015 [5] with the ion chromatographic analytical procedure of NIOSH Method 6701 [6] and OSHA Method ID-188 [3]. This method used HPIC-CS3 cation separator, HPIC-CG3 cation guard and CMMS-1 cation micromembrane suppressor. This method will serve as an alternate analytical procedure to the automated spectrophotometric procedure of NIOSH Method 6015 [5]. Although the methods from which this method is derived are fully evaluated methods, the combination of the sulfuric acid-treated silica gel sampler and IC analysis has not received a full evaluation, as such. During the development of the passive monitor method for ammonia (6701), sulfuric acid-treated silica gel tubes were used as one of the reference methods [6]. The silica gel samples with IC analysis showed good agreement with the other reference methods, bubbler collection with colorimetric analysis using Nessler's Reagent, and bubbler collection with IC analysis.

A storage stability study compared the sulfuric acid-treated silica gel tube and sulfuric acid-treated carbon beads used in OSHA Method ID-188 [3]. When stored at room temperature for five days and then

refrigerated for 21 days, silica gel samples had a mean recovery of 102 ± 3.8% (n = 8), while carbon beads had a mean recovery of 95 ± 1.6% (n = 8). The samples stored on carbon beads for 35 days showed significantly lower (although still acceptable) recovery compared to samples stored for 14 days: 103 ± 3.8% for silica gel (n = 12), and 108 ± 7.0% for carbon beads (n = 12) [2].

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METHOD WRITTEN BY:

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CARBON MONOXIDE 6604

CO MW: 28.00 CAS: 630-08-0 RTECS: FG3500000

METHOD: 6004, Issue 2 **EVALUATION:** FULL **Issue 1:** 15 May 1996
Issue 2: 16 March 2016

OSHA: 50 ppm
NIOSH: 35 ppm; C 200 ppm

PROPERTIES: colorless, odorless gas; BP -192 °C MP -207 °C; vapor density (air=1) 0.97; flammable (explosive) limits in air: 12.5 to 74.2%

SYNONYMS: monoxide; carbon oxide; carbonic oxide; flue gas

SAMPLING

SAMPLER: PORTABLE ELECTROCHEMICAL DIRECT-READING CO MONITOR

FLOW RATE: instrument dependent

VOL-MIN: 10 L
-MAX: none

SHIPMENT: routine shipment of instrumentation

SAMPLE STABILITY: at least 7 days @ 25 °C [1] (aluminized air bags)

BLANKS: fresh air or compressed CO-free air from cylinder

ACCURACY

RANGE STUDIED: 0 to 200 ppm

BIAS: - 1.7% [2]

OVERALL PRECISION ($\hat{S}_{rT}$): 0.022 [2]

ACCURACY: ± 6.0%

MEASUREMENT

TECHNIQUE: ELECTROCHEMICAL SENSOR

ANALYTE: carbon monoxide (CO)

CALIBRATION
-ZERO: CO-free air
-SPAN: standard cylinders of span gas in the desired range

RANGE: 0 to 200 ppm

ESTIMATED LOD: 1 ppm

PRECISION ($\bar{S}_r$): 0.035 @ 20 ppm
0.012 @ 50 ppm
0.008 @ 100 ppm [2]

APPLICABILITY: Portable, direct-reading carbon monoxide monitors are applicable to any work environment for personal or area monitoring.

INTERFERENCES: Several gaseous pollutants (e.g., NO_2, SO_2) may cause an interference at levels over 5 ppm. If these or other pollutants are known or suspected to be present, use a monitor with a chemical interference scrubber over the sensor. Unknown pollutants may require further experimentation to determine their effect on the sensor. As tested, SO_2 (5 ppm), CO_2 (5000 ppm), methylene chloride (500 ppm), diesel fuel (6 µL/L, about 0.3 ppm benzene), and gasoline vapor (1 µL/L, about 1 ppm benzene) had no impact on most monitor readings [2]. Some monitors are equipped with a chemical interference scrubber while others offer this as an option.

OTHER METHODS: OSHA methods ID 209 (CO by direct-reading monitor) [3] and ID 210 (CO by gas bag sampling) [4] are similar techniques.

REAGENTS:

1. CO* calibration gas, 20 to 50 ppm, compressed gas cylinder, appropriate pressure regulator, and other items as recommended by manufacturer for field check of monitor response.

   *See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Electrochemical carbon monoxide monitoring instrument designed and intended for industrial use (not a residential use alarm/monitor); fixed-location mountable for area alarm/monitoring, compact portable for person alarm/monitoring, or both; with integral concentration display.
2. Personal sampling pump, 0.250 L/min, with inlet and outlet, used for bag filling and sample analysis (e.g., when off-site analysis is needed).
3. Air bags, aluminized, 2-L, or other appropriate sizes (optional).
4. Replacement batteries or battery recharger, as appropriate for monitor.

SPECIAL PRECAUTIONS: Carbon monoxide is a highly flammable, dangerous fire and explosive risk, and is toxic by inhalation. Shipments of compressed calibration gases must comply with 49 CFR 1992 regulations.

SAMPLING:

1. Zero monitor with CO-free air at the same temperature and relative humidity as the work environment, if possible.
   NOTE 1: Monitors are more sensitive to temperature variations than to humidity variations. Most monitors have temperature compensating circuitry.
   NOTE 2: If applicable, bag samples may be collected in aluminized bags (2-L or larger) and analyzed later by placing the calibration cap over the sensor and pumping the sample across the sensor at a nominal rate of 0.250 L/min with a personal sampling pump.
2. For personal monitoring, locate the monitor as near the worker's breathing zone as possible.
3. For area monitoring, locate monitor in an area with good air circulation about 60 to 70 inches above the floor.
   NOTE: Make sure the sensor is not obstructed in either application.

CALIBRATION AND QUALITY CONTROL:

4. Calibrate with a standard calibration mixture of CO in air (e.g., in gas bag samples of known concentrations) from a pressurized cylinder at the CO level recommended by the monitor manufacturer (normally, 20 to 50 ppm CO). The monitor should be calibrated at the temperature and relative humidity as near as possible to that of the work environment in which it will be used.
5. Check the calibration daily and recalibrate whenever the monitor reading varies from the span gas by 5% or more, or as the manufacturer recommends.

MEASUREMENT:

6. Read concentration directly (in ppm) from the monitor display.
   Some monitors (data logger models) will maintain a continuous record of the data as it is accumulated and will calculate the average, TWA, peak, etc. concentrations. These data may be read from the display at any time. Some monitors will also store this information for downloading to a computer or printer at the end of the monitoring period. Other monitors only display the current reading, requiring

the operator to manually record the data. All monitor models are equipped with alarms that will warn the user (audibly, visually or both) whenever the concentration of CO exceeds the preset level of the alarm. Many are equipped with two-level alarms [5].

EVALUATION OF METHOD:

The performance of six direct-reading carbon monoxide monitors was evaluated over a period of 12 months at CO concentrations up to 200 ppm and a range of ambient temperatures and relative humidity. Most of the tests were conducted at or near the PEL. For mean recovery studies, six different monitors were used and readings were taken approximately 1 h apart. Recovery at 20 ppm was 105% (n = 42); at 50 ppm, 99.6% (n = 36); and at 100 ppm, 99.9% (n = 30). Thus, the overall mean bias was calculated at -1.7%. The precision ($\overline{S}_r$) at 20 ppm was 0.035 (35 readings from 5 monitors over a 7-h period). At 50 ppm, $\overline{S}_r$ was 0.012 (30 readings from 5 monitors over a 6-h period), and at 100 ppm, $\overline{S}_r$ was 0.008 (36 readings from 6 monitors over a 6-h period). Tests also were conducted to determine response time, zero and span drift, alarm decibel level, battery life, life of the sensors, as well as the effects of selected interferences (gases, vapors, and RF) and the effects of handling and transporting to remote sites. See [6] for preliminary work on carbon monoxide monitoring.

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METHOD REVISED BY:

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ELEMENTS by ICP (Microwave Digestion)

7302

AW: Table 1 | CAS: Table 2 | RTECS: Table 2

METHOD: 7302, Issue 1 | **EVALUATION: FULL** | **Issue 1: 21 July 2014**

OSHA: Table 2
NIOSH: Table 2
Other OELs: [1,2]

PROPERTIES: Table 1

ELEMENTS:						
	aluminum	cadmium	lead	phosphorus	strontium	yttrium
	antimony	calcium	lithium	platinum	tellurium	zinc
	arsenic	chromium	magnesium	potassium	thallium	zirconium
	barium	cobalt	manganese	selenium	tin	
	beryllium	copper	molybdenum	silver	titanium	
	boron	iron	nickel	sodium	vanadium	

SAMPLING

SAMPLER: FILTER (mixed cellulose ester membrane (MCE), 37-mm diameter, 0.8-µm pore size)

FLOW RATE: 1 to 4 L/min

VOL-MIN:
-MAX: Table 1

SHIPMENT: Routine

SAMPLE STABILITY: Stable

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: See Table 4

ACCURACY: See Table 4

BIAS: See Table 4

OVERALL PRECISION ($\hat{S}_{rT}$): See Table 4

MEASUREMENT

TECHNIQUE: INDUCTIVELY COUPLED ARGON PLASMA, ATOMIC EMISSION SPECTROSCOPY (ICP-AES)

ANALYTE: Elements listed above

REAGENTS: 10.0 mL of 1:1 nitric (HNO_3) and ASTM Type II water

FINAL SOLUTION: 20% HNO_3, 25 mL

WAVELENGTH: Depends upon element (see Table 3)

BACKGROUND CORRECTION: Spectral wavelength shift

CALIBRATION: Elements in 20% HNO_3

RANGE: See Table 4

ESTIMATED LOD: Table 3

PRECISION ($\bar{S}_r$): Table 3

APPLICABILITY: This method is for the analysis of metal and nonmetal dust collected on MCE filters in the workplace. The working range varies from element to element. The method entails simultaneous elemental analysis using a microwave digestion approach to simplify and expedite the analysis.

INTERFERENCES: Spectral interferences are the primary interferences encountered in ICP-AES analysis. These are minimized by judicious wavelength selection, inter-element correction factors and background correction [3].

OTHER METHODS: This method complements NIOSH hotplate digestion methods 7300 and 7301 for trace elements. Flame atomic absorption spectroscopy (e.g., Methods 7013 through 7082) is an alternative analytical technique for many of these elements [4]. Graphite furnace AAS (e.g., 7102 for Be, 7105 for Pb) is usually more sensitive [4]. NMAM 7301 and 7303 contain alternative extraction procedures.

REAGENTS:

1. Nitric acid, conc., trace metal grade*
2. Calibration stock solutions, 1000 µg/mL and 10,000 µg/mL commercially available, or prepared per instrument manufacturer's recommendation (see step10)
3. Digestion acid*. 1:1 water, ASTM type II, and nitric acid*, trace metal grade
4. Argon, liquid
5. De-ionized Water, ASTM Type II [5]
6. Dilution acid*, 20% nitric acid in ASTM Type II water

* See Special Precautions

EQUIPMENT:

1. Sampler: mixed cellulose ester membrane (MCE) filter, 0.8-µm pore size, 37-mm diameter; in 2-piece cassette filter holder
2. Personal sampling pump, 1 to 4 L/min, with flexible connecting tubing
3. Inductively coupled plasma-atomic emission spectrometer, equipped as specified by the manufacturer for analysis of elements of interest
4. Regulator, two-stage for argon
5. Microwave, programmable power, active temperature control, minimum of 574 W, corrosion resistant ventilated oven and turntable
6. Microwave digestion vessels, high pressure, closed PTFE, 100-mL capacity
7. Volumetric flasks, 25 mL**
8. Assorted volumetric pipettes as needed**

** Acid wash all glassware and vessels before using.

SPECIAL PRECAUTIONS: Wear gloves, lab coat, and safety glasses while handling all chemicals. All work should be performed with adequate ventilation to personnel and equipment. Because this method involves the use of capped digestion containers, avoid the use of other acids such as perchloric acid in combination with nitric acid that could cause a violent reaction [6,7]. In the preparation of the digestion and dilution acids, it is imperative that acid be added to water in order to avoid a violent exothermic reaction.

SAMPLING

1. Calibrate each personal sampling pump with a representative sampler connected to the pump (in line).
2. Sample at an accurately known flow rate between 1 and 4 L/min. For estimated sampling volumes see Table 1. For TWA measurements see Table 2. Do not exceed a filter loading of approximately 2 mg total dust.
   NOTE: Filter overloading can be assessed by periodic visual checks. See NMAM guidance chapters for discussion on sampling.

SAMPLE PREPARATION

NOTE: If total weights are desired, weighing should be done at this step. Follow NIOSH method 0500 for gravimetric analysis [11].

3. Open the cassette filter holders and transfer the samples, blanks, and Quality Control (QC) filters to clean PTFE digestion vessels. Wipe the internal cassette surfaces with a 37-mm MCE filter, polyvinyl alcohol wipe or cellulosic wipe wetted with deionized water, and add to the digestion vessel to transfer non-filter aerosol deposits into the digestion vessels.
4. Add digestion acid up to 10 mL, and cap the vessels.

NOTE: In order to avoid a violent exothermic reaction, do not add water to concentrated nitric acid. Acid should be added after the water has been placed in the vessel.

5. Place digestion vessels in microwave, and run the preprogrammed digestion procedure for 12- vessel digestion: 1200 W power, ramp to 150 °C over 20 min, hold for 10 min at 215 °C followed by at least a 5 min cool down (power will be adjusted lower for fewer vessels).
6. Allow the samples to cool to room temperature.
7. Remove vessel lids and rinse contents into 25-ml volumetric flasks with ASTM Type II water.
8. Dilute to the mark with ASTM Type II water and mix.
9. Submit extracted and diluted samples for analysis.

CALIBRATION AND QUALITY CONTROL

10. Calibrate the spectrometer according to the manufacturer recommendations.
    NOTE: Typically an acid blank and multi-element working standards are used. The following multi-element combinations are chemically compatible in 20% HNO_3.
    a. Al, As, Ba, Be, Ca, Co, Cr, Cu, Fe, Li, Mg, Mn, Mo, Na, Ni, Pb, Se, Sr, Ti, V, Y, Zn, Zr;
    b. B, K, P, Sn, Te, Tl;
    c. Ag, Cd, Sb;
    d. Pt.
11. Analyze all applicable standards at least once every twenty (20) analyses (minimum frequency 5%).
12. Check recoveries with at least one media blank and two spiked media blanks per twenty samples. Use a spike level that is within the range of 10 to 20 times the LOQ.
    NOTE: Whenever possible, QA/QC samples should be prepared from certified reference materials in a matrix similar to the bulk material sampled. Liquid spiked filters are only surrogates for real world samples and QC data based upon certified samples are preferred.

MEASUREMENT

13. Set ICP-AES spectrometer to conditions specified by manufacturer.
14. Analyze standards and samples at applicable wavelengths for each element (target analytes are in Table 3).
    NOTE: If the values for the samples are above the linear range of the instrument, dilute the solutions with dilution acid, reanalyze, and apply the appropriate dilution factor in calculations.

CALCULATIONS

15. Obtain the solution concentrations for the sample, C_s (µg/mL), and the average media blank, C_b (µg/mL), from the instrument.
16. Using the solution volume of sample, V_s (mL), and media blank, V_b (mL), calculate the concentration for the sample, C (mg/m^3), of each element in the air volume sampled, V (L), as follows:

$$C = \frac{(C_s V_s) - (C_b V_b)}{V} \quad , mg/m^3$$

NOTE: µg/Liter is essentially equal to mg/m^3.

EVALUATION OF METHOD

Method 7302 was evaluated using multi-element filter spikes at six spiking levels, based on the estimated LOQ for each element [8]. Using microwave digestion is less time consuming and more convenient than

using the traditional mixed acid hot plate approach. The elimination of perchloric acid in the sample digestion procedure helps to improve the safety of the method. [7]

Summary data are presented in Table 3 for levels 3X LOQ (lower level in Table 3) and 300X LOQ (higher level in Table 3) and for the ranges of loadings given in Table 4. Samples were subjected to microwave digestion using a CEM MDS-2100 device according to the conditions specified in the "sample preparation" section above (see Note of step #5). The values in Tables 3 and 4 were determined using several different ICP-AES instruments which were operated according to manufacturer's instructions.The precision and recovery data, instrumental detection limits, sensitivity, and analytical wavelengths are listed in Table 3 and Table 4. All of the precision data were evaluated for homogeneity for all six concentration levels tested using the Bartlett's test and the results are listed in the method backup data report [8] and summarized in Tables 3 and 4. A statistical analysis found that the data were poolable and all elements had calculated method precision accuracies of less than 25%. This overall precision ($\hat{S}_{rT}$) and accuracy as given in Table 4 is an upper limit predictor of precision. Accuracy data (Table 4) demonstrate the utility of the method for all of the elements listed.

A discussion of metals and metalloid analysis by ICP-AES is presented in an international voluntary consensus standard [3] and the microwave digestion procedure has been evaluated against other digestion procedures through an interlaboratory trial [10].

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METHOD WRITTEN BY:

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TABLE 1. PROPERTIES AND SAMPLING VOLUMES

	Properties [9]		Air Volume, L @ OSHA PEL [11]	
Element (Symbol)	**Atomic Weight**	**MP, °C**	**MIN**	**MAX**
Aluminum (Al)	26.98	660	5	100
Antimony (Sb)	121.8	630	10[2]	2000[2]
Arsenic (As)	74.92	817	5	2000
Barium (Ba)	137.3	727	5[2]	200[2]
Beryllium (Be)	9.01	1287	1250	2000
Boron (B)[1]	10.81	2300	5	2000
Cadmium	112.41	321	12	2000
Calcium (Ca)[1]	40.08	842	5	200
Chromium (Cr)	52.00	1907	5	1000
Cobalt (Co)	58.93	1495	25	2000
Copper (Cu)	63.54	1083	5	1000
Iron (Fe)	55.85	1535	5	100
Lead (Pb)	207.19	328	50	2000
Lithium (Li)[1]	6.94	181	100	2000
Magnesium (Mg)	24.31	651	5	67
Manganese (Mn)	54.94	1245	5	200
Molybdenum (Mo)	95.94	2623	5	67
Nickel (Ni)	58.71	1455	5	1000
Phosphorus (P)	30.97	44	25	2000
Platinum (Pt)	195.09	1769	1250	2000
Potassium (K)[1]	39.10	64	5	2000
Selenium (Se)	78.96	221	13	2000
Silver (Ag)	107.87	961	250	2000
Sodium (Na)[1]	22.99	98	13	2000
Strontium (Sr)[1]	87.62	777	5	2000
Tellurium (Te)	127.60	450	25	2000
Tin (Sn)	118.69	232	20[2]	2000[2]
Thallium (Tl)	204.37	304	25	2000
Titanium (Ti)	47.87	1668	5	100
Vanadium (V)	50.94	1910	5	2000
Yttrium (Y)	88.91	1522	5	1000
Zinc (Zn)	65.37	419	5	200
Zirconium (Zr)	91.22	1855	5	200

[1] No PEL, REL, or STEL data found [1,6,11].
[2] Air volumes estimated from TWAs and LOQs (see Tables 2, 3) [1].

TABLE 2. EXPOSURE LIMITS, CAS #, RTECS [1,6,11]

Element (Symbol)	CAS #	RTECS	Exposure Limits in mg/m³ (C = ceiling limit)	
			OSHA	NIOSH
Aluminum (Al)	7429-90-5	BD0330000	15 (total dust) 5 (respirable)	10 (total dust), 2 (soluble) 5 (respirable, fume)
Arsenic (As)	7440-38-2	CG0525000	0.010 (inorganic)	C 0.002[1], 0.5
Barium (Ba)	7440-39-3		0.5 (Soluble compounds, as Ba)	0.5 (Soluble compounds, as Ba)
Beryllium (Be)	7440-41-7	DS1750000	0.002, C 0.005	C 0.0005[1]
Boron (B)	7440-42-8	ED7350000	15 as oxide	10 as oxide
Cadmium (Cd)	7440-43-9	EU9800000	0.005	lowest feasible conc.[1]
Calcium (Ca)	7440-70-2	EV8040000	No OELs	No OELs
Chromium (Cr)	7440-47-3	GB4200000	0.5 (II & III), 0.005 (VI) 1 (metals, insoluble salts)	0.5
Cobalt (Co)	7440-48-4	GF8750000	0.1 (dust, fume)	0.05 (dust, fume)
Copper (Cu)	7440-50-8	GL5325000	1(dust, mists) 0.1 (fume)	1 (dust, mists) 0.1 (fume)
Iron (Fe)	7439-89-6	NO4565500	10 (fume) as oxide	5 (dust, fume) as oxide
Lead (Pb)	7439-92-1	OF7525000	0.05	0.05
Lithium (Li)	7439-93-2	OJ5540000		
Magnesium (Mg)	7439-95-4	OM2100000	15 (dust) as oxide	--
Manganese (Mn)	7439-96-5	OO9275000	C 5	1; STEL 3
Molybdenum (Mo)	7439-98-7	QA4680000	5 (soluble) 15 (total insoluble)	
Nickel (Ni)	7440-02-0	QR5950000	1	0.015, Ca
Phosphorus (P)	7723-14-0	TH3500000	0.1	0.1
Platinum (Pt)	7440-06-4	TP2160000	0.002 (soluble)	1 (metal) 0.002 (soluble)
Potassium (K)	7740-09-7	TS6460000		
Antimony (Sb)	7440-36-0	CC4025000	0.5	0.5
Selenium (Se)	7782-49-2	VS7700000	0.2	0.2
Silver (Ag)	7440-22-4	VW3500000	0.01 (dust, fume, metal)	0.01 (dust, fume, metal)
Sodium (Na)	7440-23-5	VY0686000		
Strontium (Sr)	7440-24-6	WK7700000		
Tellurium (Te)	13494-80-9	WY2625000	0.1	0.1
Tin (Sn)	7440-31-5	XP7320000	2	2
Titanium (Ti)	7440-32-6	XR1700000	15 (as TiO_2)	lowest feasible[1]
Thallium (Tl)	7440-28-0	XG3425000	0.1 (soluble) skin	0.1 (soluble) skin
Vanadium (V)	7440-62-2	YW1355000	C 0.5 (respirable) as V_2O_5 C 0.1 (fume) as V_2O_5	C 0.05 as V_2O_5
Yttrium (Y)	7440-65-5	ZG2980000	1	1
Zinc (Zn)	7440-66-6	ZG8600000	5 (ZnO fume) 15 (ZnO dust) 5 (ZnO respirable)	5; STEL 10 (ZnO fume) 5; C 15 (ZnO dust)
Zirconium (Zr)	7440-67-7	ZH7070000	5	5, STEL 10

(1) Carcinogen

TABLE 3. MEASUREMENT WAVELENGTHS AND RECOVERY DATA [8]

			Lower Level			Higher Level		
Element[1]	Wavelength (nm)[6]	LOD (µg/sample)	µg/sample	% Recovery N=6)	% RSD	µg/sample	% Recovery (N=6)	% RSD
Ag	328.1	0.1	1.50	95.5	1.01	150	99.0	0.497
Al	308.2	1	7.50	92.7	0.981	750	98.7	0.462
As	193.8	1	7.50	101	2.22	750	107	0.340
B	249.7	0.5	3.75	112	2.96	375	99.5	0.454
Ba	493.4	0.06	0.752	104	3.09	75.2	101	0.438
Be	313.0	0.009	0.076	95.8	2.36	7.60	103	0.714
Ca	315.9	2	22.5	107	2.87	2250	99.0	0.620
Cd	228.8	0.1	1.50	98.8	3.46	150	104	0.701
Co	228.6	0.3	3.75	99.7	1.72	375	104	0.566
Cr[2]	267.7	0.4	3.75	103	7.87	375	103	3.36
Cu	324.8	0.07	0.752	98.8	3.47	75.2	94.2	0.371
Fe	259.9	2	15.0	112	2.43	1500	101	0.263
K	766.5	2	15.0	98.3	5.70	1500	103	0.472
Li	670.8	0.03	0.752	92.4	2.98	75.2	98.8	0.749
Mg	279.1	0.5	7.50	89.3	3.52	750	95.1	0.309
Mn	257.6	0.02	0.752	86.2	2.38	75.2	98.2	0.389
Mo	202.0	0.2	2.25	96.8	5.41	225	103	0.373
Na	589.0	4	37.5	100	0.823	3750	110	0.457
Ni	231.6	0.2	2.25	98.3	5.21	225	97.7	0.592
P	214.9	2	15.0	100	5.67	1500	104	0.315
Pb	220.4	0.6	7.50	98.9	3.94	750	104	0.570
Pt[2]	265.9	8	75.0	98.3	0.282	10000	95.7	1.49
Sb	206.8	0.4	7.50	94.4	3.21	750	103	0.255
Se	196.1	3	37.5	104	3.21	3750	106	0.270
Sn[2]	189.9	0.8	37.5	105	5.04	3750	90.3	3.23
Sr	421.6	0.02	3.75	92.6	2.36	375	97.5	0.553
Te[2]	214.3	2	15.0	90.1	21.8	1500	103	0.614
Ti	337.3	0.2	1.50	101	1.70	150	98.8	0.575
Tl	190.9	0.9	7.5	103	4.14	750	99.3	0.352
V	292.4	0.1	0.752	93.7	4.74	75.2	103	0.341
Y[2]	371.0	0.02	0.376	107	4.44	37.6	102	3.33
Zn[2]	213.9	0.1	1.50	106	13.1	150	97.4	3.42
Zr	339.2	0.06	0.750	93.1	5.35	75.0	95.4	0.971

(1) Values reported were obtained with a Fisons ARL Accuris ICP-AES; performance may vary with instrument and should be independently verified.

(2) Values reported were obtained with a Perkin Elmer Optima 3000 DV ICP-AES. Sample concentration was based on Fisons ICP LOD data.

TABLE 4. PRECISION AND ACCURACY DATA BY ELEMENT [8]

Element (µg/sample)	Range (µg/sample)	Bias	$\hat{S}_{rT}$ (%)	Accuracy
Ag	0.5 to 150	-0.0175	0.668	2.85
Al	2.5 to 750	0.0505	1.455	7.41
As	2.5 to 750	-0.2249	0.554	23.40
Ba	0.25 to 75.2	-0.0330	0.920	4.82
Be	0.025 to 7.60	0.0297	0.863	4.39
Ca	7.43 to 2250	-0.0081	0.836	2.18
Cd	0.50 to 150	-0.0082	0.729	2.02
Co	1.24 to 375	-0.0161	0.574	2.56
Cr	1.24 to 375	-0.0204	0.655	3.12
Cu	0.248 to 75.2	0.0160	0.984	3.21
Fe	5.00 to 1500	-0.0039	1.637	3.30
K	5.00 to 1500	0.1487	1.665	17.61
La	12.6 to 50.1	-0.0136	0.920	2.87
Li	0.25 to 75.2	0.2241	1.209	24.40
Mg	2.5 to 750	0.0180	0.844	3.19
Mn	0.25 to 75.2	-0.0348	0.865	4.91
Mo	0.75 to 225	0.0140	1.469	3.82
Ni	0.75 to 225	-0.0063	0.672	1.73
P	5.0 to 1500	0.0669	1.212	8.69
Pb	2.5 to 750	-0.0246	0.544	3.36
Sb	2.5 to 750	0.0172	0.722	2.91
Se	12.4 to 3750	0.0538	0.758	6.63
Sn	12.4 to 3750	0.0561	0.936	7.15
Sr	1.24 to 375	-0.0074	0.710	1.90
Te	5.0 to 1500	0.0161	0.892	3.08
Ti	0.5 to 150	0.0212	1.043	3.84
Tl	2.5 to 750	-0.0293	0.602	3.92
V	0.25 to 75.2	0.0175	1.223	3.76
Y	0.12 to 37.6	-0.0179	1.115	3.62
Zn	0.5 to 150	0.0075	1.343	3.02
Zr	0.25 to 75.0	0.0314	0.980	4.76

ELEMENTS by ICP Microwave Digestion

7304

MW: Table 1 | CAS: Table 2 | RTECS: Table 2

METHOD: 7304, Issue 1 | **EVALUATION: FULL** | **Issue 1: 25 May 2014**

OSHA: Table 2
NIOSH: Table 2
Other OELs: [1,2]

PROPERTIES: Table 1

ELEMENTS:

aluminum	cadmium	iron	molybdenum	selenium	titanium
arsenic	calcium	lead	nickel	sodium	vanadium
barium	chromium	lithium	phosphorus	strontium	yttrium
beryllium	cobalt	magnesium	platinum	tellurium	zinc
boron	copper	manganese	potassium	thallium	zirconium

SAMPLING

SAMPLER: FILTER, (polyvinyl chloride (PVC), 37-mm diameter, 5.0 µm pore size)

FLOW RATE: 1 to 4 L/min

VOL-MIN:
-MAX: Table 1

SHIPMENT: Routine

SAMPLE STABILITY: Stable

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: See Table 4

ACCURACY: See Table 4

BIAS: See Table 4

OVERALL PRECISION ($\hat{S}_{rT}$): See Table 4

MEASUREMENT

TECHNIQUE: INDUCTIVELY COUPLED ARGON PLASMA, ATOMIC EMISSION SPECTROSCOPY (ICP-AES)

ANALYTE: Elements listed above

REAGENTS: 12 mL of 5:1 concentrated nitric acid and ASTM Type II water

FINAL SOLUTION: 20% HNO_3, 50 mL

WAVELENGTH: Depends upon element; Table 3

BACKGROUND CORRECTION: Spectral wavelength shift

CALIBRATION: Elements in 20% HNO_3

RANGE: See Table 4

ESTIMATED LOD: Table 3

PRECISION ($\bar{S}_r$): Table 3

APPLICABILITY: The working range of this method varies from element to element. This method is for the analysis of metal and nonmetal dust collected on PVC filters that are also used for gravimetric analysis. This is a simultaneous elemental analysis using a microwave digestion approach to simplify and expedite the analysis. Some elements such as antimony, silver, and tin do not form stable solutions in nitric acid when chloride from the PVC filters is present. In such cases a mixed cellulose ester (MCE) filter is necessary (See NMAM 7302). A different acid medium also helps but this technique is not described in this method.

INTERFERENCES: Spectral interferences are the primary interferences encountered in ICP-AES analysis. These are minimized by judicious wavelength selection, inter-element correction factors and background correction. [3,4,5,6]

OTHER METHODS: This method complements NIOSH hotplate digestion methods 7300 and 7301 for trace elements. Flame atomic absorption spectroscopy (e.g., Methods 70XX) is an alternative analytical technique for many of these elements. [7] Graphite furnace AAS (e.g., 7102 for Be, 7105 for Pb) is usually more sensitive. [7] NMAM 7301 and 7303 contain alternative extraction procedures.

REAGENTS

1. Nitric acid, conc., trace metal grade*
2. Calibration stock solutions, 1000 ug/mL and 10,000 ug/mL commercially available, or prepared per instrument manufacturer recommendation (see step 10)
3. Argon, liquid
4. De-ionized Water, ASTM Type II [8]
5. Dilution acid: 20% nitric acid in ASTM Type II water*

* See SPECIAL PRECAUTIONS

EQUIPMENT

1. Sampler: Polyvinyl chloride filter, 5.0-µm pore size, 37-mm diameter; in 2-piece cassette filter holder
2. Personal sampling pump, 1 to 4 L/min, with flexible connecting tubing
3. Inductively coupled plasma-atomic emission spectrometer, equipped as specified by the manufacturer for analysis of elements of interest
4. Regulator, two-stage for argon
5. Microwave, programmable power, active temperature control, minimum of 574 W, corrosion resistant ventilated oven and turntable
6. Microwave digestion vessels, high pressure, closed PTFE, 100-mL capacity
7. Volumetric flasks, 50 mL**
8. Assorted volumetric pipettes as needed**

** Acid wash all glassware and vessels before using.

SPECIAL PRECAUTIONS: Wear gloves, lab coat, and safety glasses while handling all chemicals. All work should be performed with adequate ventilation to personnel and equipment. Because this method involves the use of capped digestion containers, avoid the use of other acids such as perchloric acid in combination with nitric acid that could cause a violent reaction [1,9]. In the preparation of the digestion and dilution acid, it is imperative that acid be added to water in order to avoid a violent exothermic reaction.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler connected to the pump (in line.)
2. Sample at an accurately known flow rate between 1 and 4 L/min. For estimated sampling volumes see Table 1. For TWA measurements see Table 2. Do not exceed a filter loading of approximately 2 mg total dust.
   NOTE: Filter overloading can be assessed by periodic visual checks. See NMAM guidance chapters for additional discussion on filter capacity.

SAMPLE PREPARATION:

NOTE: If total weights are desired, it should be done at this step. Follow NIOSH method 0500 for gravimetric analysis [12].

3. Open the cassette filter holders and transfer the samples, blanks, and Quality Control (QC) filters to clean PTFE digestion digestion vessels. Wipe the internal cassette surfaces with a 37 mm PVC filter wetted with deionized water and add to the digestion vessel to transfer non-filter aerosol deposits into the digestion vessels.
4. Add 2 mL of ASTM Type II water followed by adding (slowly) 10 mL concentrated nitric acid, then cap each vessel.

NOTE: In order to avoid a violent exothermic reaction, do not add water to concentrated nitric acid. Acid should be added after the water has been placed in the vessel.

5. Place digestion vessels in microwave and run preprogrammed PVC digestion procedure. Example microwave conditions for 12-vessel digestion: 1200 W power, ramp to 215 °C over 20 min, hold for 10 min at 215 °C followed by at least a 5 min cool down (power will be adjusted lower for fewer vessels).
6. Allow the samples to cool to room temperature.
7. Remove vessel lids and rinse contents into 50-mL volumetric flasks with ASTM Type II water.
8. Dilute to the mark with ASTM Type II water and mix.
9. Submit samples for analysis.
   NOTE: A residual solid may be present after digestion. Filter/centrifuge the samples before analysis, as appropriate.

CALIBRATION AND QUALITY CONTROL:

10. Calibrate the spectrometer according to the manufacturers' recommendations.
    NOTE: Typically an acid blank and a single or multi-element working standard are used. The following multi-element combinations are chemically compatible in 20% HNO_3.
    a. Al, As, Ba, Be, Ca, Co, Cr, Cu, Fe, Li, Mg, Mn, Mo, Na, Ni, Pb, Se, Sr, Ti, V, Y, Zn, Zr;
    b. B, K, P, Te, Tl;
    c. Cd;
    d. Pt.
11. Analyze all applicable standards at least once every twenty (20) analyses (minimum frequency 5%).
12. Check recoveries with at least one media blank and two spiked media blanks per twenty samples. Use a spike level that is within the range of 10 to 20 times the Limit of Quantitation (LOQ.)
    NOTE: Whenever possible, QA/QC samples should be prepared from certified reference materials in a matrix similar to the bulk material sampled. Liquid spiked filters are only surrogates for real world samples and QC data based upon certified samples would be ideal.

MEASUREMENT:

13. Set the ICP-AES spectrometer to conditions specified by manufacturer.
14. Analyze standards and samples at applicable wavelengths for each element (target analytes are in Table 3).
    NOTE: If the values for the samples are above the linear range of the instrument, dilute the solutions with dilution acid, reanalyze, and apply the appropriate dilution factor in the calculations.

CALCULATIONS:

15. Obtain the solution concentrations for the sample, C_s (µg/mL), and the average media blank, C_b (µg/mL), from the instrument.
16. Using the solution volume of sample, V_s (mL), and media blank, V_b (mL), calculate the concentration for the sample, C (mg/m^3), of each element in the air volume sampled, V (L), as follows:

$$C = \frac{(C_s V_s) - (C_b V_b)}{V}, \text{ mg/m}^3$$

NOTE: µg/Liter is approximately equal to mg/m^3.

EVALUATION OF METHOD:

This method is less time consuming and more convenient than using the acid hotplate approach. The elimination of perchloric acid in the sample digestion procedure helps to improve the safety of the method. [9] Use of the PVC filters allows for the acquisition of total mass per filter in addition to total metals concentration.

The evaluation of this method, 7304, for PVC filters was determined at six concentration levels based on the LOQ for each element listed on page 1 [13]. All of the precision data was evaluated for homogeneity for all concentration levels tested using the Bartlett's test and the results are listed in the method backup data report [12] and summarized in Tables 3 and 4. In many cases the highest concentration level (300 times the LOQ) was not poolable due in every case to the precision being so small relative to the other values, usually less than CV = 0.001 (<0.1%). Therefore, the overall precision ($\hat{S}_{rT}$) and accuracy as given in Table 4 is an upper limit predictor of precision; precision at concentration levels greater than 300 times the LOQ (see Table 3) will probably be much smaller.

For many of the metals, precision at the 3 times and/or 1 times the LOQ levels was reasonable (CV less than 10%) but were not poolable due to the precisions at the higher concentration levels being so much smaller. In one case (strontium) the lowest level was not poolable because its CV was an inlier (less than 1%), being much smaller than those at the higher concentration levels. In most cases the precision appeared to be a function of concentration. This is observable in Table 3 where the CVs for the 10 times the LOQ (lower level) and 300 times the LOQ (higher) levels are compared.

Three elements, antimony, silver, and tin, had poor recoveries. It is believed that the chloride ions produced in the digestion of the PVC filters is causing the formation of precipitates. These metals are preferably sampled on MCE filters. The values in Tables 3 and 4 were determined using several different ICP-AES instruments and also several different microwave ovens. All were operated according to the manufacturer's instructions.

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Table 1. PROPERTIES AND SAMPLING VOLUMES

Element (Symbol)	Properties [13]		Air Volume, L @ OSHA PEL [4]	
	Atomic Weight	MP, °C	MIN	MAX
Aluminum (Al)	26.98	660	5	100
Arsenic (As)	74.92	817	5	2000
Barium (Ba)	137.3	727	5(2)	200(2)
Boron (B)(1)	10.81	2076	5	2000
Beryllium(Be)	9.01	1287	1250	2000
Calcium (Ca)(1)	40.08	842.5	5	200
Cadmium (Cd)(3)	112.40	321	13	2000
Cobalt (Co)	58.93	1495	25	2000
Chromium (Cr)	52.00	1907	5	1000
Copper (Cu)	63.54	1083	5	1000
Iron (Fe)	55.85	1538	5	100
Potassium (K)(1)	39.10	64	5	2000
Lithium (Li)(1)	6.94	181	100	2000
Magnesium (Mg)	24.31	651	5	67
Manganese (Mn)	54.94	1246	5	200
Molybdenum (Mo)	95.94	2623	5	67
Sodium (Na)(1)(3)	22.99	97.72	13	2000
Nickel (Ni)	58.71	1455	5	1000
Phosphorus (P)	30.97	44	25	2000
Lead (Pb)	207.19	327.2	50	2000
Platinum (Pt)(3)	195.1	1772.2	1250	2000
Selenium (Se)	78.96	221	13	2000
Strontium (Sr)(1)	87.62	777	5	2000
Tellurium (Te)	127.60	450	25	2000
Titanium (Ti)	47.90	1668	5	100
Thallium (Tl)	204.37	304	25	2000
Vanadium (V)	50.94	1910	5	2000
Yttrium (Y)	88.91	1522	5	1000
Zinc (Zn)	65.37	419	5	200
Zirconium (Zr)	91.22	1855	5	200

(1) No PEL, REL, or STEL data found [1,14].
(2) Air Volumes Estimated from TWA and LOQ's (see Tables 2, 3). [10]
(3) These metals, as well as tin and antimony, form precipitates in nitric acid when chloride from the PVC filters is present.

Table 2. EXPOSURE LIMITS, CAS #, RTECS [1,14,15]

Element (Symbol)	CAS #	RTECS #	Exposure Limits, mg/m³ (C = ceiling limit)	
			OSHA	NIOSH
Aluminum (Al)	7429-90-5	BD0330000	15 (total dust) 5 (respirable)	10 (total dust) 5 (respirable, fume)
Arsenic (As)	7440-38-2	CG0525000	0.010 (inorganic)	C 0.002(1)
Barium (Ba)	7440-39-3	CQ8370000	0.5 (soluble)	0.5 (soluble)
Beryllium (Be)	7440-41-7	DS1750000	0.002, C 0.005	C 0.0005(1)
Cadmium (Cd)	7440-43-9	EU9800000	0.005	lowest feasible conc.(1)
Calcium (Ca)	7440-70-2		No OEL	No OEL
Cobalt (Co)	7440-48-4	GF8750000	0.1	0.05 (dust, fume)
Chromium (Cr)	7440-47-3	GB4200000	0.5 (II & III), 0.005 (VI)	0.5 (II & III), 0.0002 (VI)
Cobalt (Co)	7440-48-4	GF8750000	0.1	0.05 (dust, fume)
Copper (Cu)	7440-50-8	GL5325000	1 (dust, mists) 0.1 (fume)	1 (dust, mists) 0.1 (fume)
Iron (Fe)	7439-89-6	NO4565500	10 (fume) as oxide	5 (dust, fume) as oxide
Magnesium (Mg)	7439-95-4	OM2100000	15 (dust) as oxide	--
Manganese (Mn)	7439-96-5	OO9275000	C 5	1; STEL 3
Molybdenum (Mo)	7439-98-7	QA4680000	5 (soluble) 15 (total insoluble)	--
Nickel (Ni)	7440-02-0	QR5950000	1	0.015(1)
Phosphorus (P)	7723-14-0	TH3500000	0.1	0.1
Lead (Pb)	7439-92-1	OF7525000	0.05	0.05
Platinum (Pt)	7440-06-4	TP2160000	0.002 (soluble)	1 (metal)
Selenium (Se)	7782-49-2	VS7700000	0.2	0.2
Silver (Ag)	7440-22-4	VW3500000	0.01 (soluble, metal)	0.01 (soluble, metal)
Tellurium (Te)	13494-80-9	WY2625000	0.1	0.1
Titanium (Ti)	7440-32-6	XR1700000	15 (as TiO_2)	lowest feasible(1)
Thallium (Tl)	7440-28-0	XG3425000	0.1 (soluble)	0.1(soluble)
Vanadium (V)	7440-62-2	YW1355000	C 0.5 (respirable) as V_2O_5 C 0.1 (fume) as V_2O_5	C 0.05
Yttrium (Y)	7440-65-5	ZG2980000	1	1
Zinc (Zn)	7440-66-6	ZG8600000	5 (ZnO fume) 15 (ZnO dust) 5 (ZnO respirable)	5; STEL 10 (ZnO fume) 5; C 15 (ZnO dust)
Zirconium (Zr)	7440-67-7	ZH7070000	5	5, STEL 10

(1) Carcinogen

Table 3. MEASUREMENT WAVELENGTHS AND RECOVERY DATA

Element[1]	Wavelength (nm)	LOD (µg/ sample)	Lower Level[4,5]				Higher Level[5]			
			µg/ sample	N =	Percent Recovery	Precision (S_r)	µg/ sample	N =	Percent Recovery	Precision (S_r)
Ag	328.07	0.1	3.00	5	63.01	0.0739	300	6	3.92	0.0865
Al	308.22	2	50.25[4]	6	89.78	0.0565	1500	6	100.71	0.0055
Al[2]	308.214	0.5	15.0	5	115.05	0.0199	1500	6	105.17	0.0056
As	193.76	2	15.0	5	93.29	0.0570	1500	6	115.84	0.0174
Ba	493.41	0.2	1.50	5	107.16	0.0295	150	6	102.22	0.0104
B	249.68	0.4	7.50	5	86.38	0.0277	750	6	101.19	0.0082
Be	313.04	0.008	0.152	6	102.38	0.0861	15.2	6	107.71	0.0091
Ca	315.89		151[4]	6	94.64	0.0512	4500	6	116.25	0.0153
Ca[2]	315.88	2	45.0	5	104.82	0.0090	4500	6	98.13	0.0066
Cd	228.80	0.2	3.00	5	109.65	0.0316	300	6	111.68	0.0152
Co	228.62	0.7	7.50	5	89.87	0.0338	750	6	114.15	0.0141
Cr	267.72	0.7	7.50	5	112.65	0.0233	750	6	118.65	0.0136
Cr[2]	267.71	0.3	7.50	5	102.60	0.0048	750	6	92.98	0.0066
Cu	324.75	0.08	1.50	5	106.84	0.0364	150	6	100.42	0.0058
Cu[2]	324.75	0.08	1.50	5	117.16	0.0361	150	6	103.13	0.0150
Fe	259.94	15	30	5	120.58	0.0405	3000	6	112.41	0.0083
Fe[2]	259.94	5	30	5	112.55	0.0489	3000	6	97.20	0.0085
K	766.49	3	100[4]	6	85.57	0.0254	3000	6	86.46	0.0260
K[2]	766.49		100[4]	6	99.40	0.0300	3000	6	90.02	0.0205
Li	670.78	0.06	1.50	5	97.51	0.0253	150	6	81.96	0.0378
Mg	279.08	0.9	15.0	5	105.25	0.0088	1500	6	97.47	0.0077
Mg[2]	279.07	0.4	15.0	5	107.33	0.0043	1500	6	101.75	0.0058
Mn	257.61	0.09	1.50	5	110.24	0.0150	150	6	115.56	0.0090
Mo	202.03	0.4	4.50	5	87.79	0.0433	450	6	120.57	0.0093
Mo[2]	202.029	0.3	4.50	5	89.75	0.0215	450	6	100.44	0.0154
Na	589.00	5	75.0	6	124.56	0.0859	7500	6	83.07	0.0248
Ni	231.60	0.3	4.50	5	102.93	0.0475	450	6	110.59	0.0080
Ni[2]	231.60	0.2	4.50	5	109.91	0.0047	450	6	101.77	0.0139
P	214.92	2	30.0	5	81.82	0.0511	3000	6	107.20	0.0103
P[2]	214.91	2	30.0	5	86.36	0.0077	3000	6	103.33	0.0174
Pb	220.35	1	15.0	5	95.85	0.0308	1500	6	100.54	0.0154
Pt	203.65	9	150	5	104.67	0.0182	15000	6	105.19	0.0088
Sb[3]	206.84	0.7	15.0	6	25.29	0.5861	1500	6	111.95	0.0086

(1) Values reported were obtained with a Fisons ARL Accuris ICP-AES unless otherwise noted; performance may vary with instrument and should be independently verified.
(2) Values reported were obtained with a Perkin Elmer Optima 3000 DV ICP-AES.
(3) Elements that were evaluated and found not suitable for analysis by this method.
(4) Values given (lower level) are for the 10xLOQ level due to low recoveries at the 3xLOQ level.
(5) LOQ = Estimated limit of quantitation

Table 3. MEASUREMENT WAVELENGTHS AND RECOVERY DATA

			Lower Level[4,5]				Higher Level[5]			
Element[1]	Wavelength (nm)	LOD (µg/ sample)	µg/ sample	N =	Percent Recovery	Precision (S_r)	µg/ sample	N =	Percent Recovery	Precision (S_r)
Se	196.09	5	75.0	5	102.05	0.0531	7500	6	111.35	0.0063
Se[2]	196.02	2	75.0	5	99.93	0.0051	7500	6	99.72	0.0082
Sn	189.9		75.0	5	30.82	0.0502	7500	6	79.56	0.0124
Sn[2,3]	189.9	0.4	75.0	5	37.87	0.0816	7500	6	92.34	0.0129
Sr	421.55	0.04	7.50	5	100.00	0.0049	750	6	99.54	0.0055
Te	214.27	4	30.0	5	95.80	0.0624	3000	6	110.81	0.0094
Te[2]	214.28	2	30.0	5	97.18	0.0100	3000	6	99.64	0.0074
Ti	337.28	0.2	3.00	5	81.66	0.0392	300	6	103.42	0.0101
Ti[3]	334.94	0.1	3.00	5	82.68	0.0374	300	6	96.13	0.0121
Tl	190.86	2	15.0	5	96.38	0.0605	1500	6	97.25	0.0148
Tl[3]	190.79	1	15.0	5	97.75	0.0032	1500	6	92.04	0.0119
V	292.40	0.1	1.50	5	104.54	0.0528	150	6	111.15	0.0160
V[2]	292.40	0.09	1.50	5	100.99	0.0146	150	6	99.38	0.0232
Y	371.03	0.07	0.752	5	105.98	0.0245	75.2	6	105.03	0.0073
Zn	213.85	0.2	3.00	5	110.76	0.0327	300	6	116.84	0.0153
Zn[2]	213.86	0.4	3.00	5	93.45	0.0351	300	6	94.01	0.0055
Zr	339.20	0.2	1.50	5	102.61	0.0242	150	6	101.56	0.0144

(1) Values reported were obtained with a Fisons ARL Accuris ICP-AES unless otherwise noted; performance may vary with instrument and should be independently verified.
(2) Values reported were obtained with a Perkin Elmer Optima 3000 DV ICP-AES.
(3) Elements that were evaluated and found not suitable for analysis by this method.
(4) Values given (lower level) are for the 10xLOQ level due to low recoveries at the 3xLOQ level.
(5) LOQ = Estimated limit of quantitation

Table 4. OVERALL PRECISION AND ACCURACY DATA [13]

Element	Instrument[1]	Range Studied (µg/sample)		Bias	Range of Bias		Precision S_{rT}	Accuracy (%)	Lowest Level[2]
		From	To		From	To			
Aluminum	Fisons	5.025	1500	-0.0318	-0.1022	0.0240	0.0419	9.9	50.25
Aluminum	P-E Optima	5.025	1500	0.0833	0.0567	0.1505	0.0379	15.1	15
Antimony	Fisons	5.025	1500	Poor and variable recoveries across study range.					
Arsenic	Fisons	5.025	1500	0.0630	-0.0671	0.1584	0.0461	14.3	15
Barium	Fisons	0.5038	150.4	0.0433	0.0222	0.0716	0.0182	7.6	0.5
Beryllium	Fisons	0.0509	15.2	0.0652	0.0366	0.0980	0.0163	9.5	0.0509
Boron	Fisons	2.514	750.4	-0.0387	-0.1362	0.0118	0.0164	6.4	7.504
Cadmium	Fisons	1.005	300.0	0.0923	0.0718	0.1167	0.0307	14.8	1.005
Calcium	Fisons	15.08	4500	0.0779	-0.0536	0.1624	0.0313	13.4	150.75
Calcium	P-E Optima	15.08	4500	0.0453	0.0098	0.0963	0.0245	8.8	15.08
Chromium	Fisons	2.514	750.4	0.1395	0.0974	0.1865	0.0214	18	2.514
Chromium	P-E Optima	2.514	750.4	-0.0018	-0.0701	0.1245	0.0131	<5	2.514
Cobalt	Fisons	2.514	750.4	0.0592	-0.1013	0.1508	0.0264	10.4	7.504
Copper	Fisons	0.5038	150.4	0.0475	0.0272	0.0684	0.0240	8.9	0.5038
Copper	P-E Optima	0.5038	150.4	0.0829	0.0313	0.1716	0.0217	12.1	1.504
Iron	Fisons	10.05	3000	0.1101	0.0630	0.2057	0.0397	18.6	30
Iron	Fisons	10.05	3000	0.0836	0.0630	0.0974	0.0396	15.4	100.5
Iron	P-E Optima	10.05	3000	0.0445	-0.0205	0.1255	0.0404	11.4	30
Lead	Fisons	5.025	1500	-0.0241	-0.0668	0.0124	0.0279	6.9	5.025
Lithium	Fisons	0.5038	150.4	-0.0690	-0.1804	0.0132	0.0276	11.1	0.5038
Magnesium	Fisons	5.025	1500	0.0156	-0.0253	0.0524	0.0171	<5	5.025
Magnesium	P-E Optima	5.025	1500	0.0715	0.0421	0.1372	0.0249	11.5	5.025
Manganese	Fisons	0.5038	150.4	0.1357	0.1005	0.1755	0.0201	17.3	0.5038
	Fisons	1.509	450.4	-0.0388	-0.1597	0.1353	0.0795	16.7	1.509
	P-E Optima	1.509	450.4	-0.0489	-0.2033	0.0969	0.0179	7.7	1.509
Nickel	Fisons	1.509	450.4	0.0787	0.0293	0.1274	0.0338	13.8	4.504
Nickel	P-E Optima	1.509	450.4	0.0645	0.0177	0.1406	0.0159	9.2	1.509
Phosphorus	Fisons	10.05	3000	-0.0546	-0.1818	0.0011	0.0417	12	30
Phosphorus	P-E Optima	10.05	3000	-0.0163	-0.1364	0.0333	0.0124	<5	10.05
Platinum	Fisons	50	15000	0.0423	0.0097	0.0671	0.0226	8.2	150
Potassium	Fisons	10.05	3000	-0.0909	-0.1443	-0.0316	0.0265	13.1	100.5
Potassium	P-E Optima	10.05	3000	-0.0499	-0.0998	-0.0060	0.0249	8.8	100.5
Selenium	Fisons	25.12	7500	0.0941	0.0675	0.1150	0.0150	12.1	25.12
Selenium	P-E Optima	25.12	7500	0.0026	-0.0027	0.0115	0.0127	<5	25.12
Silver	Fisons	1.005	300	Poor and variable recoveries across study range.					
Sodium	Fisons	25.12	7500	-0.0492	-0.1694	0.0718	0.0246	8.8	251.2
Strontium	Fisons	2.514	750.4	0.0172	-0.00002	0.0373	0.0153	<5	2.514
Tellurium	Fisons	10.05	3000	0.0295	-0.0420	0.1037	0.0404	9.8	30

(1) Values reported were obtained with a Fisons ARL Accuris ICP-AES or a Perkin Elmer Optima 3000 DV ICP-AES.
(2) Lowest level in range studied at which recoveries were between 81 and 121% recovery and relative standard deviation (S_r) less than 0.1100 on 5 or 6 replicates. Performance may vary with instrument and should be independently verified.

Table 4. OVERALL PRECISION AND ACCURACY DATA [13]

Element	Instrument[1]	Range Studied (µg/sample)		Bias	Range of Bias		Precision S_{rT}	Accuracy (%)	Lowest Level[2]
		From	To		From	To			
Tellurium	P-E Optima	10.05	3000	-0.0043	-0.0282	0.0163	0.0155	<5	10.05
Thallium	Fisons	5.025	1500	-0.0081	-0.0362	0.0334	0.0407	8.2	15
Thallium	P-E Optima	5.025	1500	-0.0505	-0.0688	-0.0048	0.0250	9	5.025
Tin	Fisons	25.12	7500	Poor and variable recoveries across study range.					
Tin	P-E Optima	25.12	7500	Poor and variable recoveries across study range.					
Titanium	Fisons	1.005	300	-0.0827	-0.1834	0.0342	0.0269	12.3	3
Titanium	P-E Optima	1.005	300	-0.1072	-0.1732	-0.0387	0.0321	15.3	1.005
Vanadium	Fisons	0.5038	150.4	0.0704	0.0438	0.1114	0.0195	10.5	0.5038
Vanadium	P-E Optima	0.5038	150.4	-0.0063	-0.0217	0.0099	0.0198	<5	0.5038
Yttrium	Fisons	0.2519	75.2	0.0598	0.0466	0.0795	0.0164	8.9	0.2519
Zinc	Fisons	1.005	300	0.1452	0.0630	0.2976	0.0340	22	1.005
Zinc	Fisons	1.005	300	0.1190	0.0630	0.1683	0.0356	18.7	3
Zinc	P-E Optima	1.005	300	-0.0502	-0.0655	-0.0388	0.0295	9.6	3
Zirconium	Fisons	0.5025	150	0.0164	-0.0096	0.0350	0.0175	<5	0.5025

(1) Values reported were obtained with a Fisons ARL Accuris ICP-AES or a Perkin Elmer Optima 3000 DV ICP-AES.
(2) Lowest level in range studied at which recoveries were between 81 and 121% recovery and relative standard deviation (S_r) less than 0.1100 on 5 or 6 replicates. Performance may vary with instrument and should be independently verified.

ELEMENTS by Cellulosic Internal Capsule Sampler

AW: Table 1 | CAS: Table 2 | RTECS: Table 2

METHOD: 7306, Issue 1 | **EVALUATION: FULL** | **Issue 1: 10 September 2015**

OSHA PELs: Table 2
NIOSH RELs: Table 2
OTHER OELs: [1,2]

PROPERTIES: Table 1

ELEMENTS:

aluminum	cadmium	indium	magnesium	potassium	tellurium	yttrium
antimony	calcium	iron	manganese	selenium	thallium	zirconium
arsenic	chromium	lanthanum	molybdenum	silver	titanium	zinc
barium	cobalt	lead	nickel	strontium	tungsten	
beryllium	copper	lithium	phosphorus	tin	vanadium	

SAMPLING

SAMPLER: Internal capsule, cellulose acetate dome with inlet opening, attached to 0.8-µm pore size mixed cellulose ester (MCE) membrane filter and housed within a 2-piece, closed-face cassette (CFC) filter holder, 37-mm diameter

FLOWRATE: 1 to 4 L/min

VOL-MIN: Table 1
-MAX: Table 1

SHIPMENT: Routine

SAMPLE STABILITY: Stable

BLANKS: Minimum of 2 field blanks per set

ACCURACY

RANGES STUDIED: Tables 3 and 4

BIAS: Table 4

OVERALL PRECISION ($\hat{S}_{rt}$) Table 4

ACCURACY: Table 4

MEASUREMENT

TECHNIQUE: INDUCTIVELY COUPLED PLASMA – ATOMIC EMISSION SPECTROMETRY (ICP-AES)

ANALYTES: Elements above

SAMPLE DISSOLUTION: Hotplate digestion (NIOSH 7300 or 7301), microwave digestion (NIOSH 7302) or hot block extraction (NIOSH 7303)

SOLUTION: Dependent upon sample preparation method

WAVELENGTH: Depends upon element; See Table 3

BACKGROUND CORRECTION: Spectral wavelength shift

CALIBRATION: Elements in acid matrix-matched to the sample; varies depending on sample preparation method

RANGE: Varies with element

ESTIMATED LOD: Table 3

PRECISION ($\bar{S}_r$): Table 4

APPLICABILITY: The working range of this method is 4×10^{-5} mg/m^3 to 10 mg/m^3 for each element in a 500-L air sample. This is simultaneous elemental analysis, not compound specific. Verify that the types of compounds in the samples are soluble with the dissolution procedure selected. Some compounds of these elements require special sample treatment.

INTERFERNCES: Spectral interferences are the primary interferences encountered in ICP-AES analysis. These are minimized by judicious wavelength selection, interelement correction factors and background correction [3,4].

OTHER METHODS: The internal capsule sampler used in this method is a recommended alternative to filter-only sampling [5] of NIOSH methods 7300 [6], 7301 [7], 7302 [8] and 7303 [9]. Use of an internal capsule sampler is an efficient means to account for sampler wall deposits that would otherwise be excluded by filter-only sampling. Unless other means are used to account for non-filter deposits inside the cassettes (e.g. within-cassette extraction, rinsing or wiping), internal capsule samplers should be used. OSHA method ID-125G [10] describes ICP-AES multielement analysis after hotplate digestion using nitric acid, sulfuric acid and hydrogen peroxide. ASTM D7035 [11] and ISO 15202 [12] are related voluntary consensus standard ICP-AES methods for multielement sampling and analysis of workplace atmospheres.

REAGENTS:

1. Nitric acid (HNO_3)*, concentrated, Trace metal grade
2. Hydrochloric acid (HCl)*, conc., Trace metal grade (only required if hydrochloric acid digestion is to be carried out)
3. Perchloric acid ($HClO_4$)*, conc., optima (only required if perchloric acid digestion is to be carried out)
4. Calibration stock solutions, 1000 µg/L: Commercially available; or prepared per instrument manufacturer's recommendation
5. Dilution acid: 20% nitric acid* (7302); 4% nitric acid:1% perchloric acid* (7300); 5% aqua regia (7301)*; or 5% nitric acid: 5% hydrochloric acid* (7303) [dilution acid is dependent upon sample preparation method used]
6. Argon, as specified by ICP-AES manufacturer
7. Deionized water, ASTM Type II [13] or equivalent

* See SPECIAL PRECAUTIONS

EQUIPMENT:

1. Sampler: cellulose acetate internal capsule attached to mixed cellulose ester membrane filter, 0.8-µm pore size; 37-mm diameter, in 2-piece, closed-face cassette filter holder
2. Personal sampling pump, 1 to 4 L/min, with flexible connecting tubing, capable of maintaining constant flow
3. Inductively coupled plasma-atomic emission spectrometer, equipped as specified by the manufacturer for analysis of elements of interest
4. Regulator, two-stage, for argon
5. Beakers, Phillips, 125-mL, or Griffin, 50-mL, with watch glass covers**
6. Volumetric flasks, 10-, 25-, 100-mL, and 1-L**
7. Assorted volumetric pipets, as needed**
8. Forceps, plastic or plastic-tipped
9. Hotplate (NIOSH 7300 or 7301), microwave oven (NIOSH 7302) or hot block (NIOSH 7303) [6-9].
10. Centrifuge tubes, 50-mL or sized appropriately for hot block apparatus.

** Clean all glassware with conc. nitric acid and rinse thoroughly in deionized water before use

SPECIAL PRECAUTIONS: All perchloric acid digestions must be carried out in a perchloric acid fume hood. When working with concentrated acids, wear protective clothing, safety goggles and gloves. All work should be performed with adequate ventilation for personnel and equipment. It is imperative that acid be added to water in order to avoid a violent exothermic reaction.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
   NOTE: See NMAM guidance chapters for discussion on sampling.
2. Sample at an accurately known flow rate between 1 and 4 L/min (± 5%) for a total sample size of <1 to 2000 L (see Table 1) for TWA measurements. Do not exceed a sampler loading of approximately 5 mg total dust.
   NOTE: Filter overloading can be assessed by periodic visual checks. See NMAM guidance chapters for additional discussion on filter capacity.

SAMPLE PREPARATION:

3. Open the cassette filter holders and, using nonmetal forceps, transfer the samples and blanks to clean digestion vessels.
   NOTE: Samples may not easily fit into the digestion vessels. Care must be taken to ensure no sample is lost during the placement of the samples in the digestion vessels.

4. Carry out sample dissolution in accordance with one of the sample preparation procedures described in NIOSH 7300, 7301, 7302, or 7303 [6-9].
   NOTE: The dissolution acid level within the vessel should cover the internal capsule.
5. After allowing to cool to room temperature, transfer the solutions quantitatively to 25-mL volumetric flasks.
6. Dilute to volume.
   NOTE: If greater sensitivity is required, the final sample volume may be held to 10 mL.

CALIBRATION AND QUALITY CONTROL:

7. Calibrate the spectrometer according to the manufacturer recommendations.
   NOTE: Typically, an acid blank and 1.0 µg/mL multielement calibration standards are used.
   The following multielement combinations are chemically compatible in 5% HNO_3:
   a. Al, As, Ba, Be, Ca, Cd, Co, Cr, Cu, Fe, La, In, Na
   b. Ag, K, Li, Mg, Mn, Ni, P, Pb, Se, Sr, Tl, V, Y, Zn, Sc
   c. Mo, Sb, Sn, Te, Ti, W, Zr
8. Analyze at least one calibration standard per ten samples.
9. Check recoveries with at least one media blank and two spiked media blanks per twenty samples. Media should be spiked with analytes of interest.
   NOTE: Whenever possible, QA/QC samples should be prepared from certified reference materials in a matrix similar to the bulk material sampled. Liquid spiked filters are only surrogates for real world samples and QC data based upon certified samples are preferred.

MEASUREMENT:

10. Set ICP-AES spectrometer to conditions specified by manufacturer.
11. Analyze standards and samples by ICP-AES in accordance with manufacturer recommendations.
    NOTE: If the values for the samples are above the range of the standards, dilute the solutions (ensuring the samples remain acid matrix-matched to the calibration standards), reanalyze and apply the appropriate dilution factor in the calculations.

CALCULATIONS:

12. Obtain the solution concentrations for the sample, C_s (µg/mL), and the average media blank , C_b (µg/mL), from the instrument.
13. Using the solution volumes of sample, V_s (mL), and media blank, V_b (mL), calculate the concentration, C mg/m^3), of each element in the air volume sampled, V (L):

$$C = \frac{(C_s V_s) - (C_b V_b)}{V} \quad , \text{mg/m}^3$$

NOTE: µg/L is approximately equal to mg/m^3

EVALUATION OF METHOD:

A previous interlaboratory investigation of aerosol-loaded cellulosic capsules (provided by SKC, Inc., Eighty-Four, PA) provided the background information for the development of this method [14]. That investigation yielded data for Cd, Cr, Co, Cu, Fe, Mn, Ni and Pb [14]. Recoveries for these elements were quantitative and values of overall relative standard deviation were <0.20 [14], which compare favorably with the variability typically observed in interlaboratory multielement analysis of air samples [15,16].
To obtain performance data for additional elements, interlaboratory performance data were obtained using 37-mm diameter cellulose acetate internal capsules attached to mixed-cellulose ester filters (Solu-sert™ from

Zefon International, Ocala, FL). Solu-sert™ capsules were dosed with 33 elements at three different spiking levels (spike levels certified by High-Purity Standards, North Charleston, SC), listed in Table 3. Sets of the spiked samples were conveyed to participating volunteer laboratories and analyzed by ICP-AES after sample dissolution. A variety of sample preparation procedures were used by the labs including NIOSH 7300, 7301, 7302, 7303, hot plate digestion utilizing nitric acid, sulfuric acid and hydrogen peroxide (modified NIOSH 7300), and microwave assisted digestion using nitric acid and hydrogen peroxide (modified NIOSH 7302). Results were received from 9 laboratories; however, not every spiked element was reported by each laboratory. Individual sample results may be found in the backup data report [17]. Statistical calculations were performed using SAS Software (version 9.2, SAS Institute Inc., Cary, NC). For each data subset, Grubbs' test at 1% confidence level was used to identify outliers, which if identified, were removed prior to further statistical calculations. No statistically significant differences were found between the laboratory results for the spiked samples; therefore, all reported data (regardless of the sample preparation method) are included in Tables 3 & 4. Recoveries were quantitative (as defined in Kennedy, et al. [18]) and interlaboratory variability was <0.20 for most elements and loading levels (Table 3). Mean overall recoveries below 90% were found only for Cr, K, and W at low loadings and for Ag at medium and high spike levels and for In at the high spike level. RSD values > 0.20 were found only for Sn at the low spike level, Ag at medium and high spike levels, and In and K at all loadings. Results for precision, bias and accuracy are summarized in Table 4.

With the domed top, the internal capsule can be difficult to fit into standard sample digestion vessels. One way to achieve this is to place the samplers into the vessels by bending them slightly inward (using coated forceps) and to push them into the bottom of the vessel to ensure they are covered with the digestion acids. Care must be taken to ensure that sample is not lost in this process. Additional guidance is available from the internal capsule manufacturer [19].

While no statistically significant differences were found based upon the sample preparation, it is important to note that interlaboratory variation is included in those calculations. Some differences in the sample preparation methods may have been statistically significant without that variability. Of particular importance are the less than quantitative recoveries for Sb, Sn, and Ti using NIOSH 7300. This sample preparation (as written) may not be amenable to the analysis of those elements. While this method lists several options for sample preparation, it is imperative that the suitability of the particular sample preparation method for the analytes of interest be considered.

Appreciable (>0.5 µg) media background levels were reported by Certified Reference Material (CRM) provider and/or the participating laboratories for several elements, notably Al, Ca, Cr, Fe, In, K, Mg, P, Sb, Se, and Tl. Trace media background levels of a few other elements, i.e., Ba, Cu and Zn, were also obtained. This background was effectively corrected for, as evidenced by the quantitative recoveries obtained for the vast majority of the elements and loading levels. Where the background levels may pose a greater influence is in the calculation of the method LOD. Method LODs (calculated using the standard deviation of blank responses) for internal capsule samples were greater than those calculated for MCE filters alone for many of the elements [17]. Care should be taken in choosing the appropriate media in concert with the expected sample concentrations.

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METHOD WRITTEN BY:
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TABLE 1. PROPERTIES AND SAMPLING VOLUMES [21]

Element (Symbol)	Atomic Weight (AW)	MP, °C	Volume, L @ OSHA PEL[A]	
			MIN[B]	MAX[C]
Silver (Ag)	107.87	961	6	>2000[D]
Aluminum (Al)	26.98	660	<1	330
Arsenic (As)	74.92	817	32	>2000
Barium (Ba)	137.34	727	3	>2000
Beryllium (Be)	9.01	1287	10	>2000
Calcium (Ca)	40.08	842	--	--
Cadmium (Cd)	112.41	321	3	>2000
Cobalt (Co)	58.93	1495	<1	>2000
Chromium (Cr)	52.00	1907	1	>2000
Copper (Cu)	63.54	1083	<1	>2000
Iron (Fe)	55.85	1538	2	500
Indium (In)	114.82	156	8	>2000
Potassium (K)	39.10	64	--	--
Lanthanum (La)	138.91	920	--	--
Lithium (Li)	6.94	181	--	--
Magnesium (Mg)	24.31	651	<1	330
Manganese (Mn)	54.94	1246	<1	1000
Molybdenum (Mo)	95.94	2623	<1	330
Nickel (Ni)	58.71	1455	2	>2000
Phosphorus (P)	30.97	44	9	>2000
Lead (Pb)	207.19	328	4	>2000
Antimony (Sb)	121.75	631	1	>2000
Selenium (Se)	78.96	221	2	>2000
Tin (Sn)	118.69	232	<1	>2000
Strontium (Sr)	87.62	777	--	--
Tellurium (Te)	127.60	450	7	>2000
Titanium (Ti)	47.87	1668	--	--
Thallium (Tl)	204.37	304	1	>2000
Vanadium (V)	50.94	1910	--	--
Tungsten (W)	183.85	3422	--	--
Yttrium (Y)	88.91	1522	<1	>2000
Zinc (Zn)	65.37	419	--	--
Zirconium (Zr)	91.22	1855	<1	1000

[A] Exposure limits listed in Table 2.
[B] Min calculated using the method quantitation limits following NIOSH 7302 sample preparation.
[C] Max calculated using 5 mg of sample collected.
[D] Indicates that the calculated maximum volume is greater than the volume collected at the maximum flow rate (4 L/min) of the method for an 8-hour shift.

TABLE 2. EXPOSURE LIMITS, CAS#, RTECS [22]

Element (Symbol)	CAS #	RTECS #	Exposure Limits	
			OSHA PEL (mg/m^3)	NIOSH REL (mg/m^3)
Silver (Ag)	7440-22-4	VW3500000	0.01 (dust, fume, metal)	0.01 (metal, soluble)
Aluminum (Al)	7429-90-5	BD0330000	15 (total dust) 5 (respirable)	10 (total dust) 5 (respirable fume) 2 (soluble)
Arsenic (As)	7440-38-2	CG0525000	0.010	C[E] 0.002 (15 min), Ca[F] 0.5
Barium (Ba)	7440-39-3	CQ8370000	0.5	
Beryllium (Be)	7440-41-7	DS1750000	0.002, C 0.005	C 0.0005, Ca
Calcium (Ca)	7440-70-2	--	--	--
Cadmium (Cd)	7440-43-9	EU9800000	0.005	lowest feasible, Ca
Cobalt (Co)	7440-48-4	GF8750000	0.1 (dust, fume)	0.05 (dust, fume)
Chromium (Cr)	7440-47-3	GB4200000	1 (metals, insoluble salts) 0.5 (Cr II & Cr III)	0.5
Copper (Cu)	7440-50-8	GL5325000	1 (dust, mists) 0.1 (fume)	1 (dust, mists) 0.1 (fume)
Iron (Fe)	7439-89-6	NO4565500	10 (fume) as oxide	5 (dust, fume) oxide as Fe
Indium (In)	7440-74-6	NL1050000	0.1	0.1
Potassium (K)	7440-09-7	TS6460000	--	--
Lanthanum	7439-91-0	--	–	–
Lithium (Li)	7439-93-2	OJ5540000	--	--
Magnesium (Mg)	7439-95-4	OM2100000	15 (dust) as oxide	--
Manganese (Mn)	7439-96-5	OO9275000	C 5	C 1; STEL[G] 3
Molybdenum (Mo)	7439-98-7	QA4680000	5 (soluble) 15 (total insoluble dust)	--
Nickel (Ni)	7440-02-0	QR5950000	1	0.015, Ca
Phosphorus (P)	7723-14-0	TH3500000	0.1	0.1
Lead (Pb)	7439-92-1	OF7525000	0.05	0.05
Antimony (Sb)	7440-36-0	CC4025000	0.5	0.5
Selenium (Se)	7782-49-2	VS7700000	0.2	0.2
Tin (Sn)	7440-31-5	XP7320000	2	2
Strontium (Sr)	7440-24-6	WK7700000	–	–
Tellurium (Te)	13494-80-9	WY2625000	0.1	0.1
Titanium (Ti)	7440-32-6	XR1700000	15 as dioxide	Ca as the oxide
Thallium (Tl)	7440-28-0	XG3425000	0.1 (skin) (soluble)	0.1 (skin) (soluble)
Vanadium (V)	7440-62-2	YW1355000	C 0.5 (respirable) as pentoxide	C 0.05 as pentoxide
Tungsten (W)	7440-33-7	YO7175000	--	5; STEL 10
Yttrium (Y)	7440-65-5	ZG2980000	1	1
Zinc (Zn)	7440-66-6	ZG8600000	5 (fume, respirable dust) as oxide 15 (total dust) as oxide	5 (dust, fume) as oxide C 15 (dust) as oxide STEL 10 (fume) as oxide
Zirconium (Zr)	7440-67-7	ZH7070000	5	5; STEL 10

[E] C: ceiling

[F] Ca: carcinogen

[G] STEL: short-term exposure limit

TABLE 3. MEASUREMENT WAVELENGTHS (λ), DETECTION LIMITS (LOD) AND RECOVERY DATA FROM INTERLABORATORY RESULTS

Element	Wavelength[H] (λ), nm	LOD[I] (ug/sample)	Low Level (ug/sample)	% Recovery (%RSD; N[J])	Medium level (ug/ sample)	% Recovery (%RSD; N[J])	High Level (ug/ sample)	% Recovery (%RSD; N[J])
Ag	328.068	0.020	5.0	93.2 (17; 7)	10.1	83.5 (26; 7)	20.1	68.2 (52; 7)
Al	396.152	0.38	10.6	95.7 (6.1; 7)	30.9	95.7 (3.1; 7)	60.8	96.2 (2.4; 7)
As	189.042	0.099	5.0	99.4 (7.3; 7)	20.2	103 (5.3; 8)	40.1	102 (5.8; 8)
Ba	455.404	0.55	2.21	97.0 (8.4; 8)	7.3	96.9 (2.5; 7[K])	15.2	99.9 (5.0; 8)
Be	313.042	0.0064	2.01	101 (4.4; 9)	7.0	101 (6.8; 9)	14.9	100 (5.1; 9)
Ca	315.887	3.9	114	95.8 (16; 8)	165	97.4 (15; 8)	215	95.8 (13; 8)
Cd	226.502	0.0052	2.01	101 (3.6; 9)	7.0	101 (4.0; 9)	14.9	102 (1.9; 8)
Co	228.616	0.0090	2.01	103 (6.8; 9)	7.0	102 (5.7; 9)	14.9	102 (5.8; 9)
Cr	267.716	0.28	2.91	80.2 (16; 8)	7.9	96.3 (7.2; 9)	15.8	97.2 (3.5; 9)
Cu	324.754	0.15	3.16	100 (4.5; 8[K])	15.1	101 (4.0; 9)	29.9	100 (3.2; 9)
Fe	259.941	5.3	21.3	107 (15; 9)	41.0	104 (5.5; 9)	80.5	103 (5.4; 9)
In	230.606	0.26	5.0	92.1 (33; 5)	14.9	90.8 (27; 5[K])	39.7	86.2 (32; 5)
K	766.491	0.70	10.6	89.0 (36; 5)	15.7	98.0 (24; 6)	20.7	106 (20; 6)
La	408.672	0.026	3.01	101 (8.1; 4)	10.1	102 (7.2; 4)	20.1	99.9 (7.9; 4)
Li	670.780	0.010	2.01	93.0 (8.5; 7)	7.0	94.9 (7.0; 7)	14.9	98.6 (5.2; 7)
Mg	279.079	1.1	12.7	93.9 (16; 7)	27.9	98.7 (9.1; 7)	103	101 (7.2; 7)
Mn	294.921	0.031	2.01	99.8 (7.6; 9)	7.0	100 (6.1; 9)	14.9	100 (5.7; 9)
Mo	202.095	0.021	2.01	101 (6.2; 9)	7.1	102 (4.8; 9)	15.0	102 (5.2; 9)
Ni	231.604	0.56	2.01	108 (9.6; 9)	7.0	104 (7.4; 9)	14.9	103 (7.0; 9)
P	178.287	0.27	10.1	104 (9.0; 5)	24.9	103 (8.9; 6)	99	102 (1.7; 5[K])
Pb	220.353	0.062	10.0	101 (6.2; 9)	25.2	100 (5.3; 9)	100	100 (7.3; 9)

[H] Commonly used wavelength; choose wavelength appropriate for your instrument settings [3,4]

[I] LOD values calculated using the responses of 7 media blanks, prepared following the microwave sample preparation in NIOSH 7302

[J] Mean recovery & relative standard deviation for N = number of laboratories reporting results for each element

[K] Excludes outlier(s) (Grubbs' test)

Table 3 continued from page 9

TABLE 3. MEASUREMENT WAVELENGTHS (λ), DETECTION LIMITS (LOD) AND RECOVERY DATA FROM INTERLABORATORY RESULTS

Element	Wavelength[H] (λ), nm	LOD[I] (ug/sample)	Low Level (ug/sample)	% Recovery (%RSD; N[J])	Medium level (ug/ sample)	% Recovery (%RSD; N[J])	High Level (ug/ sample)	% Recovery (%RSD; N[J])
Sb	206.833	0.11	5.0	99.1 (6.7; 8)	25.1	99.0 (5.7; 9)	40.2	100 (3.6; 8[K])
Se	196.090	0.14	3.0	112 (15; 6)	15.1	109 (8.7; 8)	30.1	104 (10; 8)
Sn	189.991	0.065	2.01	98.7 (26; 4)	7.0	96.9 (18; 6)	14.9	103 (5.0; 5[K])
Sr	407.771	0.014	2.01	100 (1.9; 6[K])	7.1	102 (7.5; 7)	15.0	101 (6.1; 7)
Te	214.281	0.22	3.0	104 (18; 5)	12.6	103 (7.7; 5)	20.1	101 (12; 5)
Ti	334.941	0.042	2.01	105 (5.7; 7)	7.0	101 (10; 7)	14.9	103 (3.4; 6[K])
Tl	190.864	0.046	3.0	102 (7.1; 6)	10.1	99.6 (5.8; 7)	20.1	98.3 (7.5; 7)
V	311.071	0.0091	3.02	101 (5.7; 9)	7.0	102 (6.2; 9)	14.9	102 (5.8; 9)
W	207.911	0.055	10.1	83.0 (12; 5)	25.1	97.6 (12; 5)	40.2	96.4 (16; 5)
Y	371.030	0.0039	2.01	101 (3.8; 5)	7.1	102 (5.9; 5)	15.0	101 (4.8; 5)
Zn	213.856	0.69	5.2	101 (6.0; 9)	25.1	101 (4.9; 9)	59.7	101 (4.8; 9)
Zr	339.198	0.0099	2.01	101 (6.2; 5)	7.0	99.5 (9.2; 6)	14.9	93.1 (19; 6)

[H] Commonly used wavelength; choose wavelength appropriate for your instrument settings [3,4]

[I] LOD values calculated using the responses of 7 media blanks, prepared following the microwave sample preparation in NIOSH 7302

[J] Mean recovery & relative standard deviation for N = number of laboratories reporting results for each element

[K] Excludes outlier(s) (Grubbs' test)

TABLE 4. RANGE, BIAS, PRECISION ($\overline{S}_r$ and $\hat{S}_{rT}$) AND ACCURACY DATA FROM INTERLABORATORY RESULTS

Element	n[L]	Range, ug/sample	Bias	$\overline{S}_r$[M]	$\hat{S}_{rT}$[N]	Accuracy (%)
Ag	21	5.0 to 20.1	-0.184	0.041	0.065	29.0
Al	21	10.6 to 60.8	-0.0414	0.006	0.050	12.4
As	23	5.0 to 40.1	0.0141	0.016	0.052	10.7
Ba	23	2.21 to 15.2	-0.0206	0.036	0.062	12.8
Be	27	2.01 to 14.9	0.00536	0.025	0.056	11.0
Ca	24	114 to 215	-0.0367	0.001	0.050	11.9
Cd	26	2.01 to 14.9	0.0133	0.022	0.055	11.1
Co	27	2.01 to 14.9	0.0238	0.036	0.062	12.9
Cr	26	2.91 to 15.8	-0.0281	0.046	0.068	14.4
Cu	26	3.16 to 29.9	0.00347	0.017	0.053	10.4
Fe	27	21.3 to 80.5	0.0476	0.011	0.051	13.2
In	15	5.0 to 39.7	-0.103	0.056	0.075	22.6
K	17	10.6 to 20.7	-0.0239	0.029	0.058	12.3
La	12	3.01 to 20.1	0.0119	0.025	0.056	11.2
Li	21	2.01 to 14.9	-0.0447	0.039	0.064	14.9
Mg	21	12.7 to 103	-0.0219	0.012	0.051	10.9
Mn	27	2.01 to 14.9	0.00127	0.039	0.063	12.4
Mo	27	2.01 to 15.0	0.0169	0.032	0.060	12.1
Ni	27	2.01 to 14.9	0.0498	0.055	0.074	17.2
P	16	10.1 to 99	0.0310	0.010	0.051	11.5
Pb	27	10.0 to 100	0.00439	0.006	0.050	9.9
Sb	25	5.0 to 40.2	-0.00631	0.013	0.052	10.2
Se	22	3.0 to 30.1	0.0864	0.055	0.075	20.9
Sn	15	2.01 to 14.9	-0.00541	0.117	0.128	25.0
Sr	20	2.01 to 15.0	0.00930	0.011	0.051	10.2
Te	15	3.0 to 20.1	0.0256	0.063	0.081	16.6
Ti	20	2.01 to 14.9	0.0305	0.032	0.059	13.1
Tl	20	3.0 to 20.1	0.00128	0.030	0.058	11.4
V	27	3.02 to 14.9	0.0143	0.020	0.054	10.9
W	15	10.1 to 40.2	-0.0240	0.010	0.051	11.0
Y	15	2.01 to 15.0	0.00971	0.020	0.054	10.7
Zn	27	5.2 to 59.7	0.00873	0.013	0.052	10.3
Zr	17	2.01 to 14.9	-0.0206	0.033	0.060	12.4

[L] n = total number of results reported for each element by up to 9 participating laboratories minus outliers (Grubbs' test, 1% confidence level)

[M] $\overline{S}_r$ = precision [17]

[N] $\hat{S}_{rT}$ = overall precision = $\sqrt{\overline{S}_r^{\,2} + (0.05)^2}$; same as total precision as defined in [18,20]

ZINC OXIDE 7502

ZnO MW: 81.38 CAS: 1314-13-2 RTECS: ZH4810000

METHOD: 7502, Issue 3 **EVALUATION: FULL** **Issue 1: 15 February 1984**
Issue 3: 20 October 2015

OSHA: 5 mg/m³ (fume, resp dust); 15 mg/m³ (total dust)
NIOSH: 5 mg/m³, C 15 mg/m³ (15 min) (dust); 5 mg/m³, STEL 10 mg/m³ (fume)

PROPERTIES: Solid; d 5.61 g/cm³ @ 25 °C; MP 1975 °C

SYNONYMS: China white; zinc white; zincite

SAMPLING

SAMPLER: FILTER (0.8 µm PVC membrane, 25 mm diameter, in open-face cassette)

FLOW RATE: 1 L/min to 3 L/min

VOL-MIN: 10 L
-MAX: 400 L

SHIPMENT: Routine

SAMPLE STABILITY: Stable

BLANKS: 2 to 10 field blanks per set

BULK SAMPLE: High-volume air sample required

ACCURACY

RANGE STUDIED: 0.1 mg/m³ to 11 mg/m³ [1,2] (180 L samples)

BIAS: 2.7% [2,3,4]

OVERALL PRECISION ($\hat{S}_{rT}$): 0.09 [2]

ACCURACY: ±21.6%

MEASUREMENT

TECHNIQUE: X-RAY POWDER DIFFRACTION

ANALYTE: Crystalline zinc oxide; direct analysis on filter

XRD: Copper target X-ray tube; optimize for intensity; 1° slit; graphite monochromator; scintillation detector; slow step scan, 0.02 degrees per 10 seconds; integrated intensity with background subtraction

CALIBRATION: Suspensions of zinc oxide in 2-propanol

RANGE: 50 µg to 2000 µg per sample

ESTIMATED LOD: 5 µg per sample

PRECISION ($\bar{S}_r$): 0.15 @ 1 mg/m³; 0.05 for greater than 2 mg/m³

APPLICABILITY: The working range is 0.25 mg/m³ to 10 mg/m³ for a 200 L air sample. The method does not distinguish zinc oxide fume from zinc oxide dust.

INTERFERENCES: Major interferences include ferric oxide, zinc, diamminedichlorozinc, triammonium pentachlorozincate(3–), diammonium tetrachlorozincate(2–), and diammonium zinc disulfate hexahydrate; these are resolved by using alternate analyte peaks. Particle size affects intensity measurements.

OTHER METHODS: This method combines and replaces NIOSH methods P&CAM 222 [1] and S316 [5]. The criteria document contains an elemental analysis for zinc [6].

REAGENTS:

1. Zinc oxide, ACS reagent grade. Average particle size between 0.5 µm and 10 µm.
2. 2-Propanol.*
3. Desiccant.
4. Glue or tape for securing filters to XRD holders.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: polyvinyl chloride (PVC) or PVC-acrylonitrile membrane filters, 25 mm diameter, 0.8 µm pore size; three-piece filter cassette.
   NOTE: An extension cowl on the filter cassette is desirable to produce a more uniform deposit and to prevent contamination of the open-face filter during sampling.
2. Personal sampling pump, 1 L/min to 3 L/min, with flexible connecting tubing.
3. High-volume sampling pump, 10 L/min.
4. X-ray powder diffractometer equipped with copper target X-ray tube and scintillation detector.
5. Reference specimen (mica, Arkansas stone or other stable standard) for data normalization.
6. Filtration apparatus and side arm vacuum flask with 25 mm filter holders.
7. Analytical balance (0.01 mg), magnetic stirrer, ultrasonic bath or probe, volumetric pipettes and flasks, desiccator, reagent bottles with ground glass stoppers, drying oven, polyethylene wash bottle.

SPECIAL PRECAUTIONS: 2-Propanol is flammable.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Sample open-face at 1 L/min to 3 L/min for a total sample size of 10 L to 400 L. Do not exceed 2 mg total dust loading on the filter.
3. Take a high-volume (4000 L) air sample using a clean sampler and high-volume sampling pump in the same area as the personal sample(s) for qualitative identification.

SAMPLE PREPARATION:

4. Mount field samples and blanks on XRD sample holders using appropriate methods for securing the sample to the XRD holder.

CALIBRATION AND QUALITY CONTROL:

5. Prepare two suspensions of zinc oxide in 2-propanol by weighing 10 mg and 50 mg of the dry powder to the nearest 0.01 mg. Quantitatively transfer to a 1 L glass-stoppered bottle using 1 L 2-propanol.
6. Suspend the powder in 2-propanol by using an ultrasonic probe or bath for 20 min. Immediately move the flask to a magnetic stirrer with thermally-insulated top and add a stirring bar to the suspension. Cool the solution to room temperature before withdrawing aliquots.
7. Prepare a series of standard filters using the 10 mg/L and 50 mg/L suspensions. Using appropriate pipets, prepare a sufficient number of standards in triplicate to cover the analytical range (or sample range if known). Standards at 20 µg, 30 µg, 50 µg, 100 µg, 200 µg, and 500 µg are usually sufficient.

8. Mount a filter on the filtration apparatus. Place several mL 2-propanol on the filter surface. Turn off the stirrer and shake vigorously by hand. Within a few seconds of setting the bottle down, remove the lid and withdraw an aliquot from the center of the suspension. Do not adjust the volume in the pipet by expelling part of the suspension. If more than the desired aliquot is withdrawn, return all of the suspension to the bottle, rinse and dry the pipet. Transfer the aliquot from the pipet to the filter funnel, keeping the tip of the pipet near the surface of the liquid but not submerged.
9. Rinse the pipet with several mL of 2-propanol, draining the rinse into the funnel. Repeat the rinse several more times.
10. Apply vacuum and rapidly filter the suspension. Leave vacuum on until filter is dry. Do not wash down the sides of the funnel after the deposit is in place to avoid disturbing it. Transfer the filter to the XRD sample mount.
11. Perform step scans on the standards using the same diffraction peaks and instrumental conditions as for samples (step 16). The resulting intensities for standards, I_x^o, are normalized in the following procedure.
12. Determine the net count, I_r, of the reference specimen before or after each unknown, standard, or blank is scanned. Use a diffraction peak of high intensity that can be measured rapidly but reproducibly (less than 1% S_r). Select a convenient normalization scale factor, N, which is approximately equivalent to the net count for the reference specimen peak. This factor never changes and should be used for all measurements made on a particular diffractometer. Calculate and record the normalized intensity, $\hat{I}_x^o$, for the analyte or silver peaks on each sample, field blank, media blank, and standard:

$$\hat{I}_x^o = \frac{I_x^o}{I_r} N.$$

NOTE: Normalizing to the reference specimen intensity compensates for long-term drift in X-ray tube intensity. If intensity measurements are stable, the reference specimen may be run less frequently. In this case, the net intensities of the analyte, I_x, should be normalized to the most recently measured reference intensity.

13. Prepare a calibration graph ($\hat{I}_x^o$ vs. W µg of analyte).
NOTE: Poor reproducibility at any given level indicates problems in the sample preparation technique and new standards should be made. The data should lie along a straight line. A weighted least squares ($1/\sigma^2$ weighting) is preferable. Curvature can be eliminated with absorption corrections based on the mass absorption coefficient of the analyte [7,8,9].
14. Determine the initial slope, m, of the linear portion of the calibration graph in counts per microgram. The intercept, b, of the line with the $\hat{I}_x^o$ axis should be approximately zero.
NOTE: A large negative intercept indicates an error in determining the background. This may arise from incorrectly measuring the baseline or from interference by another phase at the angle of background measurement. A large positive intercept indicates an error in determining the baseline or that an impurity is included in the measured peak.

MEASUREMENT:

15. Obtain a qualitative X-ray diffraction scan (broad 2-theta range) of the high-volume respirable sample to determine the presence of zinc oxide and any matrix interference. The expected diffraction peaks are as follows:

Zinc Oxide Peak (2-Theta Degrees)		
Primary	Secondary	Tertiary
36.26	31.75	34.44

16. Analyze the sample filters by step-scanning the most intense interference-free diffraction peak of zinc oxide and determine the integrated intensity. Measure the background on each side of the peak

for one half the time used for peak scanning and add the counts from each side for a total (average) background. Determine the 2-theta position of the background for each sample. The net count or intensity, I_x, is the difference between the peak integrated count and the total background count. The net intensity is normalized as in step 12 to obtain $\hat{I}_x$.

17. Scan each field blank over the same 2-theta range used for the analyte. These analyses serve only to verify that contamination of the filters has not occurred. The analyte peak should be absent.

CALCULATIONS:

18. The concentration, C, of zinc oxide in the air sample is:

$$C = \frac{(\hat{I}_x - b)}{mV}, \text{ µg/L or mg/m}^3,$$

where: $\hat{I}_x$ = normalized intensity for sample peak,
b = intercept of calibration graph ($\hat{I}_x^o$ vs. W),
m = initial slope of calibration graph (counts per microgram), and
V = air volume sampled (L).

In heavily-loaded samples, particularly those rich in heavy elements, X-ray absorption may cause reduced intensities and underestimation of zinc oxide. If this is suspected, an absorption correction can be made [8]. The collection filters and blanks are mounted on a smooth metal plate (substrate) for XRD quantitation. The substrate should have a non-interfering diffraction peak which is measured at the same time as the zinc oxide peak. By measuring the substrate peak on both samples and blanks, an absorption correction like that in the silica method (NIOSH method 7500) can be made. The absorption correction factor must be calculated for each sample from the formula in NIOSH method 7500, which takes into account the diffraction angles for the particular substrate chosen. Altree-Williams used a silver filter under the collection filter [7].

EVALUATION OF METHOD:

In a comparison of this method with atomic absorption spectrophotometry [3,4], zinc was determined on 15 Gelman DM-800 filters containing added zinc oxide in the range 250 µg to 1000 µg. The average percent difference for the 15 pairs was 2.7%. NIOSH method S316 was validated with generated samples in the range of 2.4 mg/m^3 to 9.9 mg/m^3 [2,5,10]. A pooled $\hat{S}_{rT}$ of 0.088 was found for 18 samples of 180 L collected from the aerosol.

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METHOD WRITTEN BY:

D. D. Dollberg, Ph.D, and M. T. Abell, NIOSH/DPSE.

CHROMIUM, HEXAVALENT 7600

Cr(VI) AW: 52.00 CAS: 18540-29-9 RTECS: GB6262000
CrO_3 MW: 99.99 CAS: 1333-82-0 RTECS: GB6650000

METHOD: 7600, Issue 3 **EVALUATION: FULL** **Issue 1: 15 May 1989**
Issue 3: 20 October 2015

OSHA: 0.005 mg/m³ (1910.1026); C 0.1 mg/m³ as CrO_3 (exceptions to 1910.1026)
NIOSH: 0.0002 mg/m³ (8 h); carcinogen

PROPERTIES: Oxidizing agent

SYNONYMS: Vary depending upon the compound

SAMPLING

SAMPLER: FILTER (5.0 µm PVC membrane)

FLOW RATE: 1 L/min to 4 L/min

VOL-MIN: 34 L @ 0.005 mg/m³
-MAX: 400 L

SHIPMENT: Routine

SAMPLE STABILITY: Analyze within 2 weeks [1]

FIELD BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 0.05 mg/m³ to 0.2 mg/m³ [2] (22 L samples)

BIAS: −5.48%

OVERALL PRECISION ($\hat{S}_{rT}$): 0.084 [2]

ACCURACY: ±18.6%

MEASUREMENT

TECHNIQUE: VISIBLE ABSORPTION SPECTROPHOTOMETRY

ANALYTE: Chromium-diphenylcarbazone complex

EXTRACTION SOLUTION: 0.25 mol/L sulfuric acid or solution of 20 g/L sodium hydroxide and 30 g/L sodium carbonate (see steps 4 and 5)

WAVELENGTH: 540 nm; 5 cm path length

CALIBRATION: Standard solutions of potassium chromate in 0.25 mol/L sulfuric acid

RANGE: 0.2 µg to 7 µg per sample

ESTIMATED LOD: 0.05 µg per sample

PRECISION ($\bar{S}_r$): 0.029 @ 0.3 µg to 1.2 µg per sample [3]

APPLICABILITY: The working range is 0.00042 mg/m³ to 3.6 mg/m³ for a 400 L air sample. This method may be used for the determination of soluble hexavalent chromium (using the acidic extraction solution) or insoluble hexavalent chromium (using the basic extraction solution) [3].

INTERFERENCES: Possible interferences are iron, copper, nickel, and vanadium; 10 µg of any of these causes an absorbance equivalent to about 0.02 µg hexavalent chromium due to formation of colored complexes. Interference due to reducing agents (e.g., elemental iron, divalent iron) is minimized by alkaline extraction (step 5).

OTHER METHODS: This method combines and replaces NIOSH methods P&CAM 169 [1], S317 [2], and P&CAM 319 [3]; the hexavalent chromium criteria document [4] contains a summary of more recent methods for air analysis, wipe analysis, and biological monitoring.

REAGENTS:

1. Sulfuric acid,* concentrated (98% mass fraction), reagent grade.
2. Sulfuric acid, 3 mol/L. Add 167 mL concentrated sulfuric acid to water in a 1 L flask; dilute to the mark.
3. Acidic extraction solution, sulfuric acid, 0.25 mol/L. Add 14.0 mL concentrated sulfuric acid to water in a 1 L flask; dilute to the mark.
4. Sodium carbonate, anhydrous, reagent grade.
5. Sodium hydroxide,* reagent grade.
6. Potassium chromate,* reagent grade.
7. Diphenylcarbazide solution. Dissolve 500 mg sym-diphenylcarbazide in 100 mL acetone and 100 mL water.
8. Hexavalent chromium standard,* 1000 µg/mL. Dissolve 3.735 g potassium chromate in deionized water to make 1 L, or use commercially available solution.
9. Calibration stock solution,* 10 µg/mL. Dilute 1000 µg/mL hexavalent chromium standard 1:100 with deionized water.
10. Basic extraction solution. Dissolve 20 g sodium hydroxide and 30 g sodium carbonate in deionized water to make 1 L of solution.
11. Glassware cleaning solution.* Add a volume of concentrated nitric acid to an equal volume of deionized water.
12. Nitrogen, purified.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: Polyvinyl chloride (PVC) filter, 5.0 µm pore size, 37 mm diameter in polystyrene cassette filter holder.
   NOTE: Some PVC filters promote reduction of hexavalent chromium. Check each lot of filters for recovery of hexavalent chromium standard.
2. Personal sampling pump, 1 L/min to 4 L/min, with flexible connecting tubing.
3. Vials, scintillation, 20 mL glass, PTFE-lined screw cap.†
4. Forceps, plastic.
5. Spectrophotometer, UV-visible (540 nm), with cuvettes, 5 cm path length.
6. Filtration apparatus, vacuum.†
7. Beakers, borosilicate, 50 mL.†
8. Watch glass.†
9. Volumetric flasks, 25 mL, 100 mL, and 1000 mL.†
10. Hotplate, 120 °C to 400 °C.
11. Micropipettes, 10 µL to 1 mL.
12. Centrifuge tubes, 40 mL, graduated, with plastic stoppers.†
13. Büchner funnel.†
14. Pipettes, TD, 5 mL.†

†Clean all glassware with the glassware cleaning solution and rinse thoroughly before use.

SPECIAL PRECAUTIONS: NIOSH considers all hexavalent chromium compounds to be suspect occupational carcinogens [4]. Concentrated acids are highly corrosive, and sodium hydroxide is caustic. All work with these compounds should be performed in a hood. Use proper protective clothing including gloves, safety glasses, and laboratory coat. Potassium chromate is a strong oxidizer with risk of fire and explosion upon contact with combustible substances and reducing agents.

SAMPLING:

1. Calibrate the sampling pump with a representative sampler in line.
2. Sample at an accurately known flow rate in the range 1 L/min to 4 L/min for a sample size of 34 L to 400 L. Do not exceed 1 mg total dust loading on the filter.
3. Remove the filter from the cassette within 1 h of completion of sampling and place it in a vial to be shipped to the laboratory. Handle the filter only with forceps. Discard the backup pad.

SAMPLE PREPARATION:

NOTE: There are two sample preparation techniques outlined below. For soluble chromates or chromic acid, follow step 4; for insoluble chromate or hexavalent chromium in the presence of iron, divalent iron, or other reducing agents, follow step 5.

4. Sample preparation for soluble chromates and chromic acid.
   a. Remove the blank and sample filters from the vials, then fold and place them into centrifuge tubes.
   b. Add 6 mL to 7 mL of acidic extraction solution to each tube, cap, and shake to wash all surfaces of the filter. Allow filter to remain in tube 5 min to 10 min [5].
   c. Remove the filter from the tube with plastic forceps, carefully washing all surfaces with an additional 1 mL to 2 mL of acidic extraction solution. Discard the filters. Start reagent blanks at this point.
   d. Filter the solution through a moistened PVC filter in a Büchner funnel to remove interferences from suspended dust. Collect the filtrate in a clean centrifuge tube. Rinse the bottle, which contained the filter, with 2 mL to 3 mL of acidic extraction solution and pour into the funnel. Rinse the funnel and filter with 5 mL to 8 mL of acidic extraction solution.
   e. Add 0.5 mL diphenylcarbazide solution to each centrifuge tube. Bring the total volume in each centrifuge tube to 25 mL with acidic extraction solution. Shake to mix and allow color to develop (at least 2 min but no longer than 40 min [5]). Transfer the solution to a clean 5 cm cuvette and analyze within 40 min of mixing (steps 9, 10, and 11).
5. Sample preparation for insoluble chromates and for hexavalent chromium in the presence of iron or other reducing agents:
   NOTE: If significant amounts of trivalent chromium are expected to be present, degas the sample solution by bubbling nitrogen through it for 5 min before proceeding and purge the headspace above the solution during step 5.a.
   a. Remove the PVC filter from the bottle, place it in a 50 mL beaker, and add 5.0 mL of basic extraction solution. Start reagent blanks at this point. Purge the headspace above the solution with nitrogen throughout the extraction process to avoid oxidation of any trivalent chromium. Cover the beaker with a watch glass and heat it to near the boiling point on a hotplate with occasional swirling for 30 min to 45 min. Do not boil the solution or heat longer than 45 min. Do not allow the solution to evaporate to dryness because hexavalent chromium may be lost owing to reaction with the PVC filter. An indication that hexavalent chromium has been lost in this manner is a brown-colored PVC filter.
   b. Cool the solution and transfer it quantitatively with distilled water rinses to a 25 mL volumetric flask, keeping the total volume about 20 mL.
      NOTE: If the solution is cloudy, filter it through a PVC filter in a vacuum filtration apparatus using distilled water rinses.
   c. Add 1.90 mL of 3 mol/L sulfuric acid to the volumetric flask and swirl to mix.
      CAUTION: Carbon dioxide will be evolved causing increased pressure in the flask. Let the solution stand for several minutes until vigorous gas evolution ceases.
   d. Add 0.5 mL diphenylcarbazide solution, dilute to the mark with distilled water and invert several times to mix thoroughly. Pour out about one-half of the contents of the flask, stopper the flask and shake it vigorously several times, removing the stopper each time to relieve pressure.
      NOTE: This step releases bubbles of carbon dioxide which otherwise would cause high and erratic readings.
   e. Transfer an aliquot of the solution remaining in the flask to a 5 cm cuvette and analyze (steps 9, 10, and 11).

CALIBRATION AND QUALITY CONTROL:

6. Calibrate daily with at least six working standards. Transfer 6 mL to 7 mL of acidic extraction solution to each of a series of 25 mL volumetric flasks. Pipet 0 mL to 0.7 mL of 10 µg/mL calibration stock solution into the volumetric flasks. Add 0.5 mL diphenylcarbazide solution to each flask and sufficient acidic extraction solution to bring the volume to 25 mL. These working standards contain 0 µg to 7 µg hexavalent chromium.
7. Analyze the working standards together with blanks and samples (steps 9, 10, and 11).

8. Prepare a calibration graph [absorbance vs. µg hexavalent chromium].

MEASUREMENT:

9. Set wavelength on the spectrophotometer to 540 nm.
10. Set to zero using an acidic extraction solution reagent blank.
11. Transfer sample solution to a cuvette and record the absorbance.
    NOTE 1: A sample containing 1.5 µg hexavalent chromium in 25 mL gives about 0.2 absorbance.
    NOTE 2: If the absorbance values for the samples are higher than the standards, dilute using acidic extraction solution, repeat this step, and multiply the resulting absorbance by the appropriate dilution factor.

CALCULATIONS:

12. From the calibration graph, determine the mass of hexavalent chromium in each sample, W (µg), and in the average blank, B (µg).
13. Calculate the concentration, C (mg/m^3), of hexavalent chromium in the air volume sampled, V (L).

$$C = \frac{(W - B)}{V}, \text{ µg/L or mg/m}^3.$$

NOTE: If the hexavalent chromium concentration is to be reported as chromic acid (CrO_3), multiply C by 1.92 (MW of chromic acid divided by AW of chromium).

EVALUATION OF METHOD:

P&CAM 169 and S317 are essentially the same method and are suitable for soluble chromate and chromic acid. Method S317 was validated with generated samples of chromic acid mist [2,5], and P&CAM 169 was tested with field samples [1,6]. P&CAM 319 was developed because a method was needed to analyze for insoluble chromates [3]. This method was tested with insoluble chromates in matrices such as paints, primer, and ceramic powders [3].

Precision, analytical range, recovery data, etc., for the three methods pooled are as follows:

Total $\hat{S}_{rT}$: 0.084
Measurement $\overline{S}_r$ [1,2,3]: 0.02 to 0.04
Range [3]: 0.5 µg/m^3 to 10 µg/m^3
Collection efficiency [5]: 94.5%
Sampling rate [1,3]: 1.5 L/min to 2.5 L/min
Stability (two weeks) [1]: 96% recovery

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METHOD REVISED BY:

Martin T. Abell, NIOSH/DPSE; NIOSH method S317 validated under NIOSH Contract CDC-99-74-45.

CHROMIUM, HEXAVALENT by Ion Chromatography

7605

Cr(VI) MW: 52.00 (Cr); 99.99 (CrO_3) CAS: 18540-29-9 RTECS: GB6262000

METHOD: 7605, Issue 2 **EVALUATION:** FULL **Issue 1:** 15 March 2003 **Issue 2:** 10 March 2016

OSHA: 0.005 mg/m³ (1910.1026); C 0.1 mg/m³ as CrO_3 (exceptions to 1910.1026)
NIOSH: 0.0002 mg/m³ (8 h); carcinogen

PROPERTIES: oxidizing agent

SYNONYMS: Vary depending upon the compound; chromate commonly used; "chrome six."

SAMPLING

SAMPLER: FILTER (5.0-µm PVC membrane)

FLOW RATE: 1 to 4 L/min

VOL-MIN: 1 L @ 0.05 mg/m³
-MAX: 400 L

SHIPMENT: Routine. Can be shipped cold when deemed necessary

SAMPLE STABILITY: Stable for 2 weeks at room temperature. Stable for 4 weeks if stored in refrigerator.

BLANKS: 2 to 10 field blanks per set

ACCURACY

RANGE STUDIED: 0.05 to 120 µg Cr(VI) [1,2]

BIAS: -1.6% [2]

OVERALL PRECISION ($\hat{S}_{rT}$): 0.07

ACCURACY: ± 17.4% (0.6 - 960 g/m³) [1]

MEASUREMENT

TECHNIQUE: Ion chromatography with post-column derivatization and UV detection.

ANALYTE: CrO_4^{2-}-diphenylcarbazide (DPC) complex

EXTRACTION: 5 mL 2% NaOH- 3% Na_2CO_3 . Dilute to 25 mL after heating.

INJECTION VOLUME: 100 µL

COLUMN: Dionex NG1 Guard, HPIC- AS7 Separator or equivalent

MOBILE PHASE: 250 mM $(NH_4)^2SO_4$ /100 mM NH_4 OH

FLOW RATE: 1.0 mL/min; 0.7 mL/min post column

POST-COLUMN REAGENT: 2.0 mM DPC + 10% MeOH +1N H_2SO_4

DETECTOR: UV @ 540 nm

CALIBRATION: Standard solutions of $K_2Cr_2O_7$ in NaOH-Na_2CO_3 buffer

RANGE: 0.05 to 20 µg per sample

ESTIMATED LOD: 0.02 µg per sample [3]

PRECISION ($\bar{S}_r$): 0.015 @ 0.5 to 5 µg/sample [3]

APPLICABILITY: The working range is 0.00025 to 0.1 mg/m³ for a 200-L air sample. This method can be used for the determination of Cr(VI) using 2% NaOH - 3% Na_2CO_3 for extraction.

INTERFERENCES: Possible interferences are iron, copper, nickel, and vanadium; 10 µg of any of these causes an absorbance equivalent to approximately 0.02 µg Cr(VI) due to formation of colored complexes. Interference due to reducing agents (e.g., Fe, Fe^{++}) is minimized by alkaline extraction (step 5).

OTHER METHODS: Method 7703 is a field portable method for Cr(VI). OSHA Method W4001 is for the measurement of Cr(VI) in wipe samples [4]. OSHA Method ID-215 is applicable to measurement of Cr(VI) and employs precipitation to reduce Cr(III) oxidation [5]. A similar air method is ISO 16740 [6]. EPA Method 218.6 is for water matrices [7].

REAGENTS:

1. Sulfuric acid, conc. (98 % w/w).*
2. Ammonium hydroxide, conc. (28 %).*
3. Ammonium sulfate monohydrate, reagent grade.
4. Sodium carbonate, anhydrous.
5. Sodium hydroxide, reagent grade.*
6. Methanol, HPLC grade.*
7. 1,5-Diphenylcarbazide, reagent grade.
8. Potassium dichromate or potassium chromate.* Dry at 100 °C and store in a desiccator.
9. Post-Column Derivatizing Reagent: Diphenylcarbazide solution. Dissolve 500 mg 1,5-diphenylcarbazide in 100 mL HPLC-grade methanol. While stirring, add 500 mL water containing 28 mL of conc. sulfuric acid. Dilute to a final volume of one liter with water. This reagent is stable for 4 - 5 days. Prepare in one-liter quantities, as needed.
10. Cr(VI) standard, 1000 µg/mL. Dissolve 2.829 g potassium dichromate in deionized water to make one liter, or use commercially available solution.
    NOTE: 3.731 g K_2CrO_4 can also be used.
11. Calibration stock solution, 1.0 µg/mL. Dilute 1000 µg/mL Cr(VI) standard 1 :1000 with deionized water.
12. Filter extraction solution, 2% NaOH-3% Na_2CO_3. Dissolve 20 g NaOH and 30 g Na_2CO_3 in deionized water to make one liter of solution.
13. Eluent (mobile phase); 250 mM ammonium sulfate/200 mM ammonium hydroxide. Dissolve 33 g ammonium sulfate in approximately 500 mL distilled water and add 6.5 mL conc. ammonium hydroxide. Dilute to one liter with distilled water and mix.
14. Nitrogen, pre-purified.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: polyvinyl chloride (PVC) filter, 5.0-µm pore size, 37 µmm diameter in polystyrene cassette filter holder.
   NOTE: Some PVC filters promote reduction of Cr(VI). Check each lot of filters for recovery of Cr(VI) standard.
2. Personal sampling pump, 1 to 4 L/min, with flexible connecting tubing.
3. Vials, scintillation, 20-mL glass, polytetrafluoroethylene (PTFE)-lined screw cap.**
4. Forceps, nonmetallic.
5. Gloves, polypropylene or latex.
6. Liquid chromatography apparatus consisting of autosampler; pump; columns ; post-column reagent delivery system with 2.2-m high pressure tubing mixing/reaction loop with 1 min a water bath at 32 °C ± 3 °C; and UV detector.
7. Columns: NG1 (Dionex Corp.) or equivalent guard column; HPIC-AS7, 4 x 250-mm (Dionex Corp.) separator column (or equivalent);
8. Filtration apparatus, PTFE luer lock style filter syringe.
9. Beakers, borosilicate, 50 -mL.**
10. Watch glass.**
11. Volumetric flasks, 25-, 100-, and 1000-mL.**
12. Oven at 107°C, not to exceed 115°C.
    NOTE: Hot plate or ultrasonic bath can be used.
13. Micropipettes, 10-µL to 0.5-mL.
14. Pipettes, TD 5-mL.**
15. Bagged refrigerant.

**Clean all glassware with 1:1 HNO_3:H_2O and rinse thoroughly before use

SPECIAL PRECAUTIONS: Many chromate compounds are suspected human carcinogens [8]. All sample preparation should be performed in a hood. Concentrated acids and bases are toxic and corrosive. When working with concentrated acids and bases, wear protective clothing. Ammonium hydroxide is a respiratory irritant. Methanol is flammable and toxic.

SAMPLING:

1. Calibrate the sampling pump with a representative sampler in line.
2. Sample at an accurately known flow rate in the range 1 to 4 L/min for a sample size of 1 to 400 L. Do not exceed 1 mg total dust loading on the filter.
3. Filters can be left in the cassettes for shipping to the lab, but to minimize sample contamination during shipping, remove the filter from the cassette within one hour of completion of sampling and place it in a vial to be shipped to the laboratory. Handle the filter only with gloved hands and nonmetallic forceps. Discard the backup pad. As a precaution, it is recommended to ship the samples with bagged refrigerant.

SAMPLE PREPARATION:

4. Don a clean pair of disposable plastic gloves (to prevent sample contamination). Using forceps, transfer the PVC filter to a 50-mL beaker, and add 5.0 mL filter extraction solution, 2% NaOH/3% Na_2CO_3. Start media blanks at this point.
   NOTE 1: If significant amounts of Cr[III] are expected to be present in the samples, either (a) degas the sodium hydroxide/sodium carbonate extraction solution by bubbling nitrogen through it for 5 min. before proceeding, or (b) use a precipitation reagent [1].
   NOTE 2: If only soluble chromates are of interest, use ammonium sulfate buffer in place of carbonate extraction solution [9,10].
5. Cover the beaker with a watchglass and heat it to near the boiling point (100°C to 115°C) in an oven with occasional swirling for 45 min. Do not boil the solution. Longer heating times (up to 90 minutes) may be necessary for some samples (e.g., paint spray). Do not allow the solution to evaporate to dryness because hexavalent chromium may be lost due to reaction with the PVC filter and/or co-collected aerosol constituents. An indication that hexavalent chromium has been lost in this manner is a brown-colored PVC filter.
   NOTE: A hot plate, heater block, or ultrasonic bath can also be used for this step [9,11].
   a. Cool the solution and transfer it quantitatively with distilled water rinses to a 25-mL volumetric flask. Bring to volume with distilled water.
      NOTE: If the solution is cloudy, filter an aliquot through a PTFE luer lock style filter attached to a syringe.
   b. Transfer an aliquot of the solution to the appropriate vial for the chromatograph's autosampler and analyze (steps 9 through 13).

CALIBRATION AND QUALITY CONTROL:

6. Calibrate daily with at least six working standards. Transfer 5 mL of extraction solution to each of a series of 25-mL volumetric flasks. Pipet known volumes (0 to 5 mL) of calibration stock solution (1.0 µg/mL) into the volumetric flasks. For higher standards, pipet 10 - 20 µL of the 1000 µg/mL concentrated stock and bring the volume to 25 mL with distilled water. These working standards contain 0 to 20 µg Cr(VI) per sample.
7. Analyze the working standards together with blanks and samples (steps 9 through 13).
8. Prepare a calibration graph [instrument response vs. µg Cr(VI)].

MEASUREMENT:

9. Set wavelength on the detector to 540 nm.
10. Set the liquid chromatograph to manufacturer's recommendations and parameters given on page 7605-1. With a mobile phase flow rate of 1.0 mL/min., a post-column reagent flow rate of 0.7 mL/min., and a 2.2-m post-column tube, the derivative retention time should be approximately 3.7 - 4.7 minutes.

NOTE: If the instrument response for the samples is higher than the standards, dilute using a 1:5 dilution of extraction solution:water to maintain a constant ionic strength; repeat the analysis; and multiply the measured concentration by the appropriate dilution factor. Alternatively, inject a smaller volume and multiply by the appropriate factor.

11. After the analysis is complete, flush the entire system with ASTM Type II water for at least one hour at 1.0 mL/min. with all columns on line. Remove the columns and continue flushing for an additional two hours. Flush the autosampler with several injections of water. Leaving the columns in line while the system is idle is not recommended.

CALCULATIONS

12. From the calibration graph, determine the mass of Cr(VI) in each sample, W (µg), and in the average blank, B (µg).
13. Calculate concentration, C (mg/m^3), of Cr(VI) in the air volume sampled, V (L):

$$C = \frac{W - B}{V}, mg/m^3$$

NOTE: µg/L ≅ mg/m^3

EVALUATION OF METHOD:

This method was evaluated in the laboratory with spiked filters and a certified reference material containing a known loading of Cr(VI). This certified reference material (CRM) is European Commission, Institute for Reference Materials and Measurements (EC/IRMM) CRM 545, Cr(VI) and Cr(total) in welding dust loaded on a glass fiber filter [12]. This method was evaluated for extraction efficiency over the concentration range of 0.15 - 5 µg/sample testing two brands of filters, SILICAL® and GLA-5000™ [3]. In these experiments, test atmospheres were not generated; instead, Cr(VI) as the dichromate was fortified on the face of the sample filters, then 240 L of air with 35% relative humidity was pulled through at 1 L/min. A 30-day storage study using both types of filters was conducted at 1.5 µg/sample (30x LOQ) at ambient room temperature and 4 °C. The average recovery of the stored samples was 94.8%. The estimation of the limit of detection and limit of quantitation (LOD/LOQ) were determined analyzing a series of liquid standards. The LOD and LOQ, 0.02 µg/sample and 0.07 µg/sample, respectively were calculated by Burkart's method [13].

To fully evaluate this method, a field study was conducted in which side- by-side samples were taken to measure exposures to Cr(VI) during spray-painting and electroplating operations. These samples were analyzed subsequently by 4 different methods (NIOSH Method 7605, 7703, 7300 and OSHA ID-215) [1]. NIOSH method 7300 was used to measure total chromium. The results from the other 3 methods correlated very well showing no statistical difference among the 3 methods. Recoveries of 98.4 (±3.4) % were obtained for CRM 545 (n = 6) [2].

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LEAD BY PORTABLE ULTRASONIC EXTRACTION/ASV

7701

Pb MW: 207.19 (Pb), 223.19 (PbO) CAS: 7439-92-1 (Pb), 1317-36-8 (PbO) RTECS: OF7525000 (Pb), OG1750000 (PbO)

METHOD: 7701, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 January 1998 **Issue 3:** 17 February 2016

OSHA: 0.05 mg/m³
NIOSH: 0.05 mg/m³

PROPERTIES: soft gray metal; d 11.3 g/cm³ @ 20 °C; MP 327.5 °C, BP 1749 °C; valences 2+, 4+ in salts

SYNONYMS: elemental lead, lead compounds (except alkyl lead)

SAMPLING

SAMPLER: FILTER (37-mm, 0.8-µm pore, mixed cellulose ester membrane)

FLOW RATE: 1 to 4 L/min

VOL-MIN: 20 L @ 0.05 mg/m³
-MAX: 1500 L

SHIPMENT: Routine

SAMPLE STABILITY: Stable

BLANKS: Minimum of 2 field blanks per set

ACCURACY

RANGE STUDIED: 0.025 to 0.150 mg/m³ (as Pb) (based on Pb mass loadings) [4]

BIAS: None identified in laboratory studies [3-5] <10% in field study [6]

OVERALL PRECISION ($\hat{S}_{rT}$): 0.087 (screen-printed electrodes); 0.094 (Hg film on glassy carbon electrodes) [4]

ACCURACY: ± 17.2%
± 19.3%

MEASUREMENT

TECHNIQUE: PORTABLE ANODIC STRIPPING VOLTAMMETRY

ANALYTE: Lead

EXTRACTION: 10% HNO_3 10 mL; ultrasonication

ANALYSIS ALIQUOT VOL: 0.1 to 5 mL

DEPOSITION POTENTIAL: -0.8 V to -1.0 V vs. Ag/AgCl

ANODIC SWEEP: Deposition potential to 0.0 V vs. Ag/AgCl sweep rate variable [1,2]

REFERENCE ELECTRODE: Ag/AgCl or calomel

WORKING ELECTRODE: Mercury film on glassy carbon or screen printed

SUPPORTING ELECTROLYTE: Mixture of NaCl/NaOH or KCl/KOH, L-ascorbic acid

CALIBRATION: Pb^{2+} in 5% HNO_3

RANGE: 0.31 to >1000 µg Pb per sample [3,4]

ESTIMATED LOD: 0.05 µg/sample [1]

PRECISION ($\bar{S}_r$): 0.068 @ 60 µg (as Pb) per sample [3]

APPLICABILITY: The working range is (at least) 0.20 to 5.00 mg/m³ (as Pb) for a 120-L air sample. Lead determination by ultrasonic extraction/ASV method is applicable to the on-site, field-based determination of lead in air filter samples, and also may be used for laboratory-based air filter sample preparation and analysis.

INTERFERENCES: Thallium is a known interference, but its presence is unlikely in the vast majority of samples. Extremely high concentrations of copper may cause a positive bias. Surfactants can poison electrode surfaces, so if the presence of surfactants is suspected they must be eliminated during sample preparation [7,8].

OTHER METHODS: Laboratory-based methods include atomic spectrometric methods following concentrated acid hotplate digestion: NIOSH methods 7082 (flame AAS), 7105 (graphite furnace AAS), and 7300-series methods (ICP-AES) [9]. ASTM standards based on NIOSH methods for sample collection, preparation and analysis have been published [10].

REAGENTS:

1. Nitric acid,* 10% (v/v) (Prepared from concentrated nitric acid, reagent grade; spectroscopic grade if trace analysis).
2. Distilled or deionized water (ASTM Type I or better [11]).
3. Calibration stock solution, 1000 µg/mL Pb. Commercial standard, or dissolve 1.00 g Pb metal in minimum of 10 mL of 50% HCl and dilute to 1 L with 1% (v/v) HCl. Store in a polyethylene bottle. Stable for at least one year.
4. Supporting electrolyte: Aqueous inert salt mixture such as 2.5 M NaCl and 0.25 M NaOH * (reagent grade or equivalent) [3,4].
5. Dissolved oxygen scavenger such as 0.25 M L-ascorbic acid (tissue culture grade or equivalent) [3,4].
6. Mercuric nitrate (reagent grade), if required (for Hg film electrodes).
7. Certified Reference Materials (CRMs) for lead.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: Mixed cellulose ester filter, 0.8 µm pore size, 37-mm diameter, in cassette filter holder or cellulosic internal capsule.
2. Personal sampling pump, 1 to 4 L/min, with flexible connecting tubing.
3. Field-portable anodic stripping voltammeter.
4. Disposable or renewable voltammetry electrodes.
5. Ultrasonic bath, 50 watts minimum power.
6. Power source for ultrasonic bath.
7. Plastic centrifuge tubes, 50-mL, with screw caps.
8. Test tube rack (size to fit in ultrasonic bath).
9. Plastic sample cell container.
10. Mechanical pipets (class A equivalent), 0.1-mL to 10-mL, as needed.
11. Pipet tips for mechanical pipets.
12. Forceps.
13. Bottles, polyethylene, 100- to 1000-mL.
14. Volumetric flasks, 100-mL (for preparatory lab work).
15. Plastic rods.
16. Wipes (ASTM E1792 [12])
    NOTE: Clean all glassware and reusable plasticware with diluted nitric acid and rinse thoroughly with distilled or deionized water before use.

SPECIAL PRECAUTIONS: Nitric acid and sodium hydroxide are irritants and may burn skin. Perform extractions in a well-ventilated area. Wear gloves and eye protection.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in the line.
2. Sample at an accurately known flow rate between 1 and 4 L/min for up to 8 h for a total sample size of 20 to 1500 L for TWA measurements. Do not exceed a filter loading of ca. 5 mg total dust.
   NOTE: Filter overloading can be assessed by periodic visual checks. See NMAM guidance chapters for additional discussion on filter capacity.

SAMPLE PREPARATION:

3. Open the cassette filter holders and, with forceps, transfer the samples and blanks to separate 50-mL centrifuge tubes. Use internal cellulosic capsules or wipe the internal cassette surfaces with a 37 mm MCE filter or cellulosic wipe wetted with deionized water and add to the centrifuge tube to transfer non-filter aerosol deposits into the tube. See [13] for additional information. Push the filters to the bottom of the tubes with plastic rods.
   NOTE: An alternative means to include non-filter aerosol deposits is to carry out extraction directly within the cassette.
4. Add 10 mL of 10% HNO_3 and cap the centrifuge tubes.

5. Place centrifuge tubes in ultrasonic bath, and agitate at room temperature for at least 30 min.
   NOTE 1: The water level in the bath should be above the level of liquid within the centrifuge tubes.
   NOTE 2: Proper performance of the ultrasonic bath should be demonstrated before use. This can be accomplished by checking recoveries of lead from performance evaluation materials.
6. Shake tubes for 5 to 10 sec, and allow to settle.

CALIBRATION AND QUALITY CONTROL:

7. Prior to field work, prepare a series of working standards covering the range 0.25 to 20 µg/mL Pb.
   a. Add aliquots of calibration stock solution to 100-mL volumetric flasks, and dilute to volume with 10% HNO_3. Store and transport the working standards in polyethylene bottles, and prepare fresh weekly.
   b. Analyze the working standards together with the blanks and samples (steps 11 through 14).
   c. Prepare a calibration graph of instrumental response vs. lead concentration (µg/mL Pb).
      NOTE: Some portable instruments read concentration directly. Calibrate according to manufacturer's directions.
8. Analyze at least one standard for every 20 samples to check for instrument drift (steps 11 through 14).
9. Check recoveries with at least one spiked media blank per 20 samples (one per batch minimum). Use certified reference materials to substantiate recoveries. Use method of standard additions to check for matrix effects or interferences.
10. Check for lead contamination by analyzing at least one reagent and one media blank per 20 samples (minimum of one per batch) (steps 11 through 14).

MEASUREMENT:

11. Set instrument parameters as specified by the manufacturer, or use conditions specified on page 7701-1.
    NOTE: If renewable electrodes are used, clean the glassy carbon electrode and deposit a fresh mercury film prior to conducting analyses.
12. Transfer sample aliquot (1 to 5 mL) to analytical cell, and dilute with 10% HNO_3, if necessary.
    NOTE: High concentrations of lead may require analysis of diluted analyte solutions.
13. Add supporting electrolyte and oxygen scavenger to sample cell. Ensure final volume of the cell is 5 mL (disposable electrodes) or 10 mL (renewable electrodes) by diluting with distilled or deionized water.
14. Measure lead content of the sample aliquot (µg/sample or µg/mL), and record the result.
    NOTE 1: For renewable electrodes, rinse and drain electrochemical sample cell at least three times with distilled or deionized water between sample runs. For disposable electrodes, use a fresh plastic sample cell container for each sample analyzed.
    NOTE 2: If the measured value is above the linear range of the standards, dilute with 10% HNO_3, reanalyze, and apply the appropriate dilution factor in the calculations.

CALCULATIONS:

15. Using measured lead contents, calculate the corresponding concentrations (µg/mL) of lead in the original extracted sample, C_s, and average media blank, C_b, from the calibration graph.
    NOTE: Be sure to account for dilution factors.
16. Using solution volumes (mL) of the samples, V_s, and media blanks, V_b, calculate the concentration, C (mg/m^3), of lead in the air volume sampled, V (L):

$$C = \frac{C_s V_s - C_b V_b}{V}, mg/m^3$$

NOTE: µg/L ≅ mg/m^3

EVALUATION OF METHOD:

This method was evaluated with lead aerosol samples generated in the laboratory (40 to 80 µg Pb per filter) [3], and with air particulate samples collected from workplaces where abrasive blasting of leaded paint on highway bridges was being conducted [4]. For the latter, lead loadings cover the range from below the detection limit of 0.09 µg Pb per filter to loadings in excess of 1500 µg Pb per filter [4]. The method also has been evaluated with performance evaluation materials and by interlaboratory testing [3-5]. Lead recoveries from Certified Reference Materials (CRMs) were found to be quantitative (≥90%) and equivalent to recoveries obtained using confirmatory analytical methods (NIOSH 7082, 7105, and 7300 [9]).

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CHROMIUM, HEXAVALENT, by Field-Portable Spectrophotometry

7703

Cr(VI) AW: 52.00 CAS: 18540-29-9 RTECS: GB6262000
CrO_3 MW: 99.99 CAS: 1333-82-0 RTECS: GB6650000

METHOD: 7703, Issue 2 **EVALUATION: FULL** **Issue 1: 15 March 2003**
Issue 2: 20 October 2015

OSHA: 0.005 mg/m³ (1910.1026); C 0.1 mg/m³ as CrO_3 (exceptions to 1910.1026)
NIOSH: 0.0002 mg/m³ (8 h); carcinogen

PROPERTIES: Oxidizing agent

SYNONYMS: Vary depending on the compound; chromate commonly used

SAMPLING

SAMPLER: FILTER (5.0 µm PVC membrane [1,2]; 0.8 µm MCE or 1.0 µm PTFE acceptable for field analysis [3])

FLOW RATE: 1 L/min to 4 L/min

VOL-MIN: 54 L (2 L/min for 27 min)
-MAX: 1200 L (3 L/min for 400 min)

SHIPMENT: Refrigerant pack at 4 °C ± 2 °C (optional)

SAMPLE STABILITY: Analyze within 24 h; if applicable, keep samples at 4 °C ± 2 °C

BLANKS: One per twenty field samples, minimum of 2 per set

ACCURACY

RANGE STUDIED: 0.045 µg/m³ to 1146 µg/m³ (about 20 L to 200 L samples) [3,4]

BIAS: −1.00% [3]

OVERALL PRECISION ($\hat{S}_{rt}$): 0.080

ACCURACY: ±15.7%

MEASUREMENT

TECHNIQUE: FIELD-PORTABLE VISIBLE SPECTROPHOTOMETRY

ANALYTE: Chromium-diphenylcarbazone complex

EXTRACTION: 10 mL 0.05 mol/L ammonium sulfate / 0.05 mol/L ammonium hydroxide (pH = 8 ± 0.5), ultrasonic extraction 30 min

Cr(VI) ISOLATION: Strong anion exchange solid phase extraction

ELUTION SOLUTION: 0.5 mol/L ammonium sulfate / 0.1 mol/L ammonium hydroxide

WAVELENGTH: 540 nm, 1 cm path length

CALIBRATION: Standard solutions of potassium chromate in elution solution

RANGE: 1 µg to 400 µg per sample

ESTIMATED LOD: 0.08 µg hexavalent chromium per sample [3]

PRECISION ($\bar{S}_r$): 0.035 @ 3 µg to 400 µg per sample [3]

APPLICABILITY: The working range is 0.22 µg/m³ to 333 µg/m³ for a 1200 L air sample. This method may be used for the determination of soluble forms of hexavalent chromium. Insoluble hexavalent chromium requires modification of the method using ultrasonic extraction with carbonate buffer.

INTERFERENCES: Interferences from reducing agents such as divalent iron are minimized to the extent possible by the alkaline ultrasonic and solid phase extraction procedures. Interferences from other metal cations are eliminated by solid phase extraction [5]. Some reduction can occur on the filter during sampling, and is usually due to the presence of divalent iron, organic material, and/or acidic conditions [6]. Reduction of hexavalent chromium can occur over time on any filter type, and is especially problematic on MCE filters [7]. However, the use of MCE and PTFE filters has been found to be acceptable for field use, where performance has been found to be equivalent to that of PVC filters [3]. During ultrasonic extraction, oxidation of trivalent chromium in solution to hexavalent chromium is prevented by the use of an ammonium buffer [8].

OTHER METHODS: This method is designed to be used in the field, but can also be utilized in the fixed-site laboratory. It is an alternative to laboratory methods such as NIOSH method 7605 or OSHA method ID-215 (hot plate digestion and ion chromatography). NIOSH method 7600 is a similar procedure, but no separation step is used. A field method not involving hexavalent chromium isolation, MDHS method 61, has been promulgated by the British Health and Safety Executive [9].

REAGENTS:

1. Ammonium sulfate, reagent grade.
2. Ammonium hydroxide,* reagent grade.
3. Water, distilled or deionized.
4. Hydrochloric acid (37% mass fraction),* reagent grade.
5. Acetonitrile,* reagent grade.
6. 1,5-Diphenylcarbazide (DPC), reagent grade.
7. Methanol,* reagent grade.
8. Extraction solution (extraction buffer): 0.05 mol/L ammonium sulfate / 0.05 mol/L ammonium hydroxide, 1 L, aqueous in distilled or deionized water.
   NOTE: Modification of method by using carbonate buffer (e.g., sodium carbonate) is required for extraction of insoluble hexavalent chromium.
9. Elution solution (elution buffer): 0.5 mol/L ammonium sulfate / 0.1 mol/L ammonium hydroxide, 250 mL, in distilled or deionized water.
10. Potassium chromate,* reagent grade.
11. Hexavalent chromium standard,* 1000 µg/mL. Dissolve 3.735 g potassium chromate in deionized water to make 1 L, or use commercially available solution.
12. Calibration stock solution,* 100 µg/mL: dilute 1000 µg/mL hexavalent chromium standard 1:10 with extraction buffer. (Solution is stable for a month.)
13. Diphenylcarbazide complexation solution (20 mmol/L): Measure 0.48 g DPC powder and place in a 100 mL volumetric flask. Add about 80 mL of acetonitrile and dissolve the DPC. Bring up to the mark with additional acetonitrile and mix thoroughly.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Samplers: 5 µm pore size polyvinylchloride (PVC), 0.8 µm pore size mixed cellulose ester (MCE), or 1.0 µm polytetrafluoroethylene (PTFE) filters, 37 mm diameter, with backup pads, in polystyrene cassette filter holder, 2- or 3-piece.
   NOTE: MCE filters, and some PVC filters, promote reduction of hexavalent chromium on a timescale of a few days. However, either filter type is acceptable for field use if the samples are to be analyzed within 24 h of collection.
2. Personal sampling pump, 1 L/min to 4 L/min, with flexible connecting tubing.
3. Ultrasonic bath (sonicator), 100 W minimum power.
4. Solid phase extraction manifold, multi-port.
5. Portable vacuum pump with pressure metering valve.
6. Portable visible spectrophotometer, sample path length 1 cm with quartz cuvette(s).
7. Strong anion exchange solid phase extraction (SPE) cartridges, 10 mL, disposable; loaded with 500 mg or 1000 mg quaternary amine bonded silica, capacity about 1 mmol/g of singly charged anion.
8. Pipettors, mechanical, assorted volumes (e.g., 1 mL to 10 mL) with disposable tips.
9. Micropipettors, mechanical, assorted volumes (e.g., 10 µL to 100 µL) with disposable tips.
10. Centrifuge tubes, plastic, 15 mL, with screw caps.
11. Scintillation vials, 20 mL, glass, with PTFE-lined screw caps.
12. Assorted beakers (and possibly Erlenmeyer flasks), various volumes.
13. Volumetric flasks, 25 mL, 100 mL, 250 mL, and 1000 mL.
14. Forceps, PTFE-coated.
15. Glass or plastic rods.
16. Disposable gloves, plastic or latex.
17. Laboratory wipes.
18. Portable power generator (if necessary).
    NOTE: If no power supply is available at the field site, electric power can be provided by means of a portable, gasoline (or other) generator.

SPECIAL PRECAUTIONS: NIOSH considers all hexavalent chromium compounds to be suspect occupational carcinogens [10]. Efforts must be made to prevent aerosolizing chromate-containing

compounds and solutions. All sample preparation should be carried out in a well-ventilated area (vacuum hood preferable); forced ventilation should be used if no hood is available. Methanol and acetonitrile solutions are flammable and must be handled carefully, i.e., wearing of impermeable gloves and avoidance of vapors. To the extent possible, solutions should be prepared in the laboratory before taking them to the field. Concentrated hydrochloric acid is highly corrosive and ammonium hydroxide is a respiratory irritant. All work with these compounds should be performed in a hood. Use proper protective clothing including gloves, safety glasses, and laboratory coat. Potassium chromate is a strong oxidizer with risk of fire and explosion upon contact with combustible substances and reducing agents.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Sample at an accurately known flow rate in the range of 1 L/min to 4 L/min for a sample size of 54 L to 1200 L. Do not exceed 2 mg of particulate loading on the filter. Label the filter cassette.
3. Don a fresh pair of disposable plastic or latex gloves (to prevent sample contamination).
4. With PTFE-coated forceps, remove filters from cassettes after completion of sampling, and place in separate plastic 15 mL centrifuge tubes for subsequent sample preparation. Discard cellulose backup pads and gloves.

SAMPLE PREPARATION:

5. Add 10 mL of extraction solution (weak buffer) to each 15 mL centrifuge tube containing the filter sample. Ensure that the filter is covered by the extraction solution. If necessary, push the filter down with a clean glass or plastic rod to immerse the entire filter. Cap and label the tubes.
6. Place sample tubes in the ultrasonic bath (sonicator). The water level in the bath should be higher than the liquid level in the centrifuge tube. Sonicate for 30 min.
   NOTE: Numerous centrifuge tubes containing sample filters can be subjected to sonication at one time, depending upon the size of the ultrasonic bath. Ensure that the bath is warm (but < 40 °C).
7. Set up the solid phase extraction manifold.
   a. Place disposable solid phase extraction (SPE) cartridges in each port, and place scintillation vials beneath the cartridges. Label the cartridges.
   b. Attach the vacuum pump to the SPE manifold.
   c. To condition SPE cartridges, pipet 3 mL of methanol into each cartridge, and evacuate. Then pipet 3 mL of extraction solution into each cartridge, and evacuate. Repeat.
8. Extract hexavalent chromium from sample solution.
   a. Pipet 3 mL to 5 mL of each ultrasonicated sample solution from the centrifuge tubes into the disposable SPE cartridge. Dispose of the pipet tip.
   b. Adjust the vacuum to obtain an extraction rate of about one drop per second (approximately 27 kPa or 203 mmHg; no more than 34 kPa or 254 mmHg). Manually tighten cartridges by twisting, if necessary, to slow down the rate of liquid dripping.
      NOTE 1: For samples in which the expected hexavalent chromium concentration is high, smaller aliquots (1 mL to 2 mL) should be dispensed into the SPE cartridges to prevent breakthrough. High concentration of hexavalent chromium can be assessed visually by its orange color.
      NOTE 2: For samples having low hexavalent chromium concentration, additional 3 mL to 5 mL aliquots of ultrasonicated sample solution can be loaded onto SPE cartridges (step 8.a). In this manner, the cartridge can be used to preconcentrate hexavalent chromium.
   c. When it appears the solution has passed through all the cartridges, increase the vacuum to ensure that all solution passes through the cartridges. This step selectively binds hexavalent chromium to the stationary phase of each cartridge.

d. To remove residue of trivalent chromium and other potential interferences, reduce the vacuum to 0. Add 1 mL distilled or deionized water to each cartridge, adjust vacuum to obtain 1 drop per second (about 27 kPa or 203 mmHg), then reduce vacuum to 0 when completed.
e. Remove the scintillation vials beneath the cartridges and discard.
NOTE: This solution contains unwanted fractions that should contain no hexavalent chromium.

9. Place clean, labeled scintillation vials beneath correct cartridges in the SPE manifold.
   a. Add 9 mL of the elution solution (elution buffer) to each cartridge to elute hexavalent chromium, and repeat steps 8.b, 8.c, and 8.d.
   b. Remove the scintillation vials, and cap them. Dispose of the used SPE cartridges.
   NOTE: The scintillation vials now contain extracted and isolated hexavalent chromium, which is ready for subsequent analysis.
10. Uncap each scintillation vial containing extracted and isolated hexavalent chromium, and add 100 µL hydrochloric acid.
11. Add 2 mL DPC complexation solution, recap vials, and mix thoroughly. Allow to stand for at least 5 min for complete color development.

CALIBRATION AND QUALITY CONTROL:

12. Calibrate daily with at least 6 working standards over the range of 0 µg/mL to 2 µg/mL of hexavalent chromium per standard.
   a. To 10 mL volumetric flasks containing about 5 mL of elution solution (strong buffer), pipet known volumes (10 µL to 200 µL) of hexavalent chromium calibration stock solution (100 µg/mL) to produce concentrations of 0.1 µg/mL, 0.2 µg/mL, 0.5 µg/mL, 1.0 µg/mL, and 2.0 µg/mL. Add 100 µL of hydrochloric acid and 2 mL of DPC complexation solution to each. Dilute to the mark with elution solution and mix thoroughly.
   NOTE: A minimum of two of the concentration levels (e.g., 0.1 µg/mL and 1.0 µg/mL) should be run at least in triplicate.
   b. Prepare a blank by pipetting 100 µL of hydrochloric acid and 2 mL of DPC complexation solution into 10 mL volumetric flask containing about 5 mL of the elution solution (elution buffer); dilute to the mark with elution solution and mix thoroughly.
   c. Analyze the calibration solutions and the blank (steps 15, 16, 17, 18, 19, and 20).
13. Analyze at least two field blanks, one field blank per twenty samples (steps 10, 11, 15, 16, 17, 18, 19, and 20). Also analyze at least three of the calibration solutions in triplicate.
14. Prepare a calibration graph of absorbance vs, hexavalent chromium concentration.
   NOTE: As an alternative to steps 12, 13, and 14, the standard addition approach can be used [11].

MEASUREMENT:

15. Turn on the spectrophotometer, and allow for an appropriate warm-up period.
16. Set the spectrophotometer to 540 nm. Set portable spectrophotometer parameters according to the manufacturer's instructions and the conditions on page 7703-1.
17. Rinse the quartz cuvette three times with distilled or deionized water, then rinse with blank solution.
18. Measure the blank. Adjust the spectrometer to zero absorbance.
19. Uncap the scintillation vial containing the sample solution to be analyzed.
   a. Condition the cuvette by filling with the solution to be analyzed, and discard the solution.
   b. Refill the cuvette with the sample solution to be analyzed.
   c. Place the cuvette in the spectrophotometer.
   NOTE: Wipe any extra moisture or liquid off the sides of the cuvette with a dry laboratory wipe, and take care to handle the cuvette only by the frosted sides.
20. Analyze samples, standards, and blanks. Record the absorbance.
   NOTE: If the absorbance value is greater than 2 absorbance units, dilute the solution to be analyzed with elution solution (strong buffer) and reanalyze.

CALCULATIONS:

21. From the calibration graph, determine the mass of hexavalent chromium in each sample, W (µg), and in the average field blank, B (µg).
    NOTE: If standard addition method was used, make appropriate adjustments from the calibration graph obtained [11].
22. Calculate the concentration, C, of hexavalent chromium in the air volume sampled, V (L):

$$C = \frac{(W - B)}{V}, \text{ µg/L or mg/m}^3.$$

    NOTE 1: If samples were diluted during sample preparation, be sure to account for the dilution factor in the calculation.
    NOTE 2: If the hexavalent chromium concentration is to be reported as chromic acid (CrO_3), multiply C by 1.92 (MW of chromic acid divided by AW of chromium).

EVALUATION OF METHOD:

This method was evaluated in the laboratory with spiked filters [3,4,5] and a certified reference material containing a known loading of hexavalent chromium [4]. This certified reference material (CRM) is European Commission, Institute for Reference Materials and Measurements (EC/IRMM) CRM 545, hexavalent chromium and total chromium in welding dust loaded on a glass fiber filter [12]. The method has also been evaluated in the field, where samples collected during aircraft maintenance operations were analyzed on-site [3,4]. The accuracy was estimated using the protocol summarized in a NIOSH technical report [13].

Alternative filter types can also be used, e.g., PTFE, binder-free glass fiber filters, or quartz fiber filters. Filter materials should be tested before use to ensure hexavalent chromium stability. Filters can be pretreated with base to minimize hexavalent chromium reduction during sampling in high-iron or acidic environments [6].

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BERYLLIUM in Air by Fluorometry

7704

Be MW: 9.0121 CAS: 7440-41-7 RTECS: DS1750000

METHOD: 7704, Issue2 **EVALUATION:** FULL **Issue 1:** 6 April 2007 **Issue 2:** 12 December 2015

OSHA: 2 µg/m³, ceiling 5 µg/m³, peak 25 µg/m³
MSHA: 2 µg/m³
DOE: 2 µg/m³ (action level 0.2 µg/m³)
NIOSH REL: 0.5 µg/m³
OTHER OELs: see Table 5

PROPERTIES: solid, d 1.85 g/mL, MP 1,278 °C, VP 0 kPa (0 mm Hg) @ 25 °C

SYNONYMS: beryllium metal, beryllia (BeO)

SAMPLING

SAMPLER: FILTER (mixed cellulose ester or nylon membrane, 0.8 µm pore size, 25- or 37-mm diameter)

FLOW RATE: (1 to 4) L/min

VOL-MIN: 240 L
-MAX: 2,000 L

SHIPMENT: routine

SAMPLE STABILITY: stable

BLANKS: 3 field blanks min.

ACCURACY

RANGE STUDIED: 0.0001 to 6 µg per filter [1,2]

BIAS: negligible [1,2]

OVERALL PRECISION ($\hat{S}_{rT}$): 0.094

ACCURACY: 18.9%

MEASUREMENT

TECHNIQUE: UV/VIS FLUOROMETRY

ANALYTE: complex of hydroxybenzoquinoline sulfonate (HBQS) with beryllium

DISSOLUTION: ammonium bifluoride (aqueous), 10 g/L

DETECTION SOLUTION: contains 63.4 µmol/L HBQS, 2.5 mmol/L EDTA, and 50.8 mmol/L lysine monohydrochloride (optional); pH adjusted to 12.85 with 10 mol/L NaOH, as necessary

DETECTOR: excitation, 360 nm to 390 nm; emission, integrated between 470 and 480 nm ($\lambda_{max} \approx 475$ nm)

CALIBRATION: beryllium standard solutions

RANGE: (0.005 to 6) µg per filter [1]

ESTIMATED LOD: 0.0001 µg per filter [Table 4]

PRECISION ($\bar{S}_r$): 0.021 at ≈0.2 µg per filter, 0.076 at ≈1.5 µg per filter, 0.052 at ≈3 µg per filter

APPLICABILITY: The working range of the method is 0.0005 µg/m³ to 0.6 µg/m³ for an air sample of 1,000 L. The analysis is for total beryllium and is not compound specific.

INTERFERENCES: Minor interference from iron can result if iron concentrations are high. Samples high in iron demonstrate a yellow or gold coloration. This interference can be minimized by allowing the solution to sit for at least two hours, during which time the solution clears, and then filtering the sample extract before use. An alternative method is to filter the solution after 30 minutes of standing through a hydrophilic filter of pore size of 0.2 µm or smaller.

OTHER METHODS: Method 7300 (hot plate digestion and inductively coupled plasma atomic emission spectrometry) is an alternative procedure for the determination of elemental beryllium [3], but with higher detection limits. ASTM method D7202 is a similar procedure to detect elemental beryllium by fluorescence [4].

REAGENTS:

1. Ammonium bifluoride.*
2. Ethylenediaminetetraacetic acid (EDTA), disodium salt, dihydrate.
3. 10-Hydroxybenzo[h]quinoline-7-sulfonate (HBQS) [5].
4. L-Lysine monohydrochloride.
5. Sodium hydroxide.*
6. Water, deionized.
7. Dissolution solution:* aqueous ammonium bifluoride, 10 g/L (prepared by dissolving ammonium bifluoride in deionized water).
8. Detection solution:* 63.4 µmol/L HBQS, 2.5 mmol/L EDTA, and 50.8 mmol/L lysine monohydrochloride; pH adjusted to 12.85 with 10 mol/L NaOH). An alternative preparation of dye solution without lysine (lysine-free) may be made by adding 1.104 g of EDTA and 64 µmoles of the 10-HBQS dye in 900 ml of water. After a clear solution is obtained, 114.5 ml of 2.5 N NaOH is added and mixed to obtain the final dye solution. The pH of the dye solution is 13.2. The lysine-free dye solution (commercially available) may be used for all analytical purposes and also provides superior detection limits.
9. Beryllium standard solution,* 1,000 mg/L (commercially available).
10. Beryllium-spiked media* (commercially available).

    *See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: membrane filter, mixed cellulose ester (MCE) or nylon, 0.8 µm pore size, 25- or 37-mm diameter.
2. Personal sampling pump, 1 L/min to 4 L/min, with clamps and flexible connecting tubing.
3. Ultraviolet/visible (UV/Vis) fluorometer, with excitation lamp (λ = 380 nm) and time-integrating visible detector (400 nm to 700 nm, $\lambda_{max} \approx$ 475 nm) or optical filters for appropriate wavelengths (excitation of 360 nm to 390 nm; emission of ≈475 nm, with full width at half maximum of ± 5 nm).
4. Mechanical agitator, shaker, or rotator.
5. Hot block (for beryllium oxide extraction).
6. Fluorescence cuvettes, disposable, 10 mm diameter, transparent to UV/Vis radiation.
7. Centrifuge tubes, plastic, 15 mL.
8. Syringe filters, hydrophilic polypropylene, 0.2 µm pore size, 25-mm diameter, in plastic housings.
   NOTE: Polytetrafluoroethylene (PTFE) filters are unsuitable for this method.
9. Pipettors, mechanical, of assorted sizes.
10. Pipet tips, plastic, disposable, of assorted sizes.
11. Labware, plastic (e.g., beakers, flasks, graduated cylinders), of assorted sizes.
12. Tweezers, plastic or plastic-coated.
13. Laboratory wipes.
14. Personal protective wear (e.g., respirators, gloves, lab coats, safety eyewear), as needed.

SPECIAL PRECAUTIONS: Wear appropriate personal protection during sampling activities and analysis. It is essential that suitable gloves, eye protection, laboratory coat, etc., be used when working with the chemicals. Perform sample preparation and analysis in a clean, well-ventilated area that is well removed from any possible beryllium contamination. Any area of skin affected by the dissolution or detection solutions must be immediately washed with plenty of water. Ammonium bifluoride will etch glass, so it is essential that all ammonium bifluoride solutions be contained in plastic labware. Avoid exposure by contact with skin or eyes, or by inhalation of vapor.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Sample at an accurately known flow rate between 1 L/min and 4 L/min for a total sample size of 240 L to 2,000 L for TWA measurements. Do not exceed a filter loading of ≈2 mg total dust.
3. After sampling, remove the filters from the cassettes using clean tweezers, and place into labeled 15 mL plastic centrifuge tubes.

SAMPLE PREPARATION:

4. Add 5 mL of the dissolution solution (ammonium bifluoride, 10 g/L) to each 15 mL centrifuge tube containing an air filter sample, and cap each tube.
5. Place each tube into a mechanical rotator, and rotate for at least 30 min.
   NOTE: Rotator may also be substituted by a shaker or an agitator as long as the dissolution solution wets the filter well. Sonication has also been shown to be effective. For dissolution of refractory materials such as high-fired beryllium oxide, agitation of the dissolution solution with the media must be replaced by heating to 85 °C for 60 minutes or more. Any standard dissolution process is particle-size dependent [6]. The two sources of BeO used to validate the method are described in the backup data report [7].
6. Filter each solution with a hydrophilic polypropylene syringe filter into a clean tube.
   NOTE: This tube should be able to accept a cap so that the solution may be saved and used later for reanalysis if required.
7. Pipet 0.1 mL of each sample filtrate into cuvettes containing 1.9 mL of the detection solution. Cap and mix briefly.
   NOTE: The above procedure is typically used to analyze a range of 0.05 µg to 6 µg of beryllium on the sampling media. Alternative ratios of dissolution solution and detection solution may be used for analyzing alternative ranges of beryllium concentration. To test a range of 0.005 µg to 0.4 µg of beryllium on the sampling media, 0.4 mL of the sample filtrate is added to 1.6 mL of the detection solution in the cuvettes. The lysine-free dye solution may also be used for obtaining even lower detection limits at a dilution ratio of 3×, where 1.33 ml of the dye solution is mixed with 0.67 ml of the filtered solution extracts (Table 3) and beryllium in the range of 0.0005 µg to 0.4 µg may be determined.
   NOTE: If high iron or titanium concentration is suspected or is evident (owing to the appearance of suspended precipitate), allow the solution to settle and filter the solution using a hygroscopic syringe filter (e.g., polyethersulfone, or hydrophilic polypropylene).
   NOTE: The stability of the detection and the dissolution solution is more than six months and of the mixed measurement solution comprising both is greater than 30 days. The solutions must be kept in sealed containers, and the detection and mixed solutions must be stored away from light.
   NOTE: If the samples are suspected of having a contaminant that fluoresces and has excitation and emission spectra that overlap with that of the signal produced by the fluorescent dye bound to beryllium, then this contaminant needs to be removed. The presence of such a contaminant can be verified by subjecting the filtered sample to fluorescence excitation after the extraction step (without adding the fluorescent dye). If a fluorescence signal is detected, then that signal is ascribed to the presence of a fluorescent contaminant. To remove the contaminant, high-purity activated charcoal is added to the beryllium extraction solution (~10 mg/ml) and the extraction procedure is carried out at elevated temperature (80 to 90 °C for at least 45 minutes). If the beryllium extraction procedure has already been performed, then after the addition of activated charcoal, the extraction process is repeated at the elevated temperature. The solution is filtered to remove the activated charcoal before adding this to the detection solution to make the measurement solution. Details of this process have been published [8].

CALIBRATION AND QUALITY CONTROL:

8. Calibrate the fluorometer with beryllium stock standard solutions. Prepare a calibration graph of fluorescence intensity vs. beryllium concentration (ng/mL) in the stock standard.
   NOTE: To test a range of 0.05 µg to 6 µg of beryllium on the sampling media, beryllium stock standard solutions are made up using beryllium spectrometric standards diluted with the ammonium bifluoride dissolution solution. A recommended series of stock standard solutions is (800, 200, 40, 10, and 0) ng/mL. As with the samples, the stock standards are prepared for analysis by adding 0.1 mL of beryllium stock standard into 1.9 mL of detection solution (20-fold dilution). Please see Table 1. Either of the two detection solutions may be used.
   NOTE: To test a range of 0.005 µg to 0.4 µg of beryllium on the sampling media, a recommended series of stock standard solutions is (80, 20, 4, 1, and 0) ng/mL. These standards with lower beryllium concentration can be prepared by 10-fold dilution of the stock standards mentioned in the note above. As with the samples, these stock standards are prepared for analysis by adding 0.4 mL of beryllium stock standard into 1.6 mL of detection solution (5-fold dilution). Please see Table 2. Either of the two detection solutions may be used.
   NOTE: When using the lysine-free dye solution ONLY, To test a range can be tested of 0.0005 to 0.4 µg of beryllium on the media using a recommended series of stock solutions is (0, 0.15, 0.3, 0.6 and 2.4) ng/ml. These standards with lower beryllium concentration can be prepared by dilution of the stock standards mentioned in the note above. The standards are prepared for analysis by adding 0.67 mL of beryllium stock standard into 1.33 mL of detection solution (3-fold dilution). This dilution will result in 0, 0.05, 0.1, 0.2 and 0.8 ppb of beryllium in these standards. Please see Table 3. MCE air filters and cellulosic capsules with MCE filters were spiked with a solution of beryllium acetate and analyzed in triplicate after extracting beryllium in 5ml of 1% ABF solution at 85oC for 60 minutes and then mixed with lysine-free dye solution in a 3-fold dilution. The results are shown in Table 4. The difference in the average fluorescent signals from blanks and the 0 ppb standard were subtracted from the fluorescent readings of the spiked filters.
   NOTE: If alternative ratios of dissolution solution and detection solution are used for sample preparation, then a similar ratio for calibration solutions is required.
9. Analyze a stock standard, a reagent blank, and a media blank at least once every 20 samples. Ensure that the concentration range of the stock standards spans the beryllium levels found in the samples.
10. Analyze one media spike and one quality control blind spike per 20 samples (minimum of three each per sample set) to insure that percent recovery is in control (e.g., 100 ± 15). Correct sample results for the average recovery if it differs significantly from 100 %.
    NOTE: If it is suspected that beryllium oxide may be present, then it is recommended to use beryllium oxide for media and blind spikes.

MEASUREMENT:

11. For each sample, obtain the fluorescence intensity at λ_{max} or with optical filter for appropriate wavelength.
12. If the fluorescence response for any of the samples is above the range of responses for the stock standards, dilute the sample filtrate with dissolution solution, reanalyze, and apply the appropriate dilution factor (D) in subsequent calculations.

CALCULATIONS:

13. Obtain the solution concentration for each sample filtrate, C_s (ng/mL), and the average media blank, C_b (ng/mL) from the calibration graph.
14. Using the dissolution volumes (normally 5 mL) of sample, V_s (mL), and media blank, V_b (mL), calculate the concentration, C ($\mu g/m^3$), of Be in the air volume sampled, V (L), while accounting for the dilution factor (D).

$$C=D \times (C_sV_s-C_bV_b)/V \text{ ng/L or } \mu g/m^3$$

NOTE: Tables 1, 2 and 3 can be used for correlating the amount of beryllium in the sampling media with the concentrations of beryllium in solution. Table 1 is for testing media with 0.2 µg to 4 µg of beryllium at 20-fold dilution; Table 2 is for testing media with 0.02 µg to 0.4 µg of beryllium at 5-fold dilution; and Table 3 is for testing media with 0.0005 µg to 0.012 µg of beryllium at 3-fold dilution. Lysine-free dye solution may be used for any of these dilutions, but for 3x dilution, lysine-free dye solution must be used.

Table 1. Correlation of amount of Be in sampling media with Be concentration in stock standard and Be concentration as analyzed, assuming 0.1 mL of sample or stock standard is added to 1.9 mL of detection solution (20-fold dilution).

Be concentration in stock standard (ng/mL)	Be concentration as analyzed (ng/mL)	Amount of Be in the media* (ng)
0	0	0
10	0.5	50
40	2	200
200	10	1000
800	40	4000

*Equals stock standard Be concentration (ng/mL) × volume (5 mL) of dissolution solution used to extract media.

Table 2. Correlation of amount of Be in sampling media with Be concentration in stock standard and Be concentration as analyzed, assuming 0.4 mL of sample or stock standard is added to 1.6 mL of detection solution (5-fold dilution).

Be concentration in stock standard (ng/mL)	Be concentration as analyzed (ng/mL)	Amount of Be in the media* (ng)
0	0	0
1	0.2	5
4	1	25
20	4	100
80	16	400

*Equals stock standard Be concentration (ng/mL) × volume (5 mL) of dissolution solution used to extract media.

Table 3. Correlation of amount of Be in sampling media with Be concentration in stock standard and Be concentration as analyzed, assuming 0.67 mL of sample or stock standard is added to 1.33 mL of lysine-free dye solution (3-fold dilution).

Be concentration in stock standard (ng/mL)	Be concentration as analyzed (ng/mL)	Amount of Be in the media* (ng)
0	0	0
0.15	0.05	0. 75
0.3	0.1	1.5
0.6	0.2	3
2.4	0.8	12

*Equals stock standard Be concentration (ng/mL) × volume (5 mL) of dissolution solution used to extract media.

Table 4: Analysis of beryllium spiked MCE filters and cellulosic filter capsule inserts using 3-fold dilution of the extraction solution with lysine-free dye solution. Beryllium concentration of standard solutions after mixing with the dye solutions were 0, 0.05, 0.1, 0.2 and 0.8ng/ml. Samples analyzed in triplicate, averages and standard deviations shown.

Nominal Be concentration on the spiked filter, µg	Be concentration as analyzed on the spiked MCE filter (µg)	Be concentration as analyzed on the spiked cellulosic internal capsule insert (µg)
0	0.0000±1.2E-5	-0.0001±3.7E-5
0.0005	0.00044±1.9E-5	0.0005±3.6E-5
0.001	0.0009±2.4E-5	0.0009±2.6E-5
0.002	0.0018±4.0E-5	0.0020±1.1E-4
0.005	0.0043±1.3E-5	0.0045±6.4E-4
0.05	0.045±5.5E-4	0.046±1.0E-3
0.48	0.42±3.5E-3	0.45±4.0E-3

Table 5. Other published OELs and guidelines†

Country or organization	8 Hour inhalation exposure limit (µg/m³)	Short term inhalation exposure limit (µg/m³)
Germany	0.06 (respirable); 0.14 (inhalable)	0.06 (respirable); 0.14 (inhalable)
ACGIH TLV® *	0.05	
Australia, France, New Zealand, Singapore, Sweden, Switzerland, United Kingdom	2	
Canada (Quebec)	0.15	
Ireland, Poland, Spain	0.2	
Czech Republic, Japan, Latvia, Norway	1	
Finland	0.1	0.4
China	0.5	0.1
Austria	2	0.8
Denmark	1	2
Hungary	2	2
Belgium, Canada (Ontario), Korea (Republic of)	2	10

*Abbreviations: ACGIH = American Conference of Governmental Industrial Hygienists, TLV® = Threshold Limit Value

†Occupational exposure limits and guidelines other than NIOSH's recommended exposure limit (REL) have not been reviewed by NIOSH. Professional society and other country exposure limits and guidelines are provided as an aid to NMAM users seeking additional information. Inclusion of these standards and guidelines does not constitute endorsement by NIOSH.

EVALUATION OF METHOD:

The method was evaluated [1,2,7] in accordance with published guidelines [9]. Experiments were conducted using an Ocean Optics® portable fluorescence device with the following components:

> USB 200 spectrometer with spectral grating #2 (UV/Vis 600), LS-1 lamp (380 nm) in LS-450 housing, UV-2 casting, OFLV linear filter 200-850, L2 collection lens and slit-200.

Tests were carried out in relative irradiance mode using 2- or 5-second integration times.

The method was evaluated using beryllium oxide spiked onto mixed cellulose ester (MCE) filters at levels of (0, 0.02, 0.1, 0.2, 0.3, 0.4, 1.5, 3.0, and 6.0) µg (five samples at each level) [2,6].

Long-term stability of samples was verified from spikes (number [n] = 30) of 0.1 µg Be on MCE filters. Samples were analyzed at day one (n = 12) and then one week (n = 6), ten days (n = 3), two weeks (n = 3), three weeks (n = 3), and one month (n = 3) after spiking. No diminution of fluorescence signal was observed from samples prepared and analyzed after having been stored for up to thirty days.

Interference tests were carried out using solutions of 0 nmol/L, 100 nmol/L, and 1.0 µmol/L Be in the presence of 0.4 mmol/L Al, Ca, Co, Cu, Fe, Ti, Li, Ni, Pb, Sn, U, V, W, or Zn (separate experiments were carried out for each potential interferant). Interlaboratory evaluations of the method were also performed [10, 11].

The method using the lysine-free detection solution on MCE filters and SOLU-SERT™ internal capsules was compared and tested (with the detection solution containing lysine for comparison) in Table 4 and this was carried out on a Glomax™ spectrometer (From Turner Biosystems, Sunnyvale, CA) with an emission filter of 475 ± 5 nm and the excitation was at 360 nm.

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PARTICULATE FLUORIDES and HYDROFLUORIC ACID by Ion Chromatography

7906

MW: F^-, 18.998 (HF, 20.01) CAS (HF): 7664-39-3 RTECS: (HF) MW7875000

METHOD: 7906, Issue 2 **EVALUATION: FULL** **Issue 2: 20 May 2014**
Issue 1: 15 August 1994

U. S. OELs
OSHA : 2.5 mg/m³ (fluorides); 3 ppm (HF)
NIOSH: 2.5 mg/m³ (fluorides);
3 ppm (HF), STEL (HF): 6 ppm
Other OELs: **[1,2]**

PROPERTIES: HF: gas; mp = -83.1 °C; bp = 19.5 °C; sp. gr. 0.987; VP = 783 mm Hg (104.4 kPa).
Fluoride salts liberate HF vapor in the presence of acids.

SYNONYMS: Hydrogen fluoride; hydrofluoric acid; Sodium fluoride (CAS #7681-49-4)

SAMPLING

SAMPLER: PRE-FILTER, cellulose nitrate, 0.8 µm pore size, 37-mm diameter, + TREATED FILTER, cellulose nitrate impregnated with Na_2CO_3, 0.8 µm pore size, 37-mm diameter, separated by a chemically inert spacer

FLOW RATE: 1 to 2 L/min

VOL-MIN: 15 L
-MAX: 1000 L

SHIPMENT: 4 °C

SAMPLE STABILITY: Stable for at least 14 days (fluorides) / 28 days (HF) if stored at @ 20 °C for 7 days and 4 °C thereafter [1]

BLANKS: 3 minimum field blanks per set

ACCURACY*

RANGE STUDIED: 0.04 to 5.9 mg/m³ (fluorides); 0.30 to 6 ppm (HF)

BIAS*: Negligible [3]

OVERALL PRECISION*($\hat{S}_{rT}$): Fluorides, 0.074; HF, 0.125 [5,6]

EXPANDED UNCERTAINTY*: less than 20% for F^-; less than 22% for HF [4,5]

*Accuracy calculations were determined using reference 4 rather than the traditional NIOSH accuracy criterion.

MEASUREMENT

TECHNIQUE: ION CHROMATOGRAPHY (IC) with conductivity detection

ANALYTE: Fluoride ion (F^-)

EXTRACTION: Aqueous solution of sodium carbonate / sodium hydrogen carbonate

INJECTION VOLUME: 50 µL

ELUENT: 8 mM Na_2CO_3 / 1 mM $NaHCO_3$ flow rate 1.0 mL/min

COLUMNS: Pre-column, anion-exchange column and suppressor column

CALIBRATION RANGE: F^-; 0.4 to 8.0 mg/L [3,5]

ESTIMATED LOD: 0.1 mg/L / 0.009 mg/m³ (120 L air volume; as F^-) [3]

PRECISION ($\overline{S}_r$): Fluorides, 0.033; HF, 0.056 [3]

APPLICABILITY: The working range is (at least) 0.1 to 8 mg/sample for a 250 Liter air sample.

INTERFERENCES: Co-sampled formate and acetate compounds in the work environment can cause a positive interference; thus detection by ion selective electrodes is a suitable alternative if airborne formate and acetate are expected. Cations that form insoluble fluorides, such as Ca^{2+}, Fe^{3+}, and Al^{3+} can cause negative interferences. Recovery of gaseous HF is reduced at high humidity.

OTHER METHODS: This method updates NIOSH 7906 [7] by providing full method accuracy information, and specifies the use of an impregnated filter instead of a treated cellulose pad. The procedure, which is consistent with ISO 21438-3 [6], replaces NIOSH 7903 [8] for the determination of particulate fluorides and gaseous HF in workplace air samples. The advantages of this method are that it can allow for the collection of the inhalable fraction of particulate fluorides by means of the pre-filter (housed within an optional inhalable sampler) and it can provide for lower limits of detection and quantitation for gaseous HF due to higher sampling flow rates. NIOSH 7902 [9] and ASTM D4765 [10] are alternative methods that are recommended for insoluble fluorides, which rely on detection of F- by ion-selective electrode.

REAGENTS:

1. Water, deionized (DI), ≥18 MΩ-cm resistivity
2. Sodium carbonate (Na_2CO_3), anhydrous, American Chemical Society (ACS) analytical grade
3. Sodium hydrogen carbonate ($NaHCO_3$), ACS analytical grade
4. Filter impregnation solution (0.75 M Na_2CO_3); Dissolve 7.95 g Na_2CO_3 in deionized water and swirl to mix. Then bring to 100 mL in a volumetric flask, stopper and mix thoroughly.
5. Eluent stock solution: 0.8 M Na_2CO_3 / 0.1 M $NaHCO_3$; Dissolve 16.96 g Na_2CO_3 and 1.68 g $NaHCO_3$ in deionized water and swirl to mix. Then bring to 200 mL in a volumetric flask, stopper and mix thoroughly.
6. Eluent solution: 8 mM Na_2CO_3 / 1 mM $NaHCO_3$; Transfer 10 mL of 0.8 M Na_2CO_3 / 0.1 M $NaHCO_3$stock solution to a 1 Liter volumetric flask, dilute to the mark with deionized water, stopper and mix thoroughly. Prepare fresh eluent solution weekly.
7. Fluoride (F^-) standard solution, 1000 mg/L
8. Calibration stock solution, 100 mg/mL (as the anion): Place a 10 mL aliquot of fluoride standard solution into a 100 mL volumetric flask, dilute to the mark and mix thoroughly. The solution is stable for at least 4 weeks at room temperature.
9. To prepare the impregnated filter, evenly distribute 120 µL 0.75 M Na_2CO_3 over the surface of the filter and allow to dry at room temperature for several hours.

*See Special Precautions

EQUIPMENT:

1. Sampler: 37-mm diameter cellulose nitrate pre-filter, 0.8 µm pore size, 37-mm impregnated cellulose nitrate filter. The untreated filter collects particulate fluorides, while the impregnated filter collects HF vapor. Arrange the filters serially (with the pre-filter upstream of the impregnated filter) in a 37-mm diameter 3-piece chemically inert cassette filter holder.
2. Personal sampling pump, 1 to 2 L/min, with flexible connecting tubing
3. Ion chromatograph (IC), with pre-column (50 mm by 4.0 mm), anion-exchange column (200 mm by 4.0 mm), suppressor column (4 mm) and conductivity detector; and connected to data processing unit
4. Ultrasonic bath
5. Vessels, 10-mL, inert plastic, with screw caps
6. Volumetric flasks, 25- to 1000 mL
7. Pipets, 50- to 10000 µL
8. Beakers, 25- to 100 mL
9. Filtration apparatus, with filter funnel
10. Disposable filters, cellulosic, 0.45 µm pore size
11. Styrene-based sulfonic acid resin cartridges
12. Water purification system, to prepare greater than or equal to 18 MΩ-cm resistivity deionized water
13. Bottles, polyethylene, 100 mL
14. Syringes, plastic, 5 mL and/or 10 mL
15. Syringe filter cartridges, with 0.8-µm pore size polytetrafluoroethylene (PTFE) membrane filters
16. Micro-syringes, 50 µL, with 60 mm x 0.6 mm needles
17. Auto-sampler vials, polypropylene, 0.75 mL capacity.

SPECIAL PRECAUTIONS: Acids, particularly HF, are extremely corrosive to skin, eyes, and mucous membranes. HF will attack glass. Plastic labware is recommended. Wear gloves, lab coat, and safety glasses while handling acids. All work should be performed with adequate ventilation for personnel and equipment. It is imperative that acid be added to water in order to avoid a violent exothermic reaction [11,12].

SAMPLING, SAMPLE TRANSPORT AND STORAGE:

1. Prior to sampling, load each clean sampler, first with a sampling (impregnated) filter, then with a pre-filter, separating the filters with a spacer. Ensure that the configuration in which the filters are loaded leads to the sampled air passing first through the pre-filter and then through the sampling filter.
2. Calibrate each personal sampling pump with a representative sampler in the line.
3. Sample at an accurately known flow rate between 1 to 2 mL/min for a total sample size of 15 to 1000 L. Avoid sampler overloading.
4. After sampling, remove the filters from the cassette and place them in screw-cap plastic vessels. For the pre-filter portion: With approximately 2 mL eluent(extraction) solution, rinse material from the inside surfaces of the pre-filter portion of the cassette into the vessel. Add eluent solution into the vessels until a final volume of 10 mL is reached.
5. Submit at least three blank untreated filters and three blank impregnated filters as field blanks for each set of samples collected per day. Handle these in the same way as the field samples; i.e., place each filter into a vessel, add 10 mL of eluent solution and ship it to the lab along with the remaining samples.
6. Refrigerate all samples that are to be stored overnight (or longer) prior to shipment to the laboratory. Ship all samples to the laboratory in accordance with established chain-of-custody procedures [13].
7. Refrigerate the samples immediately upon receipt at the lab until ready for analysis.
8. Analyze samples within 2 weeks of receipt. The samples can be stored at room temperature for one week; for longer storage, refrigerate the samples (4 °C).

SAMPLE PREPARATION AND MEASUREMENT:

9. Remove sample vessels from storage and bring them to room temperature.
10. Sonicate the samples in an ultrasonic bath for at least 15 minutes and allow to cool for at least 30 minutes.
11. Using 5- or 10-mL syringes, filter each sample extract solution through a PTFE filter and a styrene-based sulfonic acid resin cartridge (follow the manufacturer's instructions), discard the first two milliliters and place the remaining solution in clean plastic vessels.

CALIBRATION AND QUALITY CONTROL:

12. With dilution of the calibration stock solution in eluent solution, prepare calibration working standard solutions covering the range of approximately 0.4 to 8 µg/mL of fluoride. Store working standards in tightly sealed polyethylene bottles. Prepare fresh working standards biweekly.
13. Calibrate the ion chromatograph with at least six working standards covering the range of (at least) 0.4 to 8 µg/mL of fluoride per sample by preparing a calibration graph of anion peak height (mm or µS) vs. concentration (µg/mL).
14. Analyze working standards together with samples, reagent blanks and field blanks at a frequency of at least 1 per 20 samples (3 minimum of each). Cellulose nitrate filters demonstrate variable batch-dependent blank values, thus media blank correction is essential.

MEASUREMENT

15. Set the ion chromatograph to recommended eluent flow rate, (e.g. 1.0 mL/min or approximately 13 MPa pressure), and other conditions as specified by the instrument manufacturer.
16. Inject a sample aliquot (e.g. 50 µL) into the chromatograph and measure the peak height of the fluoride peak. If the peak height exceeds the linear calibration range, dilute with eluent, reanalyze and apply the appropriate dilution factor in calculations.

CALCULATIONS:

17. Calculate the mass concentration of fluoride, C (mg/m^3), in the air volume sampled, V (L):

$$C=\{\frac{(C_1*V_1*F_d)-(C_0*V_0)}{V*\eta}\}*F_c$$

where:
C_0 = mean concentration, in µg/mL, of fluoride in the field blank test solutions;
C_1 = concentration, in µg/mL, of fluoride in the sample test solution;
V = volume, in liters, of the air sample;
V_0 = volume, in mL, of the field blank test solutions;
V_1 = volume, in mL, of the sample test solutions;
F_d = dilution factor for each sample test solution;
F_c = 1.053 = conversion factor to convert from fluoride to HF concentration (if applicable);
η = recovery.

EVALUATION OF METHOD:

This updates Issue 1, NIOSH 7906 [7], by providing full method accuracy information, and specifies the use of an impregnated filter instead of a treated cellulose pad. The procedure described in issue 2 of NIOSH 7906, which is consistent with ISO 21438-3 [6], also replaces NIOSH 7903 [8] for the determination of particulate fluorides and gaseous HF in workplace air samples.
Recovery of 100% ± 2% was found after sample collection for both F^- and HF [3,5,6], and no breakthrough of HF was observed from impregnated filters for up to 5 mg fluoride [6,14]. The component of the coefficient of variation of the method that arises from analytical variability, determined from the analysis of spiked filters, was 2.4% to 5.6% for HF and 1.7% to 3.3% for fluorides [3,6]. Laboratory testing with test atmospheres of HF (0.5 to 5 mg/m^3) demonstrated quantitative sampling efficiencies (greater than 95%) at relative humidity (RH) of 20% to 60%, but recovery was around 60% at relative humidity of 80%.
The recovery of HF as an effect of relative humidity (RH) greater than 60 percent can be calculated as follows (see also Figure 1):

$$\eta=\frac{[226.5-(2.0914 * RH)]}{100}$$

No effect of humidity (RH from 20% to 80%) was observed on recovery of particulate fluoride over the concentration range of 0.3 to 5 mg/m^3. Results for repeatability and reproducibility of the method for test atmospheres of hydrogen fluoride and fluoride aerosol (Relative humidity was approximately 50%) are shown in Table I. The method has been successfully applied in independent investigations [14] and

has been promulgated as an International Standard [6]. The back-up data and user check reports are references 3 and 14 respectively.

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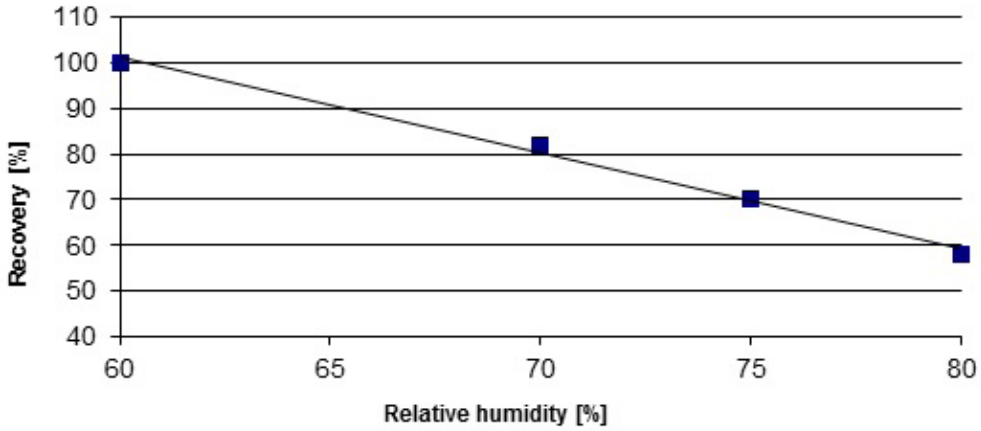

FIGURE 1. HF recovery as function of relative humidity

TABLE 1. Performance evaluation for HF and F^- ion measurements from test atmospheres [5]

Analyte	Concentration (mg/m^3)	S_r[1] (n = 6)	RSD[2](%)	U[3]
HF	0.25	0.007	3.1	0.22
HF	1.2	0.044	2.8	0.21
HF	2.3	0.026	1.1	0.20
HF	5.0	0.099	2.0	0.11
Fluoride	0.04	0.002	3.8	0.19
Fluoride	0.52	0.006	1.3	0.12
Fluoride	2.95	0.009	0.3	0.11
Fluoride	5.9	0.065	1.1	0.11

1 Standard deviation for 6 test samples
2 Relative standard deviation
3 Expanded measurement uncertainty; k = 2 (calculated in accordance with EN 482 [15])

VOLATILE ACIDS by Ion Chromatography 7907

(Hydrogen Chloride, Hydrogen Bromide, Nitric Acid)

NMAM

Formulae: 1. HCl; 2. HBr; 3. HNO_3 MW: Table 1 CAS: Table 1 RTECS: Table 1

METHOD: 7907, Issue 1 **EVALUATION: FULL** **Issue 1: 20 May 2014**

OSHA : Table 2
NIOSH: Table2
Other OELs: [1,2]

PROPERTIES: Table 3

SYNONYMS: 1) HCl: Hydrochloric acid, salt acid, muriatic acid; 2) HBr: Hydrobromic acid; 3) HNO_3: azotic acid

SAMPLING

SAMPLER: Two (2) FILTERS in series separated with a chemically inert spacer: (1) pre-filter: 37-mm diameter quartz fiber filter; (2) sampling filter: 37-mm diameter quartz fiber filter impregnated with 500 µl Na_2CO_3 solution (1 M)

FLOW RATE: 2 L/min

VOL-MIN: 30 L
-MAX: 600 L

SHIPMENT: Routine

SAMPLE STABILITY: Stable for 1 week @ 20 °C and 4 °C thereafter to at least 28 days [3]

BLANKS: 3 blanks minimum per set

ACCURACY*

RANGE STUDIED: HCl: 0.04 to 1.6 mg/sample; HBr: 0.03 to 2.3 mg/sample; HNO_3: 0.04 to 1.5 mg/sample

BIAS*: Negligible [4]

OVERALL PRECISION ($\hat{S}_{rT}$)*: HCl, 0.06; HBr, 0.06; HNO_3, 0.07 [4]

EXPANDED UNCERTAINTY*: Less than 12% for HCl and HBr; less than 14 % for HNO_3 [3,5]

*Accuracy calculations were determined using ISO Guide 98 [5] rather than the traditional NIOSH accuracy criterion.

MEASUREMENT

TECHNIQUE: ION CHROMATOGRAPHY (IC) with conductivity detection

ANALYTES: Chloride (Cl^-), bromide (Br^-) and nitrate (NO_3^-) ion

EXTRACTION: Aqueous solution of sodium carbonate / sodium hydrogen carbonate

INJECTION VOLUME: 25 µL

ELUENT: 3.1 mM Na_2CO_3 / 0.35 mM $NaHCO_3$, flow rate 1.5 mL/min

COLUMNS: Pre-column, anion-exchange column and suppressor column

CALIBRATION RANGE: Chloride, bromide and nitrate at 0.4 mg/L to 4 mg/L

ESTIMATED LOD: 0.003 mg/sample for all three acids; or 0.0012 mg/m³ for a 240 L air volume [4]

PRECISION ($\bar{S}_r$): 0.01 for all three acids [3]

APPLICABILITY: The working range is (at least) 0.01 to 2.0 mg/sample for a 240 Liter air sample [3,4].

INTERFERENCES: Inorganic acids can react with co-sampled particulate matter on the pre-filter, leading to low results. One such example is in the galvanizing industry, where the presence of zinc oxide can be a major confounding factor in the measurement of HCl. Potentially interfering particulate chlorides and nitrates removed by the pre-filter can react with the sampled acids and liberate HCl and HNO_3 that is subsequently collected on the sampling filter, leading to high results [6].

OTHER METHODS: This procedure, which is consistent with ISO 21438-2 [4], replaces NIOSH 7903 [7] for the determination of HCl, HBr and HNO_3 in workplace air samples by IC. The main advantage of this method is that it provides for lower limits of detection and quantitation for volatile acids due to higher sampling flow rates.

REAGENTS:

1. Water, deionized (DI), ≥18 MΩ-cm resistivity
2. Sodium carbonate (Na_2CO_3), anhydrous, American Chemical Society (ACS) analytical grade
3. Sodium hydrogen carbonate ($NaHCO_3$), ACS analytical grade
4. Extraction & eluent stock solution: 0.62 M Na_2CO_3 / 0.069 M $NaHCO_3$; Dissolve 13.14 g Na_2CO_3 and 1.15 g $NaHCO_3$ in 50 mL of deionized water and swirl to mix. Then bring to 200 mL in a volumetric flask, stopper and mix thoroughly.
5. Extraction and eluent solution; 0.0031 M Na_2CO_3/ 0.00035 M $NaHCO_3$: transfer 10 mL 0.62 M Na_2CO_3 / 0.069 M $NaHCO_3$ stock solution to a 2 liter volumetric flask, dilute to the mark with deionized water, stopper and mix thoroughly.
6. Chloride (Cl^-), bromide (Br^-) and nitrate (NO_3^-) standard solutions, 1000 mg/L.
7. Calibration stock solution, 100 µg/mL (as the anion): Transfer 10 mL aliquots of chloride, bromide and nitrate standard solution into a 100 mL volumetric flask, dilute to the mark with deionized water, stopper and mix thoroughly.
8. Sodium carbonate solution, for impregnation of 37 mm diameter quartz fiber filters, 1 mol/L: dissolve 10.6 g Na_2CO_3 in deionized water, quantitatively transfer the solution into a 100 ml volumetric flask, dilute to the mark with deionized water, stopper and mix thoroughly.
9. Preparation of the sampling filter: Apply 500 µL of the sodium carbonate solution, 1 mol/L, evenly on the 37 mm quartz fiber filter and allow to dry for 6 hours in a desiccator. (See NOTE 1, Step 1, p 7907-3.) Good for 14 days.

*See Special Precautions

EQUIPMENT:

1. Sampler: filter, 37-mm diameter quartz fiber impregnated with 500 µl 1 M Na_2CO_3; and pre-filter, 37-mm diameter quartz fiber filter separated by a spacer in a chemically inert cassette filter holder
2. Spacers, of 37-mm diameter suitable for use with the samplers, manufactured from a chemically inert material, e.g. polypropylene sleeves
3. Personal sampling pump, 1 to 5 L/min, with flexible connecting tubing
4. Ion chromatograph (IC), with pre-column (50 mm by 4.0 mm), anion-exchange column (200 mm by 4.0 mm), suppressor column (4 mm) and conductivity detector; and connected to data processing unit
5. Ultrasonic bath
6. Vessels, 15-mL, plastic, with screw caps
7. Volumetric flasks, 10- to 2000 mL
8. Pipets, 10 to 5000 µL
9. Beakers, 25 to 100 mL
10. Water purification system, to prepare ≥18 MΩ-cm resistivity deionized water
11. Bottles, polyethylene, 100 mL
12. Syringes, plastic, 5 mL
13. Syringe filter cartridges, with 0.45-µm pore size polytetrafluoroethylene (PTFE) membrane filters
14. Micro-syringes, 50 µL, with 60 mm x 0.6 mm needles
15. Auto-sampler vials, with slotted septum, 2 mL capacity
16. Analytical balance, with capability of weighing to nearest 0.01 mg

SPECIAL PRECAUTIONS: Wear gloves, lab coat, and safety glasses while handling acids. All work should be performed with adequate ventilation for personnel and equipment. It is imperative that acid be added to water in order to avoid a violent exothermic reaction. Avoid direct contact since acids are both corrosive and irritants to eyes, skin, and the respiratory system [8,9].

SAMPLING, SAMPLE TRANSPORT AND STORAGE:

1. Prior to sampling, load each clean sampler, first with a sampling (impregnated) filter, then with a pre-filter, separating the filters with a spacer. Ensure that the configuration in which the filters are loaded leads to the sampled air passing first through the pre-filter and then through the sampling filter.
   Note 1: Three-piece polystyrene cassettes are appropriate, with the middle ring section of the cassette acting as the spacer. Impregnated filters that are stored in a desiccator can be prepared up to 14 days prior to their use for sampling.
   Note 2: Silica gel sorbent tubes [7] can be used in lieu of impregnated filters, but each sorbent tube must be preceded by a pre-filter.
2. Calibrate each personal sampling pump with a representative sampler in the line.
3. Sample accurately at 2 L/min for a total sample size of 30 to 500 L. Avoid sampler overloading [6].
4. Transport the samples to the laboratory in a manner that prevents contamination or damage to the filters.
5. Submit at least three blank impregnated filters as field blanks for each set of samples collected per day. Handle these in the same way as the field samples.
6. Ship all samples to the laboratory in accordance with established chain-of-custody procedures [10].
7. The samples can be stored at room temperature for one week; for longer storage, refrigerate the samples (4 °C).
8. Analyze samples between 4 days and 4 weeks of sample collection.

SAMPLE PREPARATION:

9. Prior to carrying out sample dissolution, store the sampling filter for at least four days (to avoid nitric acid losses).
10. Remove sample cassettes from storage and bring them to room temperature. Discard the pre-filters.
    NOTE: If desired, the pre-filters can be analyzed for determination of particulate chlorides, bromides and nitrates. If this analysis is carried out, it is recommended to rinse the inside surfaces of the sampler with a few mL of DI water so as to include wall deposits along with material collected on the prefilter.
11. Place the sampling filters (i.e., impregnated filter samples) in 15-mL plastic screw-cap vessels and add 10 mL of extraction solution or deionzied water to each sample. Securely cap the vessels.
12. Sonicate the samples in an ultrasonic bath for at least 15 minutes, and allow to cool for approx. 30 minutes.
13. Using 5-mL syringes, filter 5-mL aliquots of each sample extract solution through a PTFE filter into clean auto-sampler vials.

CALIBRATION AND QUALITY CONTROL:

14. With dilution of the calibration stock solution in eluent solution, prepare calibration working standard solutions covering the range of approximately 0.4 to 4 mg/L of chloride, bromide and nitrate. Store working standards in tightly sealed polyethylene bottles. Prepare fresh working standards weekly.
15. Calibrate the ion chromatograph with at least six working standards covering the range of 0.4 to 4 mg/L of chloride, bromide and nitrate per sample by preparing a calibration graph of anion peak height (mm or µS [micro-siemens]) vs. concentration (mg/L).

16. Analyze working standards together with samples, reagent blanks and field blanks at a frequency of at least 1 per 20 samples (3 minimum of each).

MEASUREMENT:

17. Set the ion chromatograph to recommended eluent flow rate (e.g., 1.5 mL/min) and recommended pressure (e.g., 1.1 x 10^5 kPa), and other conditions as specified by the instrument manufacturer.
18. Inject a sample aliquot, e.g., 25-µL, into the chromatograph, and measure the peak heights of the chloride, bromide and nitrate peaks (at retention times of approx. 5 min, 9 min and 12 min, respectively). If the peak height exceeds the linear calibration range, dilute with eluent, reanalyze and apply the appropriate dilution factor in calculations.

CALCULATIONS:

19. Calculate the mass concentration of each anion, C (mg/m^3), in the air volume sampled, V (L):

$$C = \{\frac{(C_1 * V_1 * F_d) - (C_0 * V_0)}{V}\} * F_c$$

where:
C_0 = mean concentration, in mg/L, of anion in the field blank test solutions;
C_1 = concentration, in mg/L, of anion in the sample test solution;
V = volume, in liters, of the air sample;
V_0 = volume, in mL, of the field blank test solutions;
V_1 = volume, in mL, of the sample test solutions
F_d = dilution factor for each sample test solution
F_c = conversion factor to convert from anion to acid concentration (F_c = 1.0284 for chloride, 1.0126 for bromide, and 1.0163 for nitrate)

EVALUATION OF METHOD:

On impregnated quartz fiber filters, greater than 95 % recovery of hydrochloric and nitric acid was found four weeks after sample collection, and no breakthrough was observed at sample loadings of up to 2.5 mg HCl or 5 mg HNO_3 [3,4,11]. Mean analytical recovery determined from the analysis of spiked filters has been found to be in the range of 97 to 100% for HBr, HCl and HNO_3 [3,11]. The component of the coefficient of variation of the method that arises from analytical variability, determined from the analysis of filters sampled at a dynamic test gas apparatus, was 0.8% to 1.3% for hydrogen chloride and 1.1% to 8.8% for nitric acid; and as determined from the analyses of spiked samples of hydrogen bromide, this value was 0.8% to 1.4% [3]. The method has been independently verified for all three acids, in accordance with applicable performance criteria [11,12]. An interlaboratory study with 5 participants found negligible biases and good agreement for hydrogen chloride and nitric acid at concentrations between 0.6 and 8 mg/m^3 for HCl and 0.8 and 10 mg/m^3 for HNO_3 [6]. The back-up data and user check reports are references 6 and 11, respectively.

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TABLE 1. General Information

Acid	MW	CAS Number	RTECS Number
HCl	36.46	7647-01-0	MW4025000
HBr	80.91	10035-10-6	MW3850000
HNO_3	63.01	7697-37-2	QU5775000

TABLE 2. Occupational Exposure Limits

Acid	OSHA	NIOSH
HCl	C[a] 5 ppm, 7 mg/m^3	C[a] 5 ppm, 7 mg/m^3
HBr	8 hr TWA[b] 3 ppm 10 mg/m^3	C[a] 3 ppm, 10 mg/m^3
HNO_3	8 hr TWA[b] 2 ppm 5 mg/m^3	TWA[c] 2 ppm 5 mg/m^3 STEL[d] 4 ppm 10 mg/m^3

a Ceiling Limit
b Time-Weighted Average
c Up to 10 hr TWA in a 40 hr work week
d Short Term Exposure Limit

TABLE 3. Properties

Acid	Physical State	MP (°C)	BP (°C)	Vapor Pressure (VP)
HCl	gas	-114	-84.9	(38%) 28.3 kPa
	liquid	--	110	(azeotropic, 20.2%)
HBr	gas	-86.9	-66.8	2026.4 kPa
HNO_3	liquid	-42	--	(68% Nitric) 101.3 kPa

NON-VOLATILE ACIDS (Sulfuric Acid and Phosphoric Acid) 7908

Formulae: H_2SO_4 MW: 98.08 CAS: 7664-93-9 RTECS: WS5600000
H_3PO_4 MW: 98.0 CAS: 7664-38-2 RTECS: TB6300000

METHOD: 7908, Issue 1 **EVALUATION: FULL** **Issue 1: 10 May 2014**

U.S. OELs
OSHA : 1 mg/m³ (H_2SO_4 & H_3PO_4)
NIOSH: 1 mg/m³ (H_2SO_4 & H_3PO_4); STEL: 3 mg/m³ (H_3PO_4)
Other
OELs: [1,2]

PROPERTIES:
H_2SO_4: Liquid, mp = 3.0 °C (98%); 10 °C (100%); bp = 338 °C (98%); 330 °C (100%); VP = < 0.0001 kPa @ 20 °C
H_3PO_4: Solid (often used in an aqueous solution), mp = 42.4 °C; bp = 158 °C; vp = 0.0038 kPa @ 20 °C

SYNONYMS: H_2SO_4: hydrogen sulfate, oil of vitriol; H_3PO_4: ortho-phosphoric acid

SAMPLING

SAMPLER: FILTER, 37-mm diameter quartz fiber; or polytetrafluoroethylene (PTFE), 0.45 µm pore size

FLOW RATE: 1 to 5 L/min

VOL-MIN: 15 L
-MAX: 2000 L

SHIPMENT: 4 °C

SAMPLE STABILITY: Stable for 1 week at about 20 °C and at 4 °C thereafter to 28 days [3]

BLANKS: 3 field blanks minimum per set

ACCURACY*

RANGE STUDIED: 0.005 to 2.0 mg/sample

BIAS*: Negligible [3]

OVERALL PRECISION ($\hat{S}_{rT}$)*: H_2SO_4 = 0.086; H_3PO_4 = 0.106

EXPANDED UNCERTAINTY*: less than 23% for both H_2SO_4 and H_3PO_4 [6]

* Accuracy calculations were determined using references 5 and 6 rather than the traditional NIOSH accuracy criteria.

MEASUREMENT

TECHNIQUE: ION CHROMATOGRAPHY (IC) with conductivity detection

ANALYTES: Sulfate (SO_4^{2-}) ion, phosphate (PO_4^{3-}) ion

EXTRACTION: Aqueous solution of sodium carbonate / sodium hydrogen carbonate

INJECTION VOLUME: 50 µL

ELUENT: 2.7 mM Na_2CO_3/0.3 mM $NaHCO_3$, flow rate 1.5 mL/min

COLUMNS: Pre-column, anion-exchange column and suppressor column

CALIBRATION RANGE: H_2SO_4; 0.2 mg/L to 8 mg/L;
H_3PO_4; 0.8 mg/L to 8 mg/L [6]

ESTIMATED LOD: H_2SO_4 = 0.002 mg/m³;
H_3PO_4 = 0.003 mg/m³ (1 m³ air volume)[6]

PRECISION ($\bar{S}_r$): H_2SO_4 = 0.043;
H_3PO_4 = 0.032 [3,7]

APPLICABILITY: The working range for H_2SO_4 is (at least) 0.002 to 1.0 mg/sample, for H_3PO_4 is 0.004 to 1.0 mg/sample for a 420 Liter air sample [3,6].

INTERFERENCES: Particulate salts of sulfate or phosphate will give a positive interference.

OTHER METHODS: This procedure, which is consistent with ISO 21438-1 [6], replaces NIOSH 7903 [8] for the determination of sulfuric and phosphoric acid in workplace air samples by IC. The main advantage of NIOSH method 7908 is that it can allow for the collection of the inhalable fraction of sulfuric and phosphoric acid aerosols by means of the pre-filter (housed within an optional inhalable sampler.)

REAGENTS:

1. Water, deionized (DI), ≥18 MΩ-cm resistivity
2. Sodium carbonate (Na_2CO_3), anhydrous, American Chemical Society (ACS) analytical grade
3. Sodium hydrogen carbonate ($NaHCO_3$), ACS analytical grade
4. Extraction & eluent stock solution: 0.27 M Na_2CO_3 / 0.03 M $NaHCO_3$; dissolve 2.86 g Na_2CO_3 and 0.25 g $NaHCO_3$ in 25 mL of deionized water and swirl to mix. Then bring to 100 mL in a volumetric flask, stopper and mix thoroughly.
5. Extraction & eluent solution: 0.0027 M Na_2CO_3 / 0.0003 M $NaHCO_3$; transfer 10 mL of 0.27 M Na_2CO_3 / 0.03 M $NaHCO_3$ stock solution to a 1 L volumetric flask, dilute to the mark with deionized water, stopper and mix thoroughly.
6. Sulfate (SO_4^{2-}) ion and phosphate (PO_4^{3-}) ion standard solutions, each 1000 mg/L
7. Calibration stock solution, 100 mg/L (as the anion): Place 10 mL aliquots of sulfate and phosphate standard solution into a 100 mL volumetric flask, dilute to the mark and mix thoroughly.

*See Special Precautions

EQUIPMENT:

1. Sampler: filter, 37-mm diameter quartz fiber; or polytetrafluoroethylene (PTFE), 0.45 µm pore size, in cassette filter holder manufactured from acid-resistant (chemically inert) material
   NOTE: Quartz fiber filters should be binderless and heat-treated.
2. Personal sampling pump, 1 to 5 L/min, with flexible connecting tubing
3. Ion chromatograph, with pre-column (50 mm by 4.0 mm), anion-exchange column (200 mm by 4.0 mm), suppressor column (4 mm) and conductivity detector; and connected to data processing unit
4. Ultrasonic bath
5. Vessels, 10-mL, plastic (e.g., polypropylene), with screw caps
6. Volumetric flasks, 25- to 1000 mL
7. Pipets, 50 to 10000 µL
8. Beakers, 25 to 100 mL
9. Water purification system, to prepare greater than or equal to18 MΩ-cm resistivity deionized water
10. Bottles, polyethylene, 100 mL
11. Syringes, plastic, 5 mL
12. Syringe filter cartridges, with 0.8-µm pore size polytetrafluoroethylene (PTFE) membrane filters
13. Micro-syringes, 50 µL, with 60 mm x 0.6 mm needles
14. Tweezers, PTFE-coated
15. Auto-sampler vials, 2 mL capacity
16. Analytical balance, with capability of weighing to nearest 0.01 mg

SPECIAL PRECAUTIONS: Wear gloves, lab coat, and safety glasses while handling acids. All work should be performed with adequate ventilation for personnel and equipment. It is imperative that acid be added to water in order to avoid a violent exothermic reaction. There is risk of fire and explosion when phosphoric acid has contact with bases, combustible substances, oxidizing agents, reducing agents or water. Avoid physical contact since both sulfuric and phosphoric acid are both corrosive and irritants to eyes, skin, and the respiratory system. These are caustic materials and can react with metals to form flammable hydrogen gas. Do NOT mix with solutions containing bleach or ammonia [9,10].

SAMPLING, SAMPLE TRANSPORT AND STORAGE:

1. Calibrate each personal sampling pump with a representative sampler in-line.
2. Sample at an accurately known flow rate between 1 and 5 L/min for a total sample size of 15 to 1000 Liters. Avoid sampler overloading.
3. Immediately after sampling, remove the filter from the cassette with PTFE-coated tweezers and place it in a 10-mL screw-cap plastic vessel. With about 2 mL extraction solution (0.0027 M Na_2CO_3 / 0.0003 M $NaHCO_3$), rinse material from the inside surfaces of the

cassette into the vessel. Add additional extraction solution into the vessel until a final volume of 5 mL is reached.

4. Submit at least three field blanks for each set of samples collected per day. Handle these in the same way as the field samples; i.e., place each filter into a vessel, add 5 mL of eluent solution and ship it to the lab along with the remaining samples.
5. Refrigerate all samples that are to be stored overnight (or longer) prior to shipment to the laboratory. Ship all samples to the laboratory in accordance with established chain-of-custody procedures [11].
6. Refrigerate the samples (4 °C) immediately upon receipt at the lab until ready for analysis.
7. Analyze samples within 4 weeks of receipt.

SAMPLE PREPARATION:

8. Remove sample vessels from storage and bring them to room temperature.
9. Sonicate the samples in an ultrasonic bath for at least 15 minutes and allow to cool for at least 30 minutes.
10. Using 5-mL syringes, filter each sample extract solution through a PTFE filter into clean plastic vessels or into autosampler vials (if autosampler used).

CALIBRATION AND QUALITY CONTROL:

11. Through dilution of the calibration stock solution in eluent solution, prepare calibration working standard solutions covering the range of approximately 0.2 to 8 mg/L of sulfate and phosphate. Store working standards in tightly sealed polyethylene bottles. Prepare fresh working standards weekly.
12. Calibrate the ion chromatograph with at least six working standards covering the range of 0.2 to 8 mg/L of sulfate and phosphate ion per sample by preparing a calibration graph of anion peak height (mm or µS [micro siemens]) vs. concentration (mg/L).
13. Analyze working standards together with samples, reagent blanks and field blanks at a frequency of at least 1 per 20 samples (3 minimum of each).

MEASUREMENT:

14. Set the ion chromatograph to desired eluent flow rate, e.g.,1.5 mL/min, and column pressure, e.g., 1.1 x 10^5 kPa, and other conditions as specified by the instrument manufacturer.
15. Inject a sample aliquot, e.g., 50-µL, into the chromatograph, and measure the peak heights of the phosphate and sulfate peaks (at retention times of about 9 min and 11.6 min, respectively). If the peak height exceeds the linear calibration range, dilute with eluent, reanalyze and apply the appropriate dilution factor in calculations.

CALCULATIONS:

16. Calculate the mass concentration of each anion, C (mg/m^3), in the air volume sampled, V (L):

$$C = \{\frac{(C_1 * V_1 * F_d) - (C_0 * V_0)}{V}\} * F_c$$

where:

C_0 = mean concentration, in mg/L, of anion in the field blank test solutions;
C_1 = concentration, in mg/L, of anion in the sample test solution;
V_1 = volume, in liters, of the air sample;
V_0 = volume, in mL, of the field blank test solutions;

V_1 = volume, in mL, of the sample test solutions
F_d = dilution factor for each sample test solution
F_c = conversion factor to convert from anion to acid concentration:
F_c = 1.021 for sulfate; F_c = 1.031 for phosphate

EVALUATION OF METHOD:

Laboratory testing with generated atmospheres of sulfuric acid mist yielded a collection efficiency of greater than 95% over the range 0.5 to 10 mg/m^3 of H_2SO_4 on 0.45 µm pore size PTFE filters [4]. Greater than 95% recovery of sulfuric acid and phosphoric acid was found four weeks after sample collection. On quartz fiber filters, 97 to 100% recovery of sulfuric acid was found four weeks after sample collection, and no breakthrough was observed at sample loadings of up to 1 mg [3]. Mean analytical recovery determined from the analysis of spiked quartz fiber filters has been found to be in the range of 97 to 100% for both acids [3,4]. The component of the coefficient of variation of the method that arises from analytical variability, determined from the analysis of spiked quartz fiber filters, was 0.7% to 3.2% for phosphoric acid and 0.5% to 2.6% for sulfuric acid [3]. An interlaboratory study with 26 participants found negligible biases and interlaboratory relative standard deviations of 12 to 15% for sulfuric acid and phosphoric acid concentrations between 0.05 and 1 mg/m^3 [12]. The method has also been field tested for sulfuric acid measurements at sample volumes of up to nearly 2,000 Liters [13]. The analytical figures of merit for the method satisfy performance criteria specified in an applicable consensus standard [14]. The back-up data and user check reports are references 4 and 12 respectively.

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TOLUENE in Blood

8007

C_7H_8 MW: 92.14 CAS: 108-88-3 RTECS:XS5250000

METHOD: 8007, Issue 1 **EVALUATION: FULL** **Issue 1: 5 March 2013**

NIOSH and OSHA: NA
Because data on exposure limits and guidelines may change over time, NIOSH recommends referring to the following sources for updated limits and guidelines [1,2].

PROPERTIES: Clear liquid; bp 110.6 °C; VP 28.4 mm Hg at 25 °C; d^{20} 0.8669 g/mL.

BIOLOGICAL INDICATOR OF: Exposure to toluene

SYNONYMS: Methylbenzene, Phenylmethane, Toluol, Methylbenzol

SAMPLING

SPECIMEN: Blood (collected within 12 hours of last exposure)

VOLUME: Fill a 10-mL vacuum specimen tube as completely as possible (to reduce the amount of airspace)

PRESERVATIVE: Sodium citrate (light blue top)

SHIPMENT: Insulated container with bagged refrigerant

SAMPLE STABILITY: Stable at least 30 days at 4 °C [3]

CONTROLS: Collect and refrigerate immediately

ACCURACY

RANGE STUDIED: 0.0208-5.76 µg/mL [3]

ACCURACY: <5% [3]

BIAS: 0.0006

OVERALL PRECISION ($\hat{S}_{rT}$): 0.0157 [3]

SAMPLE STABILITY: 99.0% (Day 30) [3]

MEASUREMENT

TECHNIQUE: HEADSPACE/GAS CHROMATOGRAPHY, FID

ANALYTE: Toluene

HEADSPACE CONDITIONS: Transfer Temp,129 °C; Withdrawal, 0.80 min; Thermostat Time, 30 min; Needle, 120 °C; GC Cycle Time, 34 min; Sample Temp: 99 °C; Pressurize, 4.0 min; Inject, 0.40 min

INJECTION CONDITIONS: Direct injection onto column for 0.4 min, then split flow for the remainder of the run at 130 mL/min

TEMPERATURE-INJECTION: 129 °C
-DETECTOR: 250 °C
-COLUMN: 50 °C (hold for 2 min); 50 to 220 °C @ 10 °C/min; 220 °C (hold for 5 min)

CARRIER GAS: Helium, at 21 psi head pressure

COLUMN: Capillary, fused silica, 75-m x 0.53 mm, coated internally with 3.0 µm film 6% cyano- propylphenyl, 94% dimethylpoly-siloxane, bonded and cross-linked

CALIBRATION: Analyte in control blood; with isobutanol internal standard (IS)

Estimated LOD: 0.006 µg/mL in whole blood [3]

APPLICABILITY: Can be used in monitoring the exposure of workers and drug abusers for toluene.

INTERFERENCES: None identified. The chromatographic separation conditions may be adjusted to correct separation problems.

OTHER METHODS: NIOSH Method 8002 is a partially-evaluated, packed-column GC/FID method with lower accuracy and a higher detection limit. [4] The National Center for Environmental Health (NCEH)/CDC has a method for 31 volatile organic compounds in blood that includes toluene. This NCEH method is somewhat more complicated, comparable in accuracy, and ~1,000 times more sensitive. [5]

REAGENTS:

1. Whole blood*, citrate treated
2. Toluene* (reagent grade, >99.5%)
3. Isobutanol internal standard (IS) as a 20 mg/L solution in water*
4. Water, ASTM Type II
5. Helium, UHP or higher
6. Hydrogen, UHP or higher
7. Air, UHP or higher
8. Toluene calibration standards*
9. Ethylene glycol*

* See SPECIAL PRECAUTIONS

EQUIPMENT:

1. Gas chromatograph, with FID, column, and data collector (page 8007-1)
2. Headspace sampler, holds up to 40 vials and can thermostat up to 12 vials simultaneously for automated headspace analysis (Any instrument that can achieve the headspace settings specified on p. 8007-1 is acceptable)
3. Bagged refrigerant, and refrigerator
4. Adjustable pipette, 10-mL, tips 10-mL, plastic or serological
5. Headspace vials, 20-mL, with caps and septa
6. Micro-liter syringes, 10-µL , 25-µL, 100-µL, 1-mL
7. Volumetric flasks, 10-mL, 25-mL, 1-L
8. Syringes, twist-on fitting (luer lock style or equivalent), 5-mL, and 20 gauge needles
9. Tubes, vacuum blood collection, 10-mL, citrate coated (light blue top)

SPECIAL PRECAUTIONS: Wear gloves, lab coat, and safety glasses while handling all chemicals and blood products. Disposable plastic, glass, and paper (pipet tips, gloves, etc.) that contact blood should be placed in a biohazard container. Contact with biological samples can have serious health consequences through exposure to hepatitis, HIV, and other diseases. All personnel collecting, handling, or analyzing samples should follow universal precautions [6] and comply with the OSHA bloodborne pathogens standard [7] which includes immunization for hepatitis B. Toluene is extremely flammable. All work should be performed in a fume hood.

SAMPLING:

1. Collect the blood by filling a 10-mL vacuum blood collection tube (light blue top, citrate) as completely as possible in order to keep the air space to a minimum. Be certain to invert the blood tube several (5-10) times to mix the anticoagulant.
   NOTE: If desired, duplicate blood tubes could be drawn to allow for estimation of measurement precision, especially if collecting from numerous participants.
2. Immediately transfer the sample to a refrigerator or cooler (≤ 4 °C.)
3. Ship the sample vial in a well-insulated container equipped with blue ice or other cooling material.

SAMPLE PREPARATION:

4. Allow the blood sample to reach room temperature, then mix gently so as to not produce a froth by inverting the tubes 4 to 5 times.
5. Add 1.5 mL of the IS solution to a 20-mL headspace vial.
6. Extract 1.5 mL of sample from the vacuum vial using a 5-mL syringe with a twist-on fitting (luer lock style or equivalent) or micropipette and transfer the blood to a headspace vial.
7. Cap both sample and headspace vials immediately.
8. Mix the contents of each headspace vial thoroughly.

STOCK STANDARD PREPARATION:

9. Prepare a primary stock standard solution by diluting 20 µL of toluene to 50 mL with ethylene glycol (20 µL/50 mL = 345.7 µg/mL.) Store in a tightly capped glass container having little or no head space. NOTE: Aliquots of toluene should be introduced below the ethylene glycol to prevent loss of toluene.
10. Prepare stock standards by diluting aliquots of the primary standards with ethylene glycol. Suggested levels: 34.6 µg/mL, 3.46 µg/mL, 0.346 µg/mL.

CALIBRATION AND QUALITY CONTROL:

11. Calibrate with at least five working standards in duplicate covering the concentration range of the samples.
    a. Prepare each working standard by adding 1.5 mL of IS solution and 1.5 mL of blank blood to a headspace vial and cap the vial. Spike the mixture in the vial (through the septum using a micro-syringe) with a stock standard solution to the desired concentration of toluene and mix by shaking.
    b. Prepare at least two blanks by repeating step a. but omitting the toluene spike.
    c. Measure the peak areas of toluene and isobutanol in the chromatograms. Subtract the average toluene peak area of the blank from the toluene peak areas of the standards (see NOTE 1.) Divide the peak area of the blank-corrected toluene by the peak area from the isobutanol peak. Prepare a calibration curve of the peak area Std/area IS versus the toluene concentration of the standards.
    NOTE 1: A trace amount of toluene may be present in the blood of some donors. These levels will vary depending upon environmental exposures. If the blanks show the presence of toluene the standards need to be blank corrected, or else the sample results will be biased low. Geometric means for the U.S. population as determined from the National Health and Nutrition Examination Survey may be useful for comparison. [8]
    NOTE 2: It is also highly recommended that a reagent blank or blanks be included in the analysis. Atmospheric toluene in the lab may contribute errors to the measured values. A reagent blank using water, a blank headspace vial, or both of these options will show if the laboratory conditions are free from a quantifiable amount of toluene.
12. Prepare two levels of quality control (QC) samples by spiking toluene into whole blood. These levels could be at ~10 X LOQ and 200 X LOQ, but could be adjusted to better suit the anticipated levels of the sample set. Unspiked samples of the blood used to prepare the QC samples should be analyzed to determine the blank level and the true target level. QC samples should be analyzed with every batch such that they constitute 10% of the sample batch.
13. QC values should be within +/- 20% of the spiked values. If not, the batch is considered out of control, the batch data discarded, and corrective actions should be taken before more samples are analyzed. Alternatively, if the method has a long history in the lab allowing enough data for control charts to be constructed, the control charts could serve as the in or out of control decision guide, which could be looser or stricter than the recommended 20%.

MEASUREMENT:

14. Set the gas chromatograph according to manufacturer's recommendations and to conditions given on page 8007-1.
15. Set the headspace sampler according to manufacturer's recommendations and to conditions given on page 8007-1.
16. Inject and analyze samples, standards, QC samples, and blanks.
17. Measure the peak area of both toluene and isobutanol in the chromatograms (do not subtract the blank from the samples). Divide the peak area of the toluene peak by the area from the isobutanol peak.

CALCULATIONS:

18. Determine the concentration (µg/mL) of the toluene in each sample of blood using the calibration curve obtained in step 11c.

EVALUATION OF METHOD:

This method was evaluated over the range specified on page 8007-1. These ranges, 0.0208 to 5.76 µg/mL, represent from 1 x LOQ to 300 x LOQ. Six replicates were analyzed at each level. The average recoveries at the various levels ranged from 97% to 106% for toluene. The LOD and LOQ were determined by preparing a series of duplicate standards. Each series was made up and analyzed on a different day. The resulting data was then fitted to a quadratic curve. The LOD and LOQ were estimated according to Burkart's Method. [9] A long-term storage study was carried out at the 10 x LOQ level. Citrated whole blood samples that were spiked with toluene were stored at 24 °C and 4 °C for 1, 4, and 7 days and for 7,10, 21, and 30 days (respectively,) and then analyzed. Average recoveries were 96% at room temperature and 99% at 4 °C. Room temperature storage is not advised because if the sample clots before it is analyzed, the results will be compromised.

LIMITATION OF METHOD:

Concerning the use of isobutanol as an internal standard: While the boiling points of toluene and isobutanol are similar, their Henry's Law constants and thus their partitioning coefficients are quite different. This could lead to biases if there are differences in polarity in the samples or between the samples and the standards. This is one reason the calibration standards in this method are prepared using blood and not just solvent. An alternative approach could entail the use of an internal standard that partitions similarly to toluene, such as fully-deuterated toluene (toluene-d8). This would cause an increase in the cost of the method per sample (and would need to be validated by the end user), but is mentioned here as an option.

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METHOD WRITTEN BY:

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FLUORIDE in URINE

8308

F | MW: 19.00 | CAS: 16984-48-8 | RTECS: LM6290000

METHOD: 8308, Issue 3 **EVALUATION:** FULL **Issue 1:** 15 February 1984 **Issue 3:** 14 March 2016

BIOLOGICAL INDICATOR OF: exposure to inorganic fluorides [1,2]

SYNONYMS: None

SAMPLING

SPECIMEN: urine, pre- and post-shift

VOLUME: 50 mL in chemically clean polyethylene bottles

PRESERVATIVE: 0.2 g EDTA added to bottles before collection

SHIPMENT: in insulated containers using bagged refrigerant

SAMPLE STABILITY: 2 weeks @ 4 °C, longer if frozen

CONTROLS: collect 3 sets of specimens from unexposed workers (pre- and post-shift)

ACCURACY

RANGE STUDIED: not studied

BIAS: not determined

OVERALL PRECISION ($\hat{S}_{rT}$): not determined

ACCURACY: ± 23.6%

MEASUREMENT

TECHNIQUE: ION SELECTIVE ELECTRODE (ISE)

ANALYTE: fluoride ion (F^-)

DILUTION: mix equal volumes of urine with TISAB

CALIBRATION: solutions of sodium fluoride in water

QUALITY CONTROL: spiked urine pools; correct for creatinine content

RANGE: 1 to 100 mg/L urine

ESTIMATED LOD: 0.1 mg/L urine

RECOVERY: 0.95 [3]

PRECISION ($\bar{S}_r$): 0.04

APPLICABILITY: Any fluorine-containing substances that can be metabolized to fluoride (F-) can be monitored using this procedure. Inorganic compounds of fluoride can be absorbed by the body resulting in the excretion of fluoride ions as sodium fluoride. Dietary and domestic water sources of fluoride must be considered, as well as dental treatments.

INTERFERENCES: Hydroxide, the only positive interference, is eliminated by use of the buffer. Negative interferences from complexation of fluoride by cations, such as calcium, are minimized by EDTA preservative and the high ionic strength buffer.

OTHER METHODS: This method is P&CAM 114 [4] in a revised format. Other methods that have been used are those described in the NIOSH criteria documents on inorganic fluorides [1] and hydrogen fluoride [2].

REAGENTS:

1. Distilled or deionized water.
2. Sodium citrate tribasic dihydrate ($Na_3C_6H_3O_7 \cdot 2H_2O$), ACS reagent grade or better.
3. Ethylenediaminetetraacetic acid (EDTA) disodium salt, ACS reagent grade or better.
4. Acetic acid, glacial, ACS reagent grade or better.
5. Sodium chloride, ACS reagent grade or better.
6. Sodium hydroxide, 5 M. Dissolve 20 g NaOH in distilled water; dilute to 100 mL.
7. Sodium fluoride, ACS reagent grade or better.
8. Calibration stock solution, 100 µg F^- /mL. Dissolve 0.2211 g dry sodium fluoride in distilled water. Make 1000 mL solution.
9. Total ionic strength activity buffer (TISAB), pH 5. Add 57 mL glacial acetic acid, 58 g sodium chloride, and 0.30 g sodium citrate to a 1-L beaker containing 500 mL distilled water. Stir to dissolve. Place beaker in water bath for cooling. Slowly add 5 M sodium hydroxide until the pH is between 5.0 and 5.5. Cool to room temperature; dilute to 1 L with distilled water.
10. Fluoride in Urine Certified Reference Materials (CRMs).

EQUIPMENT:

1. Polyethylene bottles, 125-mL, wide-mouth.
2. Fluoride ion specific electrode (ISE), with reference electrode.
3. pH/millivolt meter, reading to ± 0.5 mV.
4. Stirrer, magnetic.
5. Stirring bars, PTFE-coated.
6. Beakers, plastic, 50-mL.
7. pH electrode.
8. Pipets, appropriate sizes for standards.
9. Volumetric flasks for standards.
10. Water bath.
11. Tissues, low-lint lab wipers.

SPECIAL PRECAUTIONS: Wear gloves, lab coat, and safety glasses while handling all chemicals and human urine products. Disposable plastic, glass, and paper (pipet tips, gloves, etc.) that contact urine should be placed in a biohazard container. Standard precautions should always be used when handling bodily fluids and/or extracts of bodily fluids [5]. Handle urine samples and urine extracts using proper gloves. Glacial acetic acid is flammable and corrosive and should be handled in a fume hood.

SAMPLING:

1. Collect pre- and post-shift spot urine samples in polyethylene bottles containing 0.2 g EDTA.
2. Ship samples in insulated container at about 4 °C using bagged refrigerant.

SAMPLE PREPARATION:

3. Perform a creatinine determination on an aliquot of the urine (e.g., [6]).

CALIBRATION AND QUALITY CONTROL:

4. Prepare at least five working standards in the range 0.1 to 100 µg F^- /mL by appropriate dilutions of the calibration stock solution with distilled water.

5. Analyze a set of working standards together with the samples and blanks (steps 9 through 12) starting with the lowest concentration.
   NOTE: Working standards, samples, and blanks must be analyzed under the same conditions, including temperature, for accurate results.
6. Prepare a semi-log calibration curve plotting millivolts on the linear scale (y-axis) and fluoride concentration, µg/mL, on the log scale (x-axis).
7. Maintain standardization by running a standard with every 10 specimens.
8. Run a spiked urine control specimen with every 10 specimens to maintain quality assurance.
   NOTE: Urine used for spiked controls must be analyzed before use to determine background fluoride concentration.

MEASUREMENT:

9. Add 10 mL well-mixed urine and 10 mL TISAB to a 50-mL plastic beaker.
10. Place a small stirring bar into beaker and mix continuously on a magnetic stirrer at room temperature.
11. Immerse electrodes. Allow sample to mix for 2 to 3 min and then record millivolt reading.
12. Rinse electrodes and stirring bar thoroughly with distilled water and wipe dry with tissue before next sample analysis.

CALCULATIONS:

13. Convert the millivolt readings to fluoride concentration using the calibration curve from step 6.
14. Express fluoride concentration as mg F^-/g urinary creatinine.

GUIDES TO INTERPRETATION:

Urine concentrations of fluorides in normal non-occupationally exposed workers have been reported to range from 0.2 to 3.2 mg/L depending on dietary intake [7]. Pre-shift levels of less than 4 mg/g creatinine and post-shift levels of less than 7 mg/g creatinine appears to protect workers against bony fluorosis [8]. NIOSH has recommended that post-shift urine specimens should not exceed 7 mg/L (corrected to a specific gravity of 1.024) and pre-shift specimens should not exceed 4 mg/L (corrected to a specific gravity of 1.024) [1,2].

The Biological Exposure Indices (BEI) for fluoride (as of the date of this method's publication) are 2 mg/L prior to shift and 3 mg/L at end of shift [9]. This BEI changed in 2011.

EVALUATION OF METHOD

No formal method evaluation has been reported; however, Tusl [3] reported recoveries of added fluoride from 94 to 100%. Precision based on analysis of 25 specimens in triplicate is estimated to be better than $\bar{S}_r = 0.04$. This method employs standard methodology that has been shown to provide adequate performance data for decades. Additional evaluation data may be found in, but is not limited to, the following references [10-13].

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METHOD WRITTEN BY:

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ACETONE and METHYL ETHYL KETONE in urine 8319

(1) Acetone, CH_3COCH_3	MW: 58.08	CAS: 67-64-1	RTECS: AL3150000
(2) Methyl ethyl ketone, $CH_3COCH_2CH_3$	MW: 72.11	CAS: 78-93-3	RTECS: EL6475000

METHOD: 8319, Issue 1 **EVALUATION: FULL** **Issue 1: 28 October2014**

OSHA & NIOSH: N/A
Because data on exposure limits and guidelines may change over time, NIOSH recommends referring to the following sources for updated limits and guidelines [1-4].

PROPERTIES: (1) bp 56.2 °C; d^{20} 0.789 g/mL
(2) bp 79.6 °C; d^{20} 0.805 g/mL

BIOLOGICAL INDICATOR OF:
Exposure to (1) acetone
(2) methyl ethyl ketone

SYNONYMS: (1) dimethyl ketone; 2-propanone; ketone propane; dimethyl formaldehyde; pyroacetic ether
(2) 2-butanone; MEK; butanone; methyl acetone; butan-2-one; oxobutane

SAMPLING

SPECIMEN: Two urine samples (before and after exposure)

VOLUME: Fill a 20-mL amber VOA vial leaving minimal headspace

SHIPMENT: Ship in an insulated container with bagged refrigerant

SAMPLE STABILITY: Stable at least 30 days at 4 °C [5]

CONTROLS: Collect and pool urine from matched population of unexposed workers if possible, then refrigerate immediately

ACCURACY

RANGE STUDIED: (1) 2.1 - 606 mg/L [5]
(2) 2.2 - 617 mg/L [5]

ACCURACY: (1) ± 11.5%, (2) ± 15.0%

BIAS: (1) -0.0444, (2) -0.0782

OVERALL PRECISION ($\hat{S}_{rT}$): (1) 0.0468 [5], (2) 0.0507

SAMPLE STABILITY: (1) 101% (Day 30) [5]
(2) 105% (Day 30) [5]

MEASUREMENT

TECHNIQUE: GAS CHROMATOGRAPHY, FLAME IONIZATION DETECTOR, HEADSPACE

ANALYTES: Acetone and methyl ethyl ketone

INJECTION VOLUME: 500 µL or timed (see measurement section)

TEMPERATURE
-INJECTION: 180 °C
-DETECTOR: 250 °C
-COLUMN: 40 °C (4 min); 40 to 60 °C @ 3 °C/min; 60 to 220 °C @ 20 °C/min; 220 °C (2 min)

CARRIER GAS: Helium, at 15 psi head pressure

COLUMN: Capillary, fused silica, 6% cyanopropylphenyl, 94% dimethylpolysiloxane, 75 m x 0.53 mm ID, 3.0 µm film thickness

CALIBRATION: Analyte in control urine; 2-pentanone or other appropriate internal standard

ESTIMATED LOD: (1) 0.6 mg/L in pooled urine [5]
(2) 0.6 mg/L in pooled urine [5]

APPLICABILITY: This method can be used in the analysis of acetone and methyl ethyl ketone in urine specimens. These compounds may be found in the urine of individuals exposed to acetone and methyl ethyl ketone [6,7].

INTERFERENCES: Acetone is a metabolite of 2-propanol; MEK is a metabolite of 2-butanol. Exposure to 2-propanol or 2-butanol may result in increased acetone or MEK excretion, respectively [8,9]. Diabetes and fasting also produce elevated urinary acetone levels [10]. Ethanol reduces MEK metabolism and thus increases the MEK concentration in urine [11]. Gender differences and use of hormonal contraceptives have been shown to affect the metabolism and excretion of MEK [12].

OTHER METHODS: There are several commercially-available, direct-reading, dipstick-type tests that are non-specific for ketones in urine. These are often used in hospitals or by diabetic patients. The Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) has published a headspace method for a variety of alcohols and ketones in urine and blood [13].

REAGENTS:

1. Pooled control urine collected from unexposed workers*
2. Acetone (≥99%) and MEK (≥99%) stock solution: Prepare by diluting the appropriate amounts of the pure analyte in water.* 750 µL in 10 mL gives ~60 mg/mL of each. Be certain to use the densities and purity factors when calculating the exact concentrations. [5]
3. Internal standard solution: Dilute 80 mg of 2-pentanone (≥99%) in enough water to make 1.0 L (80 mg/L).* Alternatively, 100 µL can be added to 1 L which gives roughly the same concentration.
4. Water, ASTM Type II [14]
5. Helium, purified
6. Hydrogen, prepurified
7. Air, filtered, prepurified

* See SPECIAL PRECAUTIONS

EQUIPMENT:

1. Bottles, polyethylene screw-top, 125-mL
2. Volatile organic analysis (VOA) vials, 20-mL, amber, polytetrafluoroethylene (PTFE) caps
3. Gas chromatograph, with flame ionization detector (FID), data system and column (p. 8319-1)
4. Headspace autosampler
5. Bagged refrigerant
6. Pipette, 10-mL, plastic or serological
7. Headspace vials, 20-mL, PTFE/Butyl septa, aluminum crimp cap
8. Microliter syringes, 10-µL, 100-µL, 1-mL
9. Volumetric flask, 10-mL

SPECIAL PRECAUTIONS: Wear gloves, lab coat, and safety glasses while handling all chemicals and human urine products. Disposable plastic, glass, and paper (pipet tips, gloves, etc.) that contact urine should be placed in a biohazard container. Standard precautions should always be used when handling bodily fluids and/or extracts of bodily fluids [15]. Handle urine samples and urine extracts using proper gloves. Acetone and MEK are highly flammable liquids. All work should be performed in a fume hood since both chemicals are respiratory irritants and may depress the central nervous system at high exposure levels.

SAMPLING:

1. Collect urine in a 125-mL polyethylene bottle or other suitable container. Collect at least two urine samples from each worker. Collect one sample before exposure and one sample after exposure.
   NOTE: It is important to avoid contamination of the urine samples by making sure that samples are collected in a clean area away from the source(s) of exposure and under hygienic conditions (after washing hands.)
2. For each sample, immediately transfer from the 125-mL polyethylene bottle enough urine to fill a 20-mL amber VOA vial such that a minimal headspace is left. Cap the containers tightly. When the VOA vial is inverted no air bubbles should be present. Refrigerate after collection.
3. Collect and pool urine from unexposed workers to be used for controls. Refrigerate after collection.
4. Ship the VOA vials and pooled control urine in a refrigerated, well-insulated container. Store refrigerated upon receipt.

SAMPLE PREPARATION:

5. Allow urine to reach room temperature.
6. Pipet 10.0 mL of urine from the VOA vial into a 20-mL headspace vial.
7. Add 0.5 mL of the internal standard solution.
8. Cap vial immediately.

CALIBRATION AND QUALITY CONTROL:

9. Calibrate daily with at least six working standards covering the concentration range of the method (2 to 600 mg/L).
   NOTE: If the range of concentrations of the samples is known (or expected), the calibration curve range can be adjusted accordingly.
   a. Prepare a diluted stock solution by pipetting 1 mL of the concentrated stock solution into a 10-mL volumetric flask and filling to the mark with pooled urine.
   b. Prepare each working standard by diluting a known amount of the diluted stock solution prepared in Step 9a into enough pooled urine to make a total of 10 mL.
      NOTE: A second, more dilute stock solution in urine can be prepared, if desired, so that the lowest calibration standards are made using more easily-measured spiking volumes.
   c. Prepare at least one pooled urine blank by transferring 10 mL of pooled urine (the same pooled urine used for creating the working standards) into a vial.
   d. Process the 10 mL of each working standard and each pooled urine blank using the same procedure as for the samples (steps 5 through 8).
   e. Analyze the working standards, the pooled urine blanks, and the samples together. FIGURES 1 and 2 show representative chromatograms of blank and fortified urines.
   f. Prepare a calibration graph by plotting, for each working standard, the normalized analyte response (peak area of analyte divided by the peak area of the internal standard on the same chromatogram) on the y-axis vs. μg of analyte/mL of urine on the x-axis. The simplest model that adequately describes the data should be used but either a linear (mostly likely 1/x weighted because of the range of the calibration curve) or a quadratic model may be utilized in processing the analytical data. Because humans can endogenously produce both acetone and methyl ethyl ketone, the compounds may be detected in the pooled urine blanks. Before plotting the calibration graph, subtract the normalized analyte response of the pooled urine blank from the normalized analyte response of each working standard. The standard curve should have a coefficient of determination (r^2) of equal to or greater than 0.98 to be acceptable for use. Furthermore, when each standard is substituted back into the calibration equation, the value should be within ±20% of the expected.
10. Prepare at least two levels of quality control (QC) samples by spiking both analytes in urine. These levels should be at approximately 10-fold the limit of quantitation (LOQ) and 200-fold the LOQ, but can be adjusted to better suit the anticipated levels of the sample set. Unspiked samples of the urine used to prepare the QC samples should be analyzed to determine the blank level and the true target level. QC samples should be analyzed with every batch such that they constitute 10% of the sample batch.
11. QC values should normally be within ±20% of the spiked values. If not, the batch is considered out of control, the batch data discarded, and corrective actions should be taken before more samples are analyzed.

MEASUREMENT:

12. Set gas chromatograph according to manufacturer's recommendations and to conditions given on p. 8319-1.
13. Set headspace autosampler according to manufacturer's recommendations and to the following conditions: (NOTE: different types of headspace samplers may require alternative conditions and some of these might not apply.)

a. Suggested conditions for a balanced-pressure type of headspace system:

Transfer Temp:	129 °C	Withdrawal:	0.2 min
Thermostat Time:	30 min	Needle Temp:	120 °C
GC Cycle Time:	28 min	Sample Temp:	80 °C
Pressurize:	1.0 min	Inject:	0.08 min

b. Suggested conditions for a syringe-injection type of headspace system:

Incubation Temp:	95 °C	Injection volume:	500 µL
Incubation Time:	15 min	Fill speed:	120 µL/sec
Agitation speed:	250 rpm	Delay:	5 sec
Run time:	26 min	Injection speed:	300 µL/sec
Syringe Temp:	95 °C	Delay:	500 msec

14. Measure peak area. Normalize the analyte response by dividing the peak area of the analyte by the peak area of the internal standard on the same chromatogram for each working standard, sample, and pooled urine blank.

CALCULATIONS:

15. Determine both the acetone and MEK concentrations (mg/L) in the urine sample from the calibration graph prepared in Step 9f.

EVALUATION OF METHOD:

This method was evaluated over the ranges of the two analytes specified on p. 8319-1. These ranges represent from 1 x LOQ to 300 x LOQ. Six to seven replicates were analyzed at each level. The average recoveries at the various levels ranged from 94% to 106% for acetone and 85% to 98% for MEK. The LOD and LOQ were determined by preparing and analyzing a series of standards in duplicate with the data fitted to a quadratic curve. The LOD and LOQ were estimated according to Burkart's Method [16]. A long-term storage study was carried out at the 10 x LOQ level. Pooled urine samples spiked with the analytes were stored at 4 °C for 1, 4, 7, 10, 21, or 30 days and then analyzed. All recoveries were nearly 100%. When stored at room temperature, a significant reduction in analyte recovery was observed after 7 days [5].

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FIGURE 1. Representative overlaid chromatograms from a high and low urine standard and urine blanks with and without internal standard (IS), full-scale

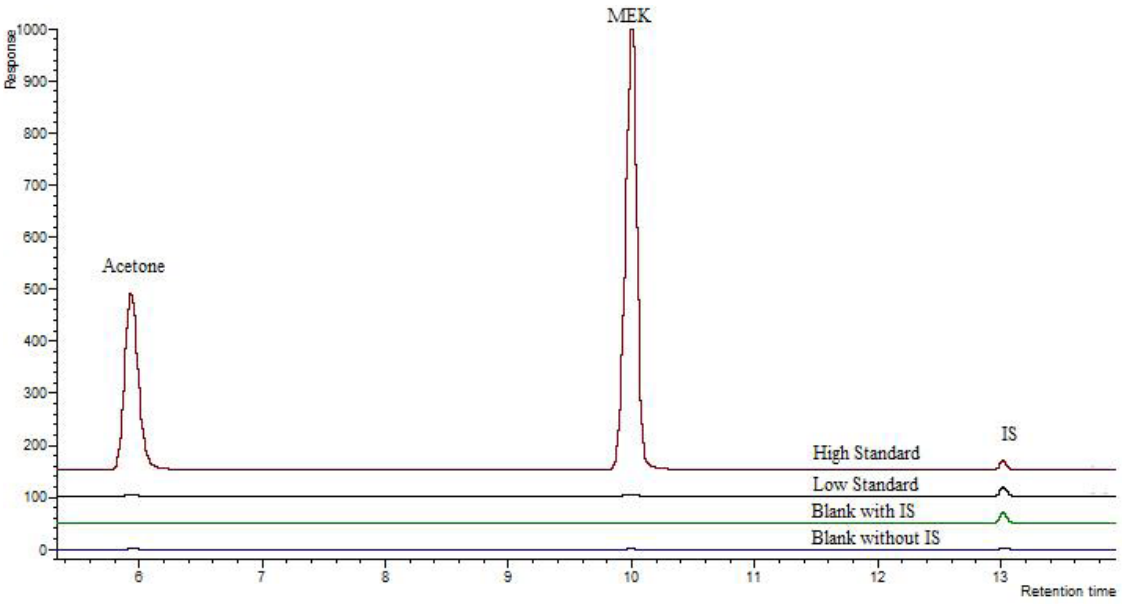
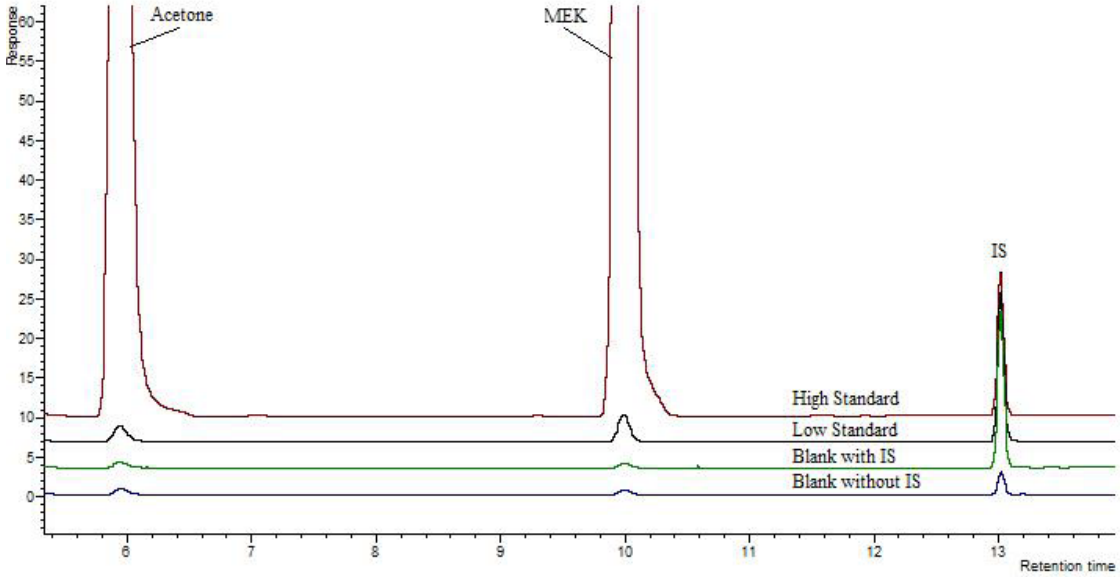


FIGURE 2. Representative overlaid chromatograms from a high and low urine standard and urine blanks with and without internal standard (IS), reduced-scale



o-CRESOL in URINE

8321

$CH_3C_6H_4OH$ MW: 108.14 CAS: 95-48-7 RTECS: GO6300000

METHOD: 8321, Issue 1 **EVALUATION:** FULL **Issue 1:** 18 March 2016

OSHA: N/A
NIOSH: N/A
Because data on exposure limits and guidelines may change over time, NIOSH recommends referring to references 1-4 for updated limits and guidelines concerning o-cresol and its use as a marker for other compounds.

PROPERTIES: colorless solid; MP 31 °C; BP 191 °C
Density (35 °C) = 1.0327 g/mL [5]

SYNONYMS: *ortho*-cresol, 2-cresol, *o*-cresylic acid, 1-hydroxy-2-methylbenzene, 2-hydroxytoluene, 2-methylphenol

SAMPLING

SPECIMEN: Urine

VOLUME: 50-100 mL in screw cap bottle; minimum of 10 mL

SHIPMENT: < 6 ºC

SAMPLE STABILITY: Stable at least 30 days at 4 °C [6]

CONTROLS: Collect urine from unexposed workers, pool and refrigerate

ACCURACY

ESTIMATED LOD: 0.01 µg/mL [6]

RANGE STUDIED: 0.0214 to 30.4 µg/mL [6]

ACCURACY: ± 21% [6]

BIAS: -0.0952 [6]

OVERALL PRECISION ($\hat{S}_{rT}$): 0.0771 [6]

RECOVERY: 92 –112 % [6]

MEASUREMENT

TECHNIQUE: GAS CHROMATOGRAPHY/MASS SPECTROMETRY with SELECTED ION MONITORING (GC/MS-SIM)

ANALYTE: *o*-Cresol

TREATMENT: Acid hydrolysis and liquid/liquid extraction

INJECTION VOLUME: 2 µL

TEMPERATURE
-INJECTION: 265 °C
-DETECTOR: 285 °C
-COLUMN: 50 °C(hold 2 min); 50 to 150 °C @ 10 °C/min; 150 to 310 °C @ 20 °C/min (hold 5 min)

CARRIER GAS: Helium, at 1.3 mL/min

COLUMN: Capillary, fused silica, phenyl arylene polymer virtually equivalent to (5% phenyl)-methylpolysiloxane (30 m x 0.32 mm ID, 0.5 µm film); close equivalent to USP G27

MS PARAMETERS: SIM (ions m/z 108, 107, 77 and 123) Quantifying ions: o-cresol: 108, nitrobenzene: 123. Confirmation ions: o-cresol: 107, nitrobenzene: 77

DWELL TIME: 30 msec

CALIBRATION: *o*-Cresol spiked in control urine and nitrobenzene as internal standard

APPLICABILITY: This method can be used for the determination of total o-cresol in urine specimens. Cresols are excreted in urine primarily as conjugates. This method uses an acid hydrolysis step to convert the conjugates to free o-cresol. (See Evaluation of Method Section.) Exposure to o-cresol will cause elevated urinary levels; however, o-cresol is a metabolite produced from toluene exposure. Not only would toluene exposure interfere with determining o-cresol exposure, but measuring o-cresol in urine is one of the recommended methods for determining toluene exposure. Recommended levels for using o-cresol to measure toluene exposure (at the time of publication of this method) include: ACGIH-TLV, 0.3 mg/g creatinine [1]; DFG-BAT, 1.5 mg/L [2]; and SUVA-VBT, 0.5 mg/L [3].

INTERFERENCES: None noted in the analytical method, but background levels of 0.032 – 0.070 µg/mL o-cresol have been observed [7-9]. These values are near and slightly above the limit of quantitation. Exposure to toluene will cause higher levels of urinary o-cresol as discussed above. p-Cresol is a normal component of human urine [10] and may, along with m-cresol, also be a co-exposure [11-12]. These two compounds have similar mass spectra to o-cresol but are chromatographically resolved under the conditions of this method [6].

OTHER METHODS: There are numerous literature methods for the determination of o-cresol in urine [10], but standardized methods from governmental agencies or consensus standards organizations are not currently available. NIOSH 8305 is a similar but only partially-validated method for phenol and p-cresol [11]. An older validated method using steam distillation and HPLC-UV detection for ~30 related compounds that includes o-cresol can be found in the German MAK collection [12].

REAGENTS:

1. *o*-Cresol* (≥99% purity) primary stock solution (PSS) about 10,000 µg/mL (0.100 g of *o*-cresol in 10 mL of methanol). Store at -10 °C ± 2 °C
2. *o*-Cresol intermediate solutions of 1,000 and 100 µg/mL (0.5 and 0.05 mL of PSS diluted to 5.0 mL with methanol). Store at -10 °C ± 2 °C
3. Human urine* provided by non-exposed individuals, store at < 6 °C**
4. Methanol*, GC grade or better
5. Hydrochloric acid*, concentrated, 33-38%, ACS reagent grade or better
6. Nitrobenzene (≥99% purity) internal standard (IS) solution of 500 µg/mL (0.125 g of nitrobenzene in 250 mL of methanol). Store at 10 °C ± 2 °C
7. Water, ASTM Type II [13]
8. Methyl tert-butyl ether* (MTBE), HPLC grade or better
9. Sodium sulfate, granular, anhydrous, ≥99% purity.
10. Helium, UHP or Grade 5

*See SPECIAL PRECAUTIONS.
**Human urine recommended due to evidence of column problems caused by synthetic urine.

EQUIPMENT:

1. GC-MS capable of selected ion monitoring with data system, autosampler, and column (page 8321-1)
2. Flasks, glass, volumetric: 5, 10 and 250 mL
3. Syringes, glass: 10, 50, 100, 500 and 2,500 µL
4. Tubes, centrifuge, 15-mL graduated polypropylene, with caps
5. Pipetter 1-10 mL, with disposable tips
6. Pasteur pipettes, glass
7. Water bath, 95 °C
8. Wash bottle
9. Vials, autosampler, amber glass
10. Cold storage for -10 °C and 4 °C
11. Bottles, 125 mL polyethylene
12. Analytical balance, to ±0.0001 g.

SPECIAL PRECAUTIONS: Wear gloves, lab coat, and safety glasses while handling all chemicals and human urine products. Disposable plastic, glass, and paper (pipet tips, gloves, etc.) that contact urine should be placed in a biohazard container. Standard precautions should always be used when handling bodily fluids and/or extracts of bodily fluids [14]. Handle urine samples and urine extracts using proper gloves. All work should be performed in a fume hood. Methanol and MTBE are both flammable. Hydrochloric acid is an extremely corrosive chemical capable of severe tissue damage.

SAMPLING:

1. Collect 50-100 mL urine in a 125 mL polyethylene bottle. Collect 2 urine specimens for each worker: one specimen before exposure and one specimen after.
2. Collect and pool urine specimens from unexposed workers to be used for controls.
3. Tightly cap each bottle and ship refrigerated or frozen in an insulated container to maintain the temperature at 6 °C or below.

SAMPLE PREPARATION:

4. Allow urine to reach room temperature and mix thoroughly.
   NOTE: If desired, remove an aliquot of urine to determine creatinine levels.
5. Dispense a 5-mL aliquot of the urine specimen into a 15-mL graduated centrifuge tube.
6. Using a Pasteur pipette, add 1 mL of concentrated HCl, up to the 6 mL calibration mark in the tube.
7. Cap the tube. Shake vigorously for one minute.
8. Place the tube in a water bath at 95 °C for 1.5 hr.
   NOTE: Covering the water bath may be required to maintain the temperature at 95 °C.
9. Remove the tube from the bath and let it cool to room temperature.
10. Add 250 µL of the nitrobenzene IS solution.
11. Add water (ASTM Type II) to the tube, filling it to the 10 mL calibration mark.
12. Pipet 2 mL of MTBE to the tube and cap it.
13. Shake the tube vigorously for 2 min.
14. Allow the phases to separate.
15. Transfer the top organic phase to an amber GC vial containing approximately 0.2 g of anhydrous sodium sulfate (to ensure the dryness of the organic fraction).
16. Cap the vials and store at <6 °C until GC-MS analysis.

CALIBRATION AND QUALITY CONTROL:

17. Calibrate daily with nine working standards containing *o*-cresol at approximately the following concentrations: 0.04, 0.1, 0.2, 1, 2, 10, 20, 40 and 60 µg/mL.
    a. Prepare the standards by adding measured amounts of *o*-cresol intermediate stock solutions to centrifuge tubes containing 5 mL of control urine.
    b. Process the standards following the same procedure used for the samples (steps 4-16).
    c. Prepare at least one method blank for every 20 samples by taking an aliquot of 5 mL control urine and processing it in the same manner as the samples (steps 4-16).
    d. Prepare at least two levels of quality control (QC) samples using a separate source of *o*-cresol and prepare in the same manner as the calibration standards within the analytical range. These levels should be at roughly 10 times the limit of quantitation (LOQ) and 100 X LOQ. Analyze at least two QC samples of different concentration for every 20 samples.
18. Prepare a calibration graph by plotting, for each working standard, the normalized analyte response (peak area of analyte divided by the peak area of the internal standard on the same chromatogram) on the y-axis vs. µg of analyte/mL of urine on the x-axis. The simplest model that adequately describes the data should be used, but either a linear (most likely 1/X weighted because of the range of the calibration curve) or a quadratic model may be utilized in processing the analytical data. Because there may be detectable levels of *o*-cresol in the pooled urine blanks, before plotting the calibration graph, subtract the normalized analyte response of the pooled urine blank from the normalized analyte response of each working standard. The standard curve should have a coefficient of determination (r^2) of equal to or greater than 0.98 to be acceptable for use. Furthermore, when each standard is substituted back into the calibration equation, the value should be within ±20% of the expected value.
19. QC values should be within ±20% of the spiked values. If not, the batch is considered out of control, the batch data discarded, and corrective actions taken before more samples are analyzed.

MEASUREMENT AND CALCULATIONS:

20. Set gas chromatograph according to manufacturer's recommendations and to conditions given on page 8321-1.
21. Set the mass spectrometer according to manufacturer's recommendations, to conditions given on page 8321-1, and to SIM for ions *m/z* 77, 107, 108, and 123.
22. Inject 2 µL of each sample, blank and QC sample.
23. Measure peak areas for *o*-cresol and nitrobenzene in the chromatograms. Divide the peak area of *o*-cresol by the peak area of nitrobenzene in the same chromatogram.

CALCULATIONS:

24. Determine concentration of *o*-cresol from the calibration curve produced in step 18.

EVALUATION OF METHOD:

This method was evaluated at five concentration levels over the range 0.0214 – 2.14 µg/mL. This range represents from 1 x LOQ to 100 x LOQ. Six replicates were analyzed at each level. The average recoveries at the various levels ranged from 86.8 to 118.4%. The limit of detection (LOD) and LOQ study was performed by analyzing a series of standards ranging from 0.0107 to 64.1 µg/mL, fitting the data to a quadratic curve, and estimating the values using "Burkart's Method" [15]. The value obtained for the LOD by this method (0.009 µg/mL) was lower than the lowest standard in the determination (0.0107 µg/mL), so the LOD used for the method was the value of the lowest standard, 0.01 µg/mL. A long-term storage study was carried out at the 30 x LOQ level: pooled urine specimens spiked with *o*-cresol at 0.854 µg/mL were stored at 4 °C for 1, 7, 10, 14, 21 and 30 days and then analyzed. The recoveries across the entire study (1-30 days) were between 92-112%. Another set of specimens stored at room temperature were analyzed after 1 and 7 days, producing recoveries ranging from 90-102% [6]. The analytical range of the method was extended during a secondary laboratory validation step. Two concentration levels were evaluated (5.06 and 30.30 µg/mL) by analyzing five replicates at each level. These levels showed recoveries of 100.2 and 92.8% with relative standard deviations of 0.63 and 1.40% respectively [6].

In order to minimize confusion among users of NIOSH Method 8321, the authors would like to re-emphasize that *p*-cresol is an endogenous human metabolite produced from protein breakdown and will always be found in human urine [10]. The mass spectrum of *p*-cresol is quite similar to that of *o*-cresol and so there is some possibility of peak misidentification. Fortunately, while the peaks are near each other in the chromatogram under the method conditions, the *p*-cresol peak elutes later, is adequately resolved, and thus will not interfere with *o*-cresol analyses [6].

Discussion concerning acid hydrolysis step: The efficiency of the acid hydrolysis step in this procedure was not evaluated. A common method of converting these conjugates (glucuronides and sulfates) back to the parent compounds is heating the sample with a mineral acid. Several literature examples that employ hydrochloric acid under very similar conditions can be found [8,9,12,16-18]. A common thread among these methods is that none of them appear to investigate the efficiency of the acid hydrolysis step. Fustinoni et al. did investigate the hydrolysis step both in terms of amount of acid used and reaction time required [19]. They found that 50 µL of concentrated HCl per 300 µL of urine and reacting for 60 min at 100 °C gave yields of greater than 97%. NIOSH Method 8321 uses 1 mL concentrated HCl per 5 mL urine, heating at 95 °C for 1.5 h, which are nearly identical conditions. These similar conditions should assure adequate efficiency of the acid hydrolysis step and have proven to not be detrimental to the *o*-cresol [6].

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TRICHLOROACETIC ACID IN URINE 8322

FORMULA: $C_2HCl_3O_2$ MW: 163.39 CAS: 76-03-9 RTECS: AJ7875000

METHOD: 8322, Issue 1 **EVALUATION: FULL** **Issue 1: 17 April 2015**

OSHA & NIOSH: N/A
Other OELS: Because data on exposure limits and guidelines may change over time, NIOSH recommends referring to the following sources for updated limits. [1 - 4]

PROPERTIES: White solid; mp 59.1 °C; bp 198.2 °C; d = 1.61 g/cm^3 [5]

BIOLOGICAL INDICATOR OF: Exposure to trichloroethylene, trichloroacetic acid, methyl chloroform, tetrachloroethene, chloral hydrate

SYNONYMS: Trichloroethanoic acid, Aceto-caustin

SAMPLING

SPECIMEN: Urine

VOLUME: At least 10 mL

PRESERVATIVE: None

SHIPMENT: Freeze urine; ship in dry ice in an insulated container.

SAMPLE STABILITY: Stable at least 30 days at -17 ºC [6]

CONTROLS: Urine specimens from matched population of non-exposed persons

ACCURACY

RANGE STUDIED: 0.9 to 100 µg/mL (as trichloroacetic acid)

BIAS: 0.0113

OVERALL PRECISION ($\hat{S}_{rT}$): 0.03656

ACCURACY: 7.5%

MEASUREMENT

TECHNIQUE GAS CHROMATOGRAPHY with ELECTRON CAPTURE DETECTOR (GC-ECD)

ANALYTES: Trichloroacetic acid (determined as the methyl ester)

PROCEDURE: Methylation of an aliquot with BF_3-methanol to form the methyl ester followed by extraction into toluene

INJECTION: 1 µL, splitless for 0.5 min

TEMPERATURES
-INJECTION: 250 ºC
-DETECTOR: 300 ºC
-OVEN: 80 ºC (hold for 0.5 min), 80 to 180 ºC at 20 ºC/min, hold for 7 min

CARRIER GAS: Helium, ~3.5 mL/min

MAKEUP GAS: Nitrogen, 40 mL/min

COLUMN: Capillary, fused silica, 6% cyanopropyl-phenyl-94% dimethylpolysiloxane, 75 m x 0.53 mm ID, 3 µm film

CALIBRATION: Trichloroacetic acid prepared in water to cover range and derivatized with the samples

ESTIMATED LOD: 0.08 µg/mL (as trichloroacetic acid) [6]

APPLICABILITY: This method can be used for the determination of trichloroacetic acid (TCAA) in urine specimens. TCAA is one of several metabolites detected after exposure to a variety of chlorinated compounds (representative compounds listed above) or from contaminated drinking water [7-11].

INTERFERENCES: None observed in the analytical method apart from some carryover issues (see Evaluation of Method section.) TCAA is a non-specific metabolite of several compounds. Urinary TCAA levels reflect exposure to any and all of these precursors. Background TCAA was detected in 76% of urine samples in a US general population sample, with a median concentration of 3.3 µg/L, approximately 300 times lower than the range of this method [12].

OTHER METHODS: There are numerous literature methods for the determination of TCAA in urine [13]. The National Center for Environmental Health/Centers for Disease Control and Prevention (NCEH/CDC) has a method that is more expensive but also significantly more sensitive [11]. This method is based on the procedure used by O'Donnell [7] with some modifications.

REAGENTS:

1. Sodium trichloroacetate [CAS #650-51-1], 97% purity or greater*
2. Boron trifluoride-methanol solution, 14%*
3. Toluene, ACS reagent grade or better*
4. Sodium sulfate, anhydrous, granular; reagent grade or better
5. Acetic acid, glacial; reagent grade or better*
6. Acetone, reagent grade or better*
7. Methanol, reagent grade or better*
8. Helium, purified
9. Nitrogen, Ultra High Purity or P5
10. Water, ASTM Type II [14]

SOLUTIONS:

1. 1:3 glacial acetic acid:deionized water
2. 1:1 acetone:methanol

*** See SPECIAL PRECAUTIONS**

EQUIPMENT:

1. Centrifuge tubes, polypropylene, ~15-mL, with screw caps, or other suitable container for specimen collection and storage
2. Gas chromatograph with electron capture detector, autosampler, data collection system and column (page 8322-1)
3. Microliter syringes, various sizes
4. Volumetric flasks, glass, various sizes
5. Adjustable pipettor with disposable plastic tips, 0.1 to 1-mL
6. Disposable Pasteur transfer pipettes, 15 and 23 cm
7. Culture tubes, 13 mm x 100 mm (~8 mL), with PTFE-lined caps
8. Vortex mixer
9. Glass wool
10. Vials, autosampler, glass, 2-mL with caps
11. Oven, capable of maintaining 60 °C

SPECIAL PRECAUTIONS: Standard precautions should always be used when handling bodily fluids and/or extracts of bodily fluids [15]. Handle urine specimens and urine extracts using powder-free latex or nitrile gloves. Acetic acid, acetone, toluene, and methanol are flammable; handle with care and use in a chemical fume hood. Handle all chemicals using the required safety precautions. Reagents with manufacturer expiration dates should be observed. The Environmental Protection Agency (EPA) has designated TCAA as a known mouse carcinogen and a possible human carcinogen [16].

SAMPLING:

1. Collect at least 10 mL of urine in ~15-mL polypropylene tubes or other suitable container.
   NOTE: Because of the relatively lengthy half-life values of TCAA, ACGIH recommends sampling at the end of shift at the end of workweek [1].
2. Freeze the urine and ship in dry ice in an insulated container.
   Reminder: Commercial shippers have special labeling requirements for packages containing biological samples and dry ice.

SAMPLE PREPARATION:

3. Thaw urine specimens, bring to room temperature, and mix thoroughly.
4. Place 200 µL of urine specimen in an 8-mL glass culture tube with a PTFE-lined cap.
5. Add 0.5 mL 14% boron trifluoride in methanol; cap and mix.
6. Heat in oven at 60 °C for a minimum of 1.5 hr (maximum 2.5 hr).
7. Cool to room temperature and then add 2.0 mL toluene.
8. Vortex or shake vigorously for 1 min.
9. After the layers separate, transfer the upper toluene layer to a drying column containing anhydrous sodium sulfate. The drying columns are prepared in 15-cm Pasteur pipettes with a glass wool plug and about 200 to 300 mg anhydrous sodium sulfate, sufficient to form a bed depth of ~1 cm.
10. Collect the eluate in a 2-mL GC vial. Cap vial.

CALIBRATION AND QUALITY CONTROL:

11. Prepare a stock solution by accurately weighing a known quantity of sodium trichloroacetate into a volumetric flask. Add a known volume of deionized water and mix. Convert the weight of the sodium trichloroacetate to TCAA by multiplying by 0.8814 (MW TCAA divided by MW sodium trichloroacetate = 0.8814). As an example, 34 mg of sodium trichloroacetate into a 10-mL flask makes a 3 mg/mL stock solution to be used in preparing the calibration standards.
    NOTE: Sodium trichloroacetate was used instead of trichloroacetic acid for all phases of this method development as well as in the preparation of standards. Trichloroacetic acid is very hygroscopic; the salt is much less so.
12. Prepare working (calibration) standards by serial dilution to cover the analytical range. A suggested working standard concentration range is 0.08 to 300 µg/mL. Withdraw 200 µL of each calibration standard and follow steps 4 through 10.
13. Determine the retention time for the analyte of interest.
14. Prepare at least one blank urine specimen without an analyte spike to verify whether the source (of blank urine) contained no detectable quantity of TCAA.
15. Prepare at least two levels of quality control spikes of TCAA, sodium salt to be analyzed with each analysis batch. These levels should be at ~10 X the limit of quantitation (LOQ) and 200 X LOQ, but can be adjusted to better suit the anticipated levels of the set of specimens. QC samples must be analyzed with every batch such that they constitute 10% of the sample batch.
16. QC values must be within ±20% of the spiked values. If not, the batch is considered out of control, the batch data discarded, and corrective actions taken before more samples are analyzed.
17. Calibrate daily with at least six liquid working standards covering the expected concentration range of the samples.

MEASUREMENT:

PRECAUTION: SYRINGE-RINSE SOLUTIONS: Toluene will extract material from some urine specimens that may eventually clog the syringe and cause injection errors unless the syringe is rinsed with the following solutions following each injection.
First rinse solution: 1:3 glacial acetic acid:deionized water
Second rinse solution: 1:1 acetone:methanol

18. Set the gas chromatograph according to manufacturer's recommendations and to conditions given on page 8322-1. With the chromatographic conditions listed, the retention time of the methyl ester of TCAA was 8.87 min [6].
19. Inject each of the samples, standards, blanks, and quality control samples.
20. Measure peak area or peak height; peak area is recommended.
    NOTE: If the sample peak area or height is greater than that of the highest calibration standard, dilute with toluene and reanalyze. Apply the appropriate dilution factor in the calculations.
21. Prepare a calibration curve by plotting instrument responses (usually peak area) for the standards vs. concentration. The simplest model that adequately describes the data should be used, but either a linear (mostly likely 1/x weighted because of the range of the calibration curve) or a quadratic model may be utilized in processing the analytical results. The standard curve must have a coefficient of determination (r^2) of equal to or greater than 0.98 to be acceptable for use. Furthermore, when each standard is plugged back into the calibration equation, the measured value must be within ±20% of the expected value.

CALCULATION OF ANALYTE PER SAMPLE:

22. Determine the concentration of TCAA in µg/mL (mg/L) using the response of each sample and the calibration curve prepared in step 21. Apply any dilution factor if applicable.
    NOTE: If the creatinine value is available, the concentration may be reported as µg/g creatinine if desired.

EVALUATION OF METHOD:

This method was evaluated over a range of 0.9-30 µg/mL. This range covers 3x, 10x, 30x, and 100x of the estimated LOQ. Six replicates were prepared and analyzed at each concentration level. The average recoveries for each of the concentration levels were 94.8% (3 x LOQ), 102.3% (10 x LOQ), 110.4% (30 x LOQ), and 97.1% (100 x LOQ). Recoveries were determined by comparison against spiked and derivatized liquid standards (standards prepared in deionized water). The upper concentration range was extended to 100 µg/mL during testing by an independent laboratory. Five samples were analyzed at this concentration and the average recovery was 105.0%. Overall accuracy was calculated to be 7.5%; bias was 0.0113, and overall precision was 0.0366 [6]. The limit of detection (LOD) and LOQ were determined by analyzing a series of derivatized spiked standards, with the data fitted to a quadratic curve, then estimated according to the Burkart method [17]. A long-term storage stability study was carried out at the 10x, 30x, and 100x LOQ levels. Urine samples were spiked with trichloroacetate and stored at -17 ºC for 7, 14, 21, 30, and 46 days and then analyzed. Recoveries at 30 and 46 days were all greater than 90% [6].

During the testing performed by the independent laboratory ("User Check"), broad, interfering carryover peaks from the urine matrix were noticed. The lab found that raising the final temperature of the GC program to 240 ºC (instead of 180 ºC) and adding a longer hold time 10 min (instead of 7 min) reduced the carryover problem, allowing more precise and accurate measurement of the peak of interest. This adjusted GC program would now be: 80 ºC for 0.5 min, heat to 240 ºC at 20 ºC/min, and hold for 10 min. Either set of conditions may be used.

NOTE: While the overall accuracy and precision for the User-Check samples were within acceptable limits [6], there were spurious results in 10% of the samples (2 out of 20.) No reason is known for these outliers, nor were the samples able to be re-injected, re-extracted, or re-analyzed. To improve user confidence in the results obtained by this method, it is suggested to randomly run duplicate analyses of 10-20% of the samples and to randomly re-inject 10-20% of the samples. If the method is used in an on-going manner and no problems or spurious results are noted, this recommendation could be lowered or eliminated.

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METHOD EDITED BY: John M. Reynolds, ALS Environmental (formerly DataChem Laboratories, Inc.), Salt Lake City, Utah and Dale A. Shoemaker, Ph.D., NIOSH/DART/CEMB.

3-BROMOPROPIONIC ACID in URINE

metabolite of 1-bromopropane

8324

FORMULA: $C_3H_5BrO_2$ MW: 152.97 CAS: 590-92-1 RTECS: UE7875000

METHOD: 8324, Issue 1 **EVALUATION: FULL** **Issue 1: 12 September 2014**

Exposure limits and guidelines:
OSHA: None
NIOSH: None
Other OELs: Because data on exposure limits and guidelines may change over time, NIOSH recommends referring to the following sources for updated limits [1 - 4].

PROPERTIES: Solid; d 1.48 g/mL at 25 °C; MP 58-62 °C

BIOLOGICAL INDICATOR OF: Exposure to 1-bromopropane

SYNONYMS: β-Bromopropionic acid; 2-carboxyethylbromide.

SAMPLING

SPECIMEN: Urine

VOLUME: At least 15 mL

PRESERVATIVE: None added
Refrigerate or freeze upon collection

SHIPMENT: Ship cold or frozen with ice or dry ice
Freeze upon receipt at the laboratory

SAMPLE STABILITY: Stable in frozen urine for at least 30 days

CONTROLS: Urine specimens obtained from non-exposed individuals

ACCURACY

RANGE STUDIED: Table 1

BIAS: None established

PRECISION: Table 1

RECOVERY ACCURACY: Full recovery (95% overall) was established by a spiked urine recovery, overall RSD was ±3.1% (Table 1).

The definitions of precision and accuracy in this method are those utilized by the US Food and Drug Administration [5].

MEASUREMENT

TECHNIQUE: GAS CHROMATOGRAPHY, MASS SPECTROMETRY with SELECTED ION MONITORING (GC/MS-SIM)

ANALYTE: tert-butyldimethylsilane derivative of 3-bromopropionic acid

EXTRACTION: Liquid-liquid extraction (LLE)

INJECTION VOLUME: 0.5 µL, splitless

TEMPERATURES
- **INJECTION:** 200 °C
- **COLUMN:** 60 °C initial, 4 °C/min to 180 °C,15 °C/min to 255 °C, post-run at 270 °C for 5 min
- **DETECTOR:** Source 230 °C, Quadrupole 150 °C; Solvent delay, 15 min

RUN TIME: Approximately 50 minute cycle time

CARRIER GAS: Helium, 0.8 mL/min constant flow

COLUMN: Capillary, fused silica, 100% dimethyl-polysiloxane, 50 m X 0.20 mm (ID), 0.33 µm film thickness

CALIBRATION: Analyte in control urine; with internal standard

QUALITY CONTROL: At least one level of spiked urine sample prepared from a separately weighed stock solution

RANGE: 2.0 to 100 µg/mL

ESTIMATED LOD: Approximately 0.01 µg/mL (IUPAC) [6]. 0.1 µg/mL is the lowest calibration standard.

APPLICABILITY: 3-Bromopropionic acid (3-BPA) has been reported to be a rat metabolite [7] and is a potential human biomarker for exposure to 1-bromopropane. This method measures the quantity of free 3-BPA in urine. 1-Bromopropane is used as an industrial solvent. In one limited study, 3-BPA was not detected in individuals exposed to low levels of 1-bromopropane [8].

INTERFERENCES: None found or identified.

OTHER METHODS: This method is from the one described by B'Hymer and Cheever [9] and further investigated by Mathias, et al. [8].

REAGENTS:

1. 3-Bromopropionic acid (3-BPA) reference standard as a 1.0 mg/mL stock solution in deionized water. Store in a refrigerator.
2. 3-Chloropropionic acid (3-CPA) reference standard, 20 µg/mL in deionized water, internal standard solution. Store in a refrigerator.
3. Ethyl acetate, HPLC grade or better*
4. N-Methyl-N-(tert-butyldimethylsilyl) trifluoroacetamide (MTBSTFA) with 1% tert-butyldimethylchlorosilane (TBDMCS)
5. Magnesium sulfate, anhydrous, powdered, ACS reagent grade
6. Hydrochloric acid, concentrated, ACS reagent grade
7. Water, deionized (ASTM type II)
8. Nitrogen, prepurified grade or better
9. Urine, non-exposed*

* See SPECIAL PRECAUTIONS

EQUIPMENT:

1. Gas chromatograph with mass spectrometric detector, column, autosampler, and data collector (page 8324-1)
2. Bottles, polypropylene, 125-mL with caps
3. Analytical balance, to ±0.0001 g
4. Analytical evaporator with nitrogen gas sweep
5. Test-tube vortex mixer
6. Heating block or oven
7. Automatic pipettor with disposable tips
8. Repeating pipet dispenser, 1 Liter
9. Tubes, disposable screw-top culture (16 X 100 mm and 16 X 150 mm), with polytetrafluoroethylene (PFTE)-lined caps
10. Metal spatula
11. Flasks, volumetric; 10, 50 and 100-mL
12. Autosampler vials, 2 mL, silanized, with caps and septa
13. Glass funnels
14. Glass wool, silanized
15. Disposable glass pipets
16. Dry ice or bagged refrigerant

SPECIAL PRECAUTIONS: Standard precautions should always be used when handling bodily fluids and/or extracts of bodily fluids [10]. Handle urine samples and urine extracts using powder-free latex or nitrile gloves. Ethyl acetate and MTBSTFA are flammable; handle with care and use in a chemical fume hood. Handle all chemicals using the required safety precautions. Manufacturer expiration dates for reagents should be observed.

SAMPLING:

1. Collect at least 15 mL urine in an appropriate polypropylene tube or bottle and cap. Refrigerate or freeze immediately after collection. Collect at least two urine specimens for each worker: one before the work shift and one after.
2. Ship the specimens stored in either wet or dry ice in an insulated container. Store frozen upon arrival at the laboratory. A reminder: commercial shippers have special labeling requirements for packages containing dry ice.

SAMPLE PREPARATION:

3. Thaw the urine specimen to room temperature.
4. Mix thoroughly to ensure urine homogeneity.
5. Transfer 2.0 mL of urine into a 16 X 100 mm (or larger) screw-capped culture tube.
6. Acidify by adding 40 µL of concentrated hydrochloric acid.
7. Add 0.5 mL of deionized water.
8. Add 0.5 mL of the 20 µg/mL 3-CPA internal standard solution.
9. Ethyl acetate extraction: Dispense 4 mL of ethyl acetate into the culture tube, cap, and vortex (or vigorously shake) for 1 minute.
10. Allow layers to separate, collect the ethyl acetate (top) layer.

11. Repeat the extraction (steps 9 and 10) three more times. Collect and combine all ethyl acetate extracts using a glass pipet into a 16 X 150 mm culture tube.
12. Dry the ethyl acetate extract by adding approximately 100 to 200 mg of anhydrous magnesium sulfate and swirl for about 15 seconds.
13. Transfer the extract solution into a 16 X 150 mm culture tube by means of a glass funnel with silanized glass wool patch to remove the wet magnesium sulfate. The glass wool patch must be packed tightly enough to prevent particles of magnesium sulfate from passing through.
14. Rinse the tube and the funnel with ethyl acetate to ensure complete transfer.
15. Concentrate the combined ethyl acetate extract for each sample to 1 mL using a nitrogen sweep at room temperature and transfer the solution to a 2-mL GC autosampler vial.
16. tert-Butyldimethylsilane derivatization: Add 50 µL of MTBSTFA with 1% TBDMCS silanizing reagent to each autosampler vial and cap immediately.
17. Heat the solution for 1.5 hours at 70 °C in a heating block or oven.

CALIBRATION AND QUALITY CONTROL:

18. 3-Bromopropionic acid (3-BPA) standards are prepared in blank, non-exposed urine. The 1 mg/mL stock 3-BPA solution is diluted in deionized water to make 0.4, 1, 2, 4, 8, 20, 80, 200, 400, 600, and 800 µg/mL 3-BPA solutions for spiking.
19. Transfer 2.0 mL of non-exposed urine into a 16 X 100 mm (or larger) screw-capped culture tube.
20. Acidify by adding 40 µL of concentrated hydrochloric acid.
21. Add 0.5 mL of the 20 µg/mL 3-CPA internal standard solution.
22. Add 0.5 mL of the appropriate 3-BPA spiking solution described in step 18 to make urine samples equivalent to 0.1, 0.25, 0.5, 1, 2, 5, 20, 50,100, 150 and 200 µg/mL of 3-BPA in the original 2.0 mL volume of urine.
23. Prepare at least one blank urine without a 3-BPA spike to verify the source of blank urine contains no detectable quantity of 3-BPA.
24. Prepare at least two levels of quality control (QC) standard of 3-BPA fortified urine using a separately weighed and prepared 3-BPA stock solution. One level should be within the lower 25% of the calibration curve and one level within the upper 25% of the calibration curve. More than two QC levels can be used. QC samples should be analyzed with every batch such that they constitute at least 5% of the sample batch.
25. QC values should be within ±20% of the spiked values. If not, the batch is considered out of control, the batch data discarded, and corrective actions should be taken before more samples are analyzed.
26. Ethyl acetate extraction: Prepare the spiked standard urine samples, the blank urine sample(s), and the QC standards the same as described in the preceding Sample Preparation section using Steps 9 through 17.

MEASUREMENT:

27. Set the gas chromatograph according to the manufacturer's recommendations and to the conditions listed on page 8324-1.
28. Set the mass selective detector to selected ion monitoring mode for ions *m/z* 211 (derivative of 3-BPA) and 165 (derivative of 3-CPA).
    NOTE: The use/non-use of qualifier ions for this method is discussed in the literature [9].
29. Inject 0.5 µL of each sample, standard, blank, and QC standard extract from Steps 17 and 26.
30. Measure the peak areas of the tert-butyldimethylsilane derivatives of 3-BPA and 3-CPA in the chromatograms of the standards.
31. Divide the peak area of the derivative of 3-BPA by the peak area from the derivative of 3-CPA in the same chromatogram.

32. Prepare a linear calibration curve of the peak Area Std./Area Int. Std. versus the concentration of the standard for 3-BPA.
33. Measure the peak areas of the derivatives of 3-BPA and 3-CPA in the remainder of the chromatograms.
34. Divide the peak area of the derivative of 3-BPA by the peak area from the derivative of 3-CPA in the same chromatogram.

CALCULATIONS:

35. Determine the concentration of 3-BPA in the extracts from the original urine (2.0 mL specimen) from the curve obtained in step 32. The results are expressed as µg/mL of 3-BPA in urine.

EVALUATION OF METHOD:

This method was evaluated and described by B'Hymer [6] and in detail by B'Hymer and Cheever [9]. A general summary of this published information is given below:

Accuracy and Precision: Two recovery studies using multiple GC columns over several days demonstrated the accuracy and precision of this test method. The first recovery study was performed over three separate experimental batch runs, and these data are presented in Table 1A. Average recovery was between 93 and 98% for the three 3-BPA spiked level urine samples investigated. For each batch run, the experimental trial consisted of three samples at three different concentration levels. The recovery for each level (n=9 samples) is displayed in Table 1A. The second recovery study (data shown in Table 1B) used spiked urine samples from 20 non-exposed volunteers and demonstrated that the procedure was accurate (95% average recovery) and precise (2.5% relative standard deviation.) No interferences were detected in the unspiked urine from the 20 volunteer specimens. Both recovery studies generated a total of 47 spiked urine samples at 2, 10, 20 and 50 µg/mL 3-BPA levels. Precision expressed as percent relative deviation (% RSD) was as high as 5.7% on the 2 µg/mL recovery samples (n = 9). Overall recovery was 95% and overall RSD was 3.1% (n = 47).

Linearity: All calibration curves used during the development of this method were linear and had correlation coefficients of 0.98 and greater. The concentration range was 0.1 to 200 µg/mL 3-BPA in urine with 2.0 mL urine sample size. Calibration curves were run at the beginning and end of all sample batch runs; calibration curve slope drift was found to be acceptable.

Specificity: The optimized chromatographic conditions developed for this procedure proved to be specific and have no major interferences. The mass spectrometric detector was useful in adding additional specificity to the method. The ion *m/z* 211 was chosen for monitoring the calibration curve used in the calculations because of its greater abundance, and it was a characteristic fragment for the tert-butyldimethylsilane (TBDMS) derivative of 3-BPA. This is the molecular ion less the tert-butyl group, *m/z* 57 (Figure 1). Ion *m/z* 165 was used to monitor the TBDMS derivative of 3-CPA, the internal standard, for the same reasons. Full-scan mass spectra of the TBDMS derivatives are presented in Figure 2. An example chromatogram for blank urine and urine spiked with 3-BPA and 3-CPA is shown in Figure 3.

Robustness: Multiple HP-1 (100% dimethylpolysiloxane) columns of different manufacturing lots were used during the recovery studies. Accuracy and precision did not appear to be affected; therefore, the method appears to be reproducible with any normal functioning HP-1 capillary column. Recovery results from individual urine samples spiked with 3-BPA indicate that the method is accurate and not significantly affected by individual urine sample matrix differences during analyte extraction.

Stability: While sample stability was not exhaustively evaluated, an aqueous stock standard solution of 3-BPA stored for two weeks at 4 °C gave full recovery assay values when compared to a freshly prepared 3-BPA standard. The 3-BPA in the urine specimens appears to be stable in frozen urine for a much

longer time frame of two months or more. Derivatized sample extracts appeared to be stable during a one week time frame.

Range: This method should be considered accurate for the estimation of 3-BPA in human urine within the 2.0 to 100 µg/mL method validation range.

REFERENCES:

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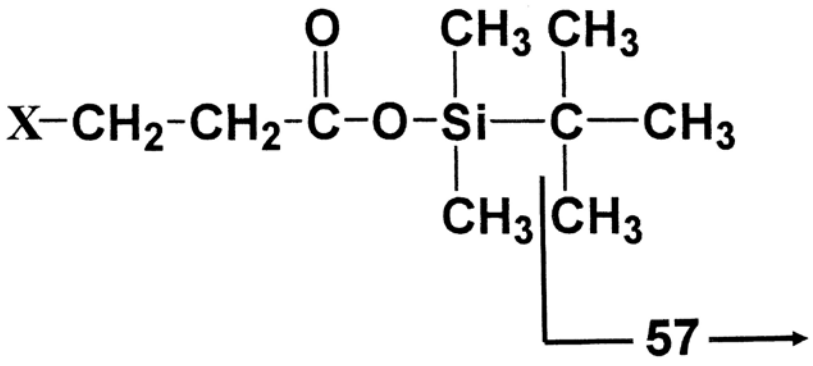
METHOD WRITTEN BY:

Clayton B'Hymer, PhD, NIOSH/DART/BHAB. Final editing performed by Dale A. Shoemaker, PhD, NIOSH/DART/CEMB.



X = ^{35}Cl, m/z = 165 or for ^{37}Cl, m/z = 167.

X = ^{79}Br, m/z = 209 or for ^{81}Br, m/z = 211.

Figure 1. The major ions monitored for the tert-butyldimethylsilane derivatives were the molecular ions less the tert-butyl group (*m/z* = 57). The ions used for quantitation are *m/z (mass to charge)* 165 for the internal standard derivative and *m/z* 211 for the 3-bromopropionic acid derivative.

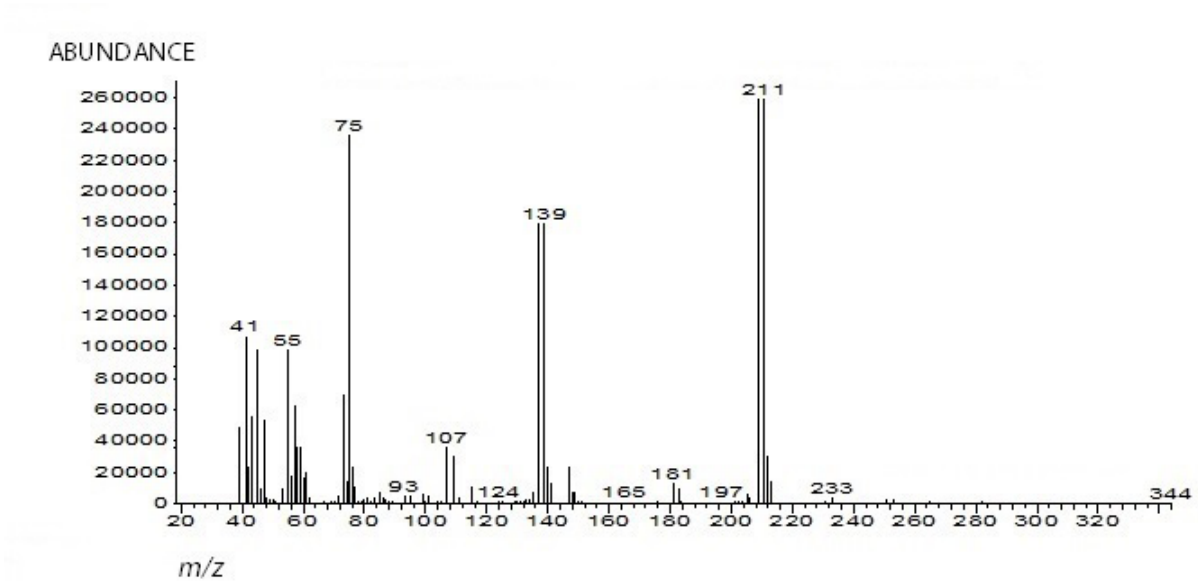


Figure 2a. **Mass spectrum for 3-Bromopropionic acid, t-butyldimethylsilyl ester**

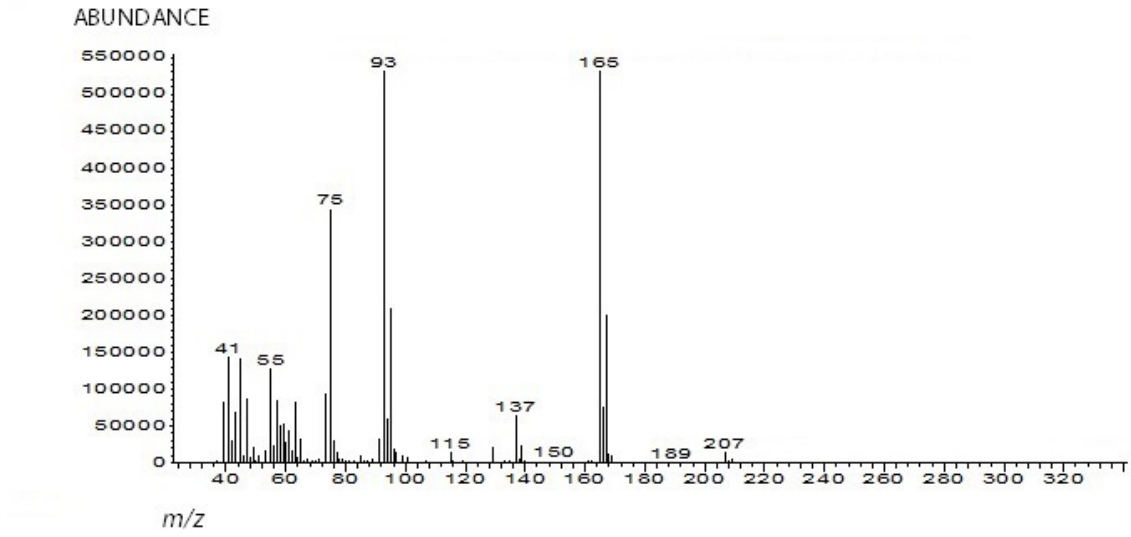


Figure 2b. **Mass spectrum for 3-Chloropropionic acid, t-butyldimethylsilyl ester**

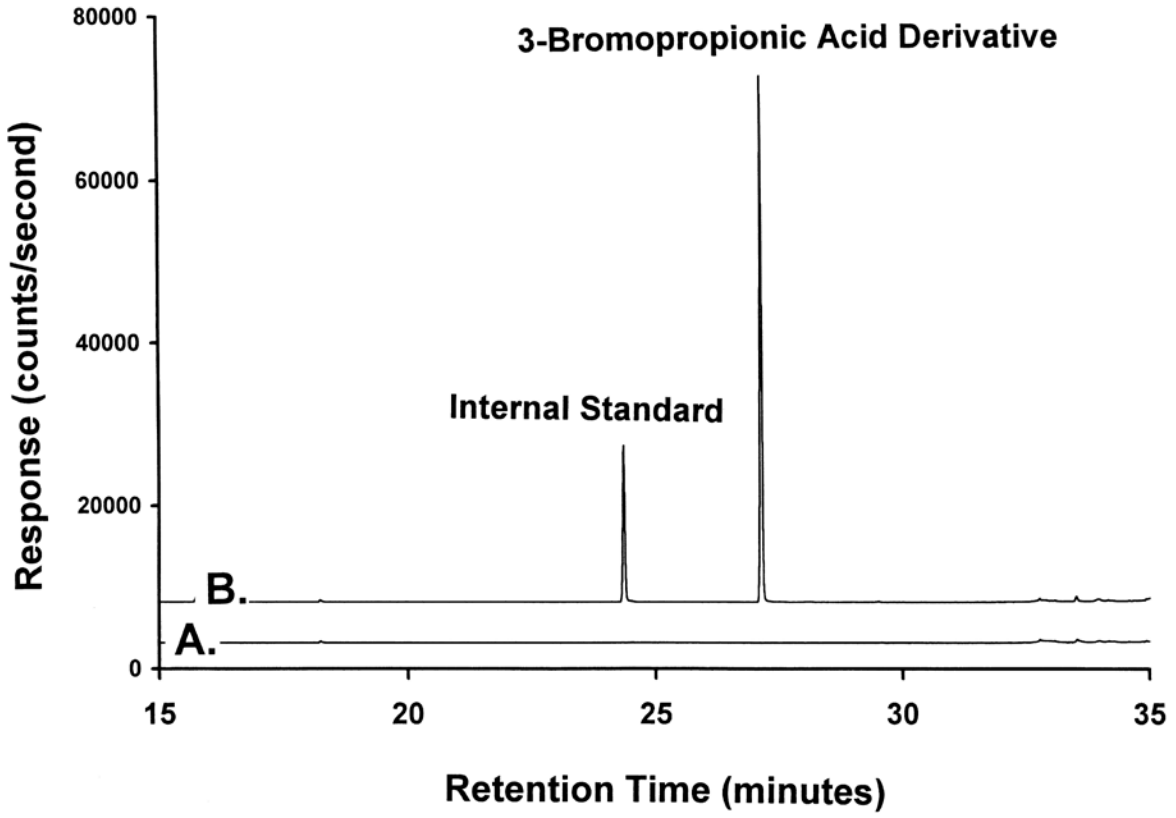


Figure 3. A total ion chromatogram of a (A) blank non-exposed volunteer urine specimen and (B) 20 µg/mL spiked 3-BPA urine solution with 5 µg/mL equivalent 3-CPA as the internal standard. No interfering peaks were evident in any of the group of 20 non-exposed volunteer specimens.

Table 1. Recovery studies of 3-bromopropionic acid:
(A) multilevel recovery study of 3-BPA from spiked urine samples1,
(B) recovery of 20 µg/mL 3-BPA spikes from individual urines of 20 non-exposed volunteers2
Note: Overall recovery of all samples was 95% and overall RSD was 3.1% (n = 47.)

(A)

Spike level (µg/mL)	Mean 3-BPA recovered, (n = 9, µg/mL)	Average % Recovery	Standard Deviation (µg/mL)	% Relative Standard Deviation
2	1.91	96	0.11	5.7
10	9.32	93	0.13	1.4
50	48.9	98	0.36	0.7

(B)

Volunteer urine Spike level (µg/mL)	Mean 3-BPA recovered (n = 20, µg/mL)	Average % Recovery	Standard Deviation (µg/mL)	% Relative Standard Deviation
20	19.0	95	0.48	2.5

[1] Three different spiked urine samples were prepared at each level and chromatographed on three separate experimental trial runs (a total of nine samples at each spike level were analyzed.)

[2] All non-spiked specimens showed no 3-BPA derivative peak in the chromatograms.

S-Benzylmercapturic acid and S-phenylmercapturic acid in urine 8326

Metabolites of toluene and benzene

1. *S*-Benzylmercapturic acid: FORMULA: $C_{12}H_{15}NO_3S$ MW: 253.3 CAS: 19542-77-9
2. *S*-Phenylmercapturic acid: FORMULA: $C_{11}H_{13}NO_3S$ MW: 239.3 CAS: 20640-68-0

METHOD: 8326, Issue 1 **EVALUATION: Full** **Issue 1: 20 May 2014**

Published limits and guidelines using these compounds as markers:

1. Toluene: OSHA and NIOSH: None

2. Benzene: OSHA and NIOSH: None

Other OELs: Because data on exposure limits and guidelines may change over time, NIOSH recommends referring to the following sources for updated limits and guidelines concerning the use of these compounds as markers for toluene and benzene [1- 4].

PROPERTIES: 1. Solid; density =1.246 g/cm^3; mp 162-163 °C
2. Solid; density = 1.28 g/cm^3; mp 155 °C

BIOLOGICAL INDICATOR OF: Exposure to 1. toluene and
2. benzene

SYNONYMS (not all inclusive):

1. *S*-Benzylmercapturic Acid (BMA): *S*-benzyl-*N*-acetyl-L-cysteine; (2*R*)-2-Acetamido-3-(phenylmethylsulfanyl)propanoic acid; Alanine, *N*-acetyl-3-(benzylthio)-; *S*-phenylmethyl-*N*-acetyl-L-cysteine
2. *S*-Phenylmercapturic acid (PMA): *S*-phenyl-*N*-acetyl-L-cysteine; (2*R*)-2-Acetamido-3-(phenylsulfanyl)propanoic acid; (2*R*)-2-Acetylamino-3-(phenylthio)propionic acid

SAMPLING

SPECIMEN: Urine

VOLUME: At least 8 mL

PRESERVATIVE: None added. Refrigerate or freeze upon collection.

SHIPMENT: Ship cold or frozen with ice or dry ice. Freeze upon receipt at the laboratory.

SAMPLE STABILITY: Stable in frozen urine for periods of a month or more and for several freeze/thaw cycles [5,6].

CONTROLS: Urine specimens obtained from non-exposed or low level exposed individuals.

ACCURACY*

RANGE STUDIED: See Table 2

BIAS: Negligible

OVERALL PRECISION ($\hat{S}_{rt}$)*: See Table 2

ACCURACY*: Overall recoveries obtained from spiked urine samples (n=48) were 103% and 106% for S-benzylmercapturic acid and S-phenylmercapturic acid, respectively. The precision as relative standard deviation was no greater than 5.0% at any concentration level (n=9, Table 2).

* The definitions of precision and accuracy in this method are those utilized by the US Food and Drug Administration [7].

MEASUREMENT

TECHNIQUE: HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY - TANDEM MASS SPECTROMETRY (HPLC/MS/MS)

ANALYTES: *S*-Benzylmercapturic acid and *S*-phenylmercapturic acid

EXTRACTION: Solid-Phase Extraction (SPE) C18

COLUMN: C18 [dimethyloctadecylsilane solid phase type, 3.5 µm particle size] (150 mm by 3 mm)

MOBILE PHASES: A = 5/95/0.1% (v/v/v) acetonitrile/water/acetic acid
B = 75/25/0.1% (v/v/v) acetonitrile/water/acetic acid

FLOW RATE: 0.3 mL/min (0.4 mL/min post run)

GRADIENT: Time (min) vs. Mobile Phase Composition

0 to 10	0 to 40% B
10 to 18	40 to 100% B
18 to 20	100% B
20 to 21	100% B Flow increased to 0.4 mL/min
21 to 28	100% B (0.4 mL/min flow)
28 to 30	100 to 0% B (re-equilibration, 0.3 mL/min)
30 to 37	0% B (re-equilibration)

INJECTION VOLUME: 8 µL

IONIZATION SOURCE: Electrospray at 3500 Volts and negative scan mode, nebulizer gas at 35 psi and 10 L/min flow

DETECTOR (MS/MS): Dwell time = 200 msec; Fragmentor at 80 Volts; Collision energy at 8 Volts; Collision gas: nitrogen at 0.06 L/min

MULTIPLE REACTION MODE: Quantification mass transitions; BMA = *m/z* 252 → 123, PMA = 238 → 109, d_5-BMA = 257 → 128, d_5-PMA = 243 → 114

TOTAL RUN TIME: Approximately 37 minute cycle time

CALIBRATION: BMA and PMA solutions with internal standards

QUALITY CONTROL: At least one level of spiked urine specimen prepared from a separately weighed stock solution

RANGE: 0.5 to 50 ng/mL for BMA and PMA

ESTIMATED LOD: Approximately 0.2 ng/mL for BMA and PMA; by lowest standard levels, BMA and PMA = 0.5 ng/mL

PRECISION ($\bar{S}_r$): See Table 2

APPLICABILITY: BMA and PMA are metabolites of toluene and benzene, respectively. PMA is a very specific biomarker for benzene. BMA can form from exposure to other sources, such as benzyl acetate or benzyl alcohol which can be found in personal care products [8]. Both toluene and benzene are common solvents with multiple occupational uses; furthermore exposure to toluene and benzene (less commonly) can occur from environmental and other sources. This method measures the quantity of the two target metabolite analytes in urine.

INTERFERENCES: None found or identified.

OTHER METHODS: This method is based on the research of B'Hymer [9,10]. There are numerous literature methods for these two compounds, but standardized methods from governmental agencies or consensus standards organizations are not currently available, though there is also a recent method developed at CDC/National Center for Environmental Health for these analytes and others [11].

REAGENTS:

1. *S*-Benzylmercapturic acid (BMA, *N*-acetyl-*S*-benzyl-DL-cysteine, CAS no. 19542-77-9) reference standard 0.20 mg/mL stock solution in methanol. Store at 4 °C in amber vials (or in the dark).
2. *S*-Phenylmercapturic acid (PMA, phenyl-*N*-acetyl-DL-cysteine, CAS no. 20640-68-0) reference standard 0.20 mg/mL stock solution in methanol. Store at 4 °C in amber vials (or in the dark).
3. Deuterated *S*-benzyl-d_5-mercapturic acid reference standard (d_5-BMA), 0.15 mg/mL stock solution in methanol. Store at 4 °C in amber vials (or in the dark).
4. Deuterated *S*-phenyl-d_5-mercapturic acid reference standard (d_5-PMA), 0.15 mg/mL stock solution in methanol. Store at 4 °C in amber vials (or in the dark).
5. Internal standard spiking solution, deuterated stock solutions diluted to approximately 30 ng/mL in water
6. Acetone, HPLC grade or better*
7. Acetonitrile, HPLC grade or better*
8. Acetic Acid, glacial, ACS reagent grade or better*
9. Methanol, HPLC grade or better*
10. Water, doubly deionized, minimum resistivity of 18 MΩ-cm
11. Water, HPLC grade
12. Acetonitrile/water (50/50%, v/v) injector rinse solution
13. Chromatographic matrix adjustment solution, 49/50/1% (v/v/v) acetonitrile/water/acetic acid
14. Mobile phase A (5/95/0.1%, v/v/v) acetonitrile/water/acetic acid, filtered through 0.7 µm glass microfiber filters
15. Mobile phase B (75/25/0.1%, v/v/v) acetonitrile/water/acetic acid, filtered through 0.7 µm glass microfiber filters
16. Synthetic urine substitute, if desired
17. Nitrogen, UHP

* See SPECIAL PRECAUTIONS*

EQUIPMENT:

1. High-Performance Liquid Chromatograph (HPLC) equipped with a tandem mass spectrometric detector with data collection system, page 8326-1
2. HPLC column (C18 [dimethyloctadecylsilane solid phase type], 150 mm X 3 mm, 3.5 µm particle size)
3. Autosampler
4. Analytical balance, 0.1 mg readability
5. Rotary vacuum concentrator with cold trap and vacuum pump or analytical evaporator with nitrogen
6. Automatic pipet with disposable tips in the 1000 µL volume delivery range
7. Solid-phase extraction (SPE) cartridges, C18, 500 mg, 3 mL
8. SPE vacuum manifold apparatus
9. Culture tubes, disposable screw-top (16 X 150 mm) with PTFE-lined caps
10. Tubes, polypropylene, disposable screw-top, 15 mL. Polypropylene bottles and caps may also be used for sample collection.
11. Metal spatula
12. Volumetric flasks: 10, 50, 100 and 200 mL
13. Autosampler vials, amber, with caps and septa
14. Disposable glass pipets
15. Sintered glass filtration apparatus and 1-L side- armed Erlenmeyer flask
16. Microfiber filters, glass, 0.7 µm; diameter to fit the filtration apparatus
17. Wet or dry ice

SPECIAL PRECAUTIONS: Standard precautions should always be used when handling bodily fluids and/or extracts of bodily fluids [12]. Handle urine specimens and urine extracts using powder-free latex or nitrile gloves. Acetic acid, acetone, acetonitrile and methanol are flammable; handle with care and use in a chemical fume hood. Handle all chemicals using the required safety precautions. Reagents with manufacturer expiration dates should be observed.

SAMPLING:

1. Collect at least 8 mL of urine in an appropriate polypropylene tube or bottle and cap. Refrigerate at 4 °C or freeze after collection. Collect at least two urine specimens for each worker, one before the work shift and one after.
2. Ship the specimen stored in either wet or dry ice in an insulated container. Freeze specimens upon arrival at the laboratory and store frozen. A reminder: commercial shippers have special labeling requirements for packages containing dry ice.

SAMPLE PREPARATION:

NOTE: BMA and PMA are somewhat light sensitive (see Evaluation of Method section). Perform the sample preparation steps in a low light environment. Extreme measures are not required.

3. Thaw the urine specimen to room temperature.
4. Mix urine specimen thoroughly to ensure homogeneity.
5. Transfer 4.0 mL of urine into a 16 X 150 mm (or larger) screw-capped culture tube.
6. Add 0.5 mL of deionized water to aid in the dissolution of solids.
7. Add 0.5 mL of the 30 ng/mL deuterated BMA/PMA internal standard solution.
8. Solid-phase extraction

NOTE: All SPE steps are performed using the vacuum manifold apparatus. The flow rate should not exceed 1 mL/min. The SPE cartridges should not be allowed to go to dryness until the end of Step 8d. Refer to manufacturers' recommendations for use of specific SPE cartridges.

a. Pre-wash the C18 SPE cartridge with 2 mL of acetone.
b. Equilibrate the SPE cartridge with 2 mL of HPLC grade water.
c. Load the 5-mL urine mixture and draw the sample through the cartridge.
d. Wash the cartridge with 1 mL of HPLC grade water. Discard any liquid collected up to this point.
e. Apply (or increase) the vacuum to pull most of the water from the cartridge.
f. Elute the analytes with 3 mL of acetone three times, collecting all of the acetone washes into a 15-mL plastic screw-capped tube.

9. Evaporate the 9 mL of acetone from the extracts to dryness by means of a vacuum rotary concentrator or by using a nitrogen sweep.
10. Cap the plastic tubes containing the dry extract and store in a refrigerator/freezer until ready for chromatographic analysis.
11. Prior to chromatographic analysis, dissolve the extract in 1 mL of HPLC mobile phase A and transfer the sample into an amber HPLC autosampler vial.

CALIBRATION AND QUALITY CONTROL:

12. Prepare a BMA/PMA standard mixture by combining 2.0 mL of each stock solution and diluting to 100 mL with deionized water to make an approximately 4 µg/mL solution concentration for each.
13. BMA/PMA standard solutions: The 4 µg/mL BMA/PMA solution is diluted in water to make 4, 8, 16, 40, 80, 320 and 400 ng/mL BMA/PMA solutions.
14. Accurately transfer 0.500 mL of each BMA/PMA solution from step 13 into a separate HPLC autosampler vial. [This delivers 2, 4, 8, 20, 40, 160 and 200 ng of each analyte to each autosampler vial.]
15. Add 0.5 mL of the deuterated internal standard spiking solution [30 ng/mL] to each vial. [This delivers 15 ng of the internal standards to each autosampler vial.]

16. Add 0.1 mL of the chromatographic matrix adjustment solution to each standard vial.
    NOTE: These standard samples are *equivalent* to 0.5 to 50 ng/mL BMA/PMA urine samples [based on the original 4.0 mL urine volume extracted and placed in each autosampler vial.]
17. Prepare one blank urine sample without analyte spikes; alternatively, prepare one blank using a urine substitute by following steps 14-16 using 0.5 mL of the unspiked urine or substitute in step 14.
18. Prepare at least one quality control (QC) standard of urine or urine substitute fortified with PMA/BMA using separately prepared stock solutions. A 10 ng/mL equivalent spike level is suggested and more than one level can be used if desired.

MEASUREMENT:

19. Set the high-performance liquid chromatograph according to the manufacturer's recommendations and to the conditions listed on page 8326-1. A needle rinse with 50/50% (v/v) acetonitrile/water is required to eliminate sample carry-over by the autosampler.
20. Set the mass spectrometric detector to multiple reaction mode (MRM) according to the manufacturer's recommendations and the conditions listed on page 8326-1. Example conditions are summarized below:

Table 1. MS/MS Conditions using negative electrospray ionization

Analyte	Precursor Ion	MS1 Resolution	Product Ion	MS2 Resolution	Dwell Time (msec)	Fragmentor Voltage	Collision Energy (volt)
d_5-BMA	257	unit	128	unit	200	80	8
BMA	252	unit	123	unit	200	80	8
d_5-PMA	243	unit	114	unit	200	80	8
PMA	238	unit	109	unit	200	80	8

21. Inject 8 µL of each sample extract, standard, QC standard, and blank. Sample chromatograms for each compound are illustrated in Figure 1.
22. Measure the peak areas of the two analytes (BMA and PMA) and those for the deuterated internal standards (d_5-BMA and d_5-PMA) in the chromatograms. Divide the peak area of the analytes by the peak area from the matching deuterated internal standard.
23. Prepare calibration curves of the peak Area Std./Area Internal Std. (ratio calculated in step 22) versus the *urine equivalent* concentration of the standards for the two analytes.

CALCULATIONS:

24. Determine the concentration of the two analytes in the extracts from the original urine (4.0 mL specimen) from the curves obtained in step 23. The results can be expressed as ng/mL of each analyte in urine.

EVALUATION OF METHOD:

This method was evaluated and described in detail by B'Hymer [9,10]. A general summary of this published information is given below:

Accuracy and Precision. Three recovery studies using multiple columns over several days demonstrated the accuracy and precision of this test method. The first recovery study was performed using fortified urine samples over three separate experimental batch runs, and these data are presented in Table 2. Average recoveries were between 102 and 106% for the two analytes over the four spiked

concentration levels investigated. For each batch run, the experimental trial consisted of three samples at four different concentration levels. The recovery and precision for each level (n = 9 samples) are displayed in Table 2. The relative standard deviations (RSD) observed ranged from 2.0 to 5.0%. These accuracy and precision numbers fall well within parameters established for bioanalytical methods [7].

The second recovery study was performed using a urine substitute, fortified over three separate experimental batch runs, and these data are presented in Table 3. Average recoveries were between 99 and 109% for the two analytes over the four spiked concentration levels investigated. For each batch run, the experimental trial consisted of three samples at four different concentration levels. The recovery for each level (n = 9 samples) is displayed in Table 3. As seen in the RSD column of Table 3, precision was much worse for the urine substitute recovery study. This is due to a higher level of ion suppression in the electrospray source. This was especially pronounced at the lower spiked concentration levels (1 and 2 ng/mL). The highest result for the RSD of the 9 samples fortified at 1 ng/L BMA was 29%. While the accuracy numbers meet standard criteria, the precision values at the lower concentrations do not [7]. The use of a urine substitute for QC samples is not recommended for this method.

The third recovery study used urine specimens from twelve non-exposed volunteers; six were smokers and six were non-smokers. Most participants' specimens had base levels for both BMA and PMA as are shown in Table 4. Again, reasonable accuracy and precision were demonstrated for a 6 ng/mL equivalent level spike; individual recoveries ranged from 95 to 109% for BMA and 101 to 123% for PMA (Table 4). No interferences were detected in the unspiked urine from the 12 volunteer specimens. This study illustrates two important points: 1. Levels of both metabolites can be found in the urine of non-exposed individuals, which is why aqueous standards are used in this method, and 2. It is important to ascertain smoking status and other non-occupational exposures that may cause elevated levels of these metabolites.

Linearity. All calibration curves used during the development of this method were linear and had correlation coefficients of 0.99 and greater. The concentration range was equivalent to 0.5 to 50 ng/mL BMA and PMA for the extraction of 4.0 mL urine. Calibration curves were run at the beginning and end of all sample batch runs; calibration curve slope drift was found to be minimal.

Specificity. The optimized chromatographic conditions developed for this method, along with the tandem mass spectrometric detector, proved to be specific and showed no major interferences. The mass transition ions of BMA and PMA chosen in this method had the greatest response and were the predominant daughter ions.

Robustness. Two C18 HPLC columns (Zorbax Rx-C18, Agilent Technologies, Santa Clara, CA, USA) from the same manufacturer but from different manufacturing lots were used during the recovery studies. Accuracy and precision were not affected; therefore, the method was found to be reproducible with any normal functioning C18 HPLC column. Recovery results from individual volunteer urine specimens spiked with the analytes indicate that the method is accurate and not significantly affected by individual urine specimen matrix differences during analyte extraction. The urine substitute was found to cause problems with precision, especially at lower levels; this was attributed to an increase in ion suppression over human urine within the electrospray source.

Stability. Sample stability was evaluated, whereby a six-day stability study was conducted on the final chromatographic sample solution. BMA and PMA were stable at 8 °C (the autosampler temperature) and at room temperature in the absence of light. A light stability experiment was carried out by storing this solution in a clear glass vial at room temperature on the window sill, thus creating a worst-case scenario. After 1 day of storage in light under these conditions, BMA and PMA had mean assay values of 75 and 72% (n = 3), respectively, when compared to solutions of freshly prepared reference standards. After three days of light exposure, extensive degradation was noticed; BMA mean assay values had fallen to 9% (n = 3) of the original level and PMA had fallen to 16% (n = 3). After six days of exposure to light, both analytes were nearly completely degraded. Although both analytes benefit from the use of

individual deuterated internal standards, the use of amber glass autosampler vials or other means of reducing light exposure is recommended to ensure sample stability during extended chromatographic batch runs.

Range. This method should be considered accurate for the estimation of BMA and PMA in human urine within the 0.5 to 50 ng/mL standard curve range. Field samples at higher levels can be diluted to a concentration within that range for analysis.

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METHOD WRITTEN BY:

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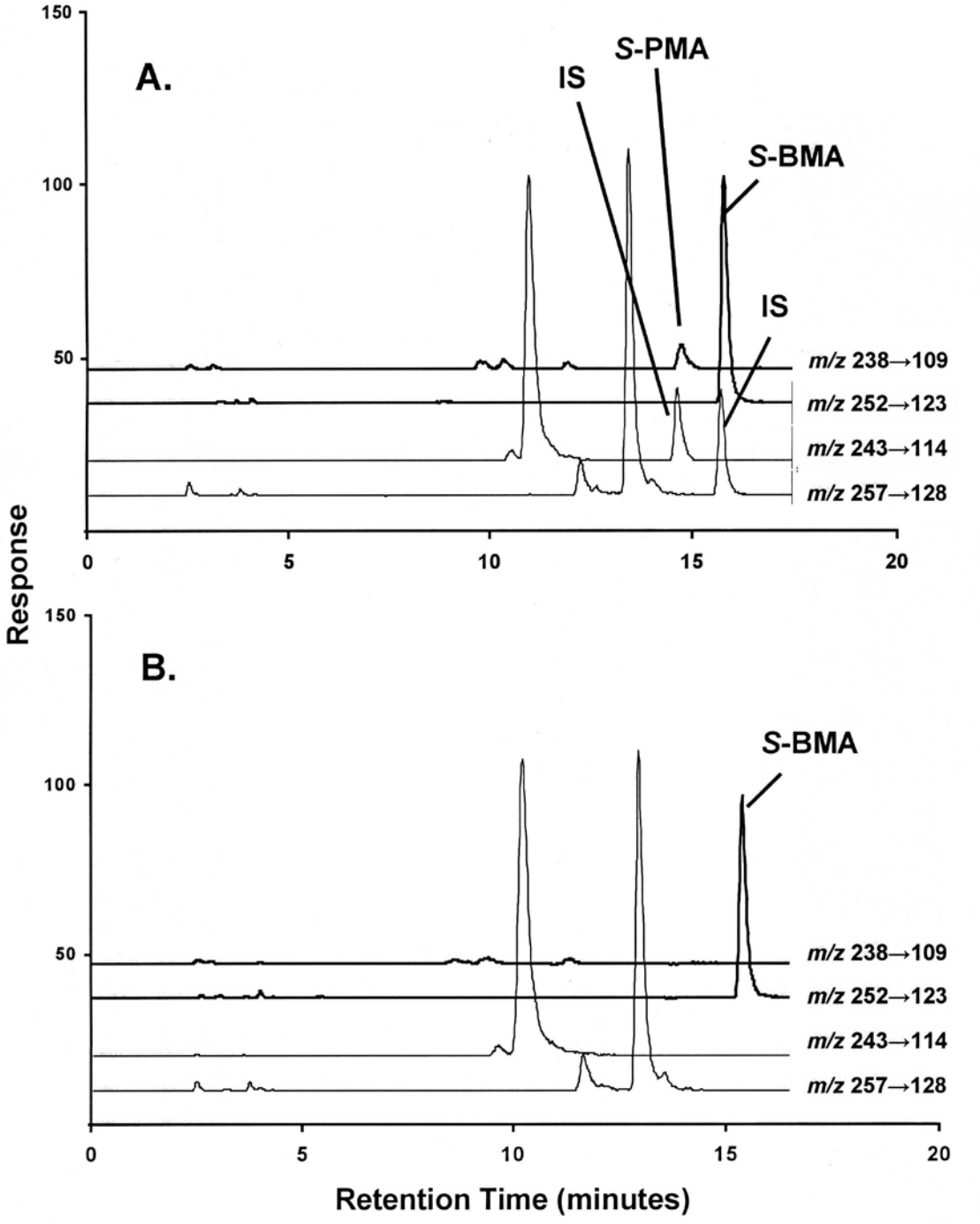

Figure 1. Chromatograms obtained using the described procedure: (A) fortified urine containing 1 ng/mL *S*-PMA, 7.2 ng/mL *S*-BMA, and 3.8 ng/mL of each of the deuterated internal standards (IS) and (B) non-fortified urine from above containing only the background level of 6.2 ng/mL *S*-BMA

Table 2. Multiple level recovery experiment of BMA and PMA from urine

Analyte	Analyte added (ng/mL)	Mean concentration (ng/mL, n = 9)	Mean background corrected concentration (ng/mL, n = 9)	Average recovery (%)	Standard deviation (ng/mL)	%RSD[1]
BMA[2]	1	7.43	7.18	103	0.37	5.0
BMA[2]	2	8.44	8.18	103	0.19	2.3
BMA[2]	8	14.6	14.2	103	0.32	2.2
BMA[2]	30	38.2	36.2	106	0.94	2.4
PMA	1	1.02	1.00	102	0.05	4.9
PMA	2	2.10	2.00	105	0.09	4.3
PMA	8	8.23	8.00	103	0.27	3.3
PMA	30	31.9	30.0	106	0.65	2.0

Notes: 1. %RSD = percent relative standard deviation
2. The non-fortified reference urine had a background level of 6.2 ng/mL BMA and no detectable level of PMA.
Three different spiked samples were prepared at each level and analyzed during three separate experimental trial runs (a total of nine samples at each spike level were analyzed). The same C18 column was used for experimental batch trials 1 and 2; a second C18 column was used on trial run 3.

Table 3. Multiple level recovery experiment of BMA and PMA from a urine substitute

Analyte	Analyte added (ng/mL)	Mean concentration (ng/mL, n = 9)	Average recovery (%)	Standard deviation (ng/mL)	%RSD[1]
BMA	1	1.07	107	0.31	29
BMA	2	2.13	106	0.34	16
BMA	8	8.31	104	0.53	6.4
BMA	30	30.7	102	0.76	2.5
PMA	1	1.09	109	0.27	25
PMA	2	1.98	99	0.16	7.9
PMA	8	7.96	100	0.48	6.0
PMA	30	31.1	104	0.91	2.9

Notes: 1. %RSD = percent relative standard deviation.
Three different spiked samples were prepared at each level and analyzed during three separate experimental trial runs (a total of nine samples at each spike level were analyzed).

Table 4. Individual smoker and non-smoker recovery experiment of BMA and PMA

	Background Level		Fortified Urine (background + 6 ng/mL)		Fortified Urine Recovery	
Individual Sample	BMA (ng/mL)	PMA (ng/mL)	BMA (ng/mL)	PMA (ng/mL)	BMA [ng/mL (percent)]	PMA [ng/mL (percent)]
Smoker 1	2.7	0.2	8.7	6.2	8.6 (99%)	6.5 (104%)
Smoker 2	28.3	0.3	34.3	6.3	34.7 (101%)	6.9 (108%)
Smoker 3	15.9	0.9	21.9	6.9	21.3 (97%)	7.9 (114%)
Smoker 4	5.7	0.3	11.7	6.3	11.6 (99%)	7.7 (121%)
Smoker 5	1.3	nd	7.3	6.0	6.9 (95%)	6.4 (106%)
Smoker 6	9.2	0.7	15.2	6.7	15.5 (102%)	7.0 (104%)
Mean	10.5	0.4	16.5	6.4	16.4 (99%)	7.1 (110%)
Non-smoker 1	0.3	nd	6.3	6.0	6.2 (98%)	6.2 (103%)
Non-smoker 2	7.1	nd	13.1	6.0	14.3 (109%)	7.4 (123%)
Non-smoker 3	6.8	nd	12.8	6.0	13.1 (102%)	6.8 (112%)
Non-smoker 4	23.3	nd	29.3	6.0	28.6 (97%)	6.3 (105%)
Non-smoker 5	4.7	nd	10.7	6.0	11.0 (103%)	6.3 (105%)
Non-smoker 6	7.2	nd	13.2	6.0	13.5 (102%)	6.1 (101%)
Mean	8.2	-	14.2	6.0	14.5 (102%)	6.5 (108%)

Notes: The instrumental limit of detection (LOD) was estimated to be approximately 0.2 ng/mL for both analytes. The lowest standard value was 0.5 ng/mL for both analytes. [Values near the LOD were reported to one significant figure.]
nd = none detected (< 0.2 ng/mL)

ASBESTOS, CHRYSOTILE by XRD 9000

$Mg_3Si_2O_5(OH)_4$ MW: ~283 CAS: 12001-29-5 RTECS: CI6478500

METHOD: 9000, Issue 3 **EVALUATION: FULL** **Issue 1: 15 May 1989**
Issue 3: 20 October 2015

EPA Standard (Bulk): 1% by weight

PROPERTIES: Solid, fibrous mineral; conversion to forsterite at 580 °C; attacked by acids; loses water above 300 °C

SYNONYMS: Chrysotile

SAMPLING

BULK SAMPLE: 1 g to 10 g

SHIPMENT: Seal securely to prevent escape of asbestos

SAMPLE STABILITY: Indefinitely

BLANKS: None required

ACCURACY

RANGE STUDIED: 1% to 100% in talc [1]

BIAS: Negligible if standards and samples are matched in particle size [1]

OVERALL PRECISION ($\hat{S}_{rT}$): Unknown; depends on matrix and concentration

ACCURACY: ±14% to ±25%

MEASUREMENT

TECHNIQUE: X-RAY POWDER DIFFRACTION

ANALYTE: Chrysotile

PREPARATION: Grind under liquid nitrogen; wet-sieve through 10 µm sieve

DEPOSIT: 5 mg dust on 0.45 µm silver membrane filter

XRD: Copper target X-ray tube; optimize for intensity; 1° slit; integrated intensity with background subtraction

CALIBRATION: Suspensions of asbestos in 2-propanol

RANGE: 1% to 100% asbestos

ESTIMATED LOD: 0.2% asbestos in talc and calcite; 0.4% asbestos in heavy X-ray absorbers such as ferric oxide

PRECISION ($\bar{S}_r$): 0.07 (5% to 100% asbestos); 0.10 (@ 3% asbestos); 0.125 (@ 1% asbestos)

APPLICABILITY: Analysis of percent chrysotile asbestos in bulk samples.

INTERFERENCES: Antigorite (massive serpentine), chlorite, kaolinite, bementite, and brushite interfere. X-ray fluorescence and absorption is a problem with some elements; fluorescence can be circumvented with a diffracted beam monochromator, and absorption is corrected for in this method.

OTHER METHODS: This is NIOSH method P&CAM 309 [2] applied to bulk samples only, since the sensitivity is not adequate for personal air samples. An EPA test method for the determination of asbestos in bulk insulation samples is similar to this one [3]. NIOSH method 7400 is an optical counting procedure for airborne fibers in personal samples. NIOSH methods 7402 (Asbestos by Transmission Electron Microscopy) and 9002 (Asbestos by Polarized Light Microscopy) are also useful for positive identification of asbestos.

REAGENTS:

1. Chrysotile,* certified reference material.
2. 2-Propanol.*
3. Desiccant.
4. Glue or tape for securing silver filters to XRD holders.

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Vials, plastic (for bulk sample).
2. Freezer mill, liquid nitrogen-cooled, grinding vials, and extractor.
3. Ultrasonic bath.
4. Sieve, 10 µm, for wet-sieving.
5. Filters, polycarbonate, 1.0 µm, 37 mm.
6. Filtration apparatus and side-arm vacuum flask with 25 mm and 37 mm filter holders.
7. Oven, drying, 110 °C.
8. Analytical balance, readable to 0.01 mg.
9. Beaker, Griffin, 50 mL, with watch glass cover.
10. Filters, silver membrane, 25 mm diameter, 0.45 µm pore size.
11. Desiccator.
12. Bottles, glass, 1 L, with ground glass stoppers.
13. Wash bottle, polyethylene.
14. Magnetic stirrer.
15. X-ray powder diffractometer with copper target X-ray tube and scintillation detector.
16. Reference specimen (mica, Arkansas stone or other stable standard) for data normalization.
17. Volumetric pipettes and flasks.

SPECIAL PRECAUTIONS: Asbestos, a human carcinogen, should be handled in a hood [4]. 2-Propanol is flammable.

SAMPLING:

1. Place several grams of the dust to be analyzed in a plastic vial, seal the vial securely, and ship in a padded carton.

SAMPLE PREPARATION:

2. Place about 0.5 g of sample dust in a grinding vial and grind in a liquid nitrogen-cooled mill for 2 min to 10 min.
3. Wet sieve the ground dust using a 10 µm sieve and 2-propanol. Place the dust on the sieve and place the sieve directly in an ultrasonic bath or in a wide dish in the bath. Use enough 2-propanol to cover the dust (put water in the bath if a dish is used to contain the 2-propanol). Apply ultrasonic power to sieve the dust.
   NOTE: It may take some time to obtain several mg of dust. Heating of the 2-propanol is likely and cooling periods may be required.
4. Recover the sieved sample dust from the 2-propanol by filtering the suspension through a non-fibrous filter (polycarbonate) or by driving off the 2-propanol on a hot plate. Dry the sieved sample in 110 °C oven for 4 h or more.
5. Weigh out about 5 mg of the sieved material onto a small square of tared weighing paper. Record the actual sample weight, W_s, to the nearest 0.01 mg. Transfer the dust to a 50 mL beaker, washing the weighing paper with several mL of 2-propanol. Add 10 mL to 15 mL 2-propanol to the beaker.
6. Cover the beaker with a watch glass. Agitate in an ultrasonic bath at least 3 min until all agglomerated particles are dispersed. Wash the underside of the watch glass with 2-propanol, collecting the washings in the beaker.

7. Place a silver filter in the filtration apparatus. Attach the funnel securely over the entire filter circumference. With no vacuum, pour 2 mL to 3 mL 2-propanol onto the filter. Pour the sample suspension from the beaker into the funnel and apply vacuum. During filtration, rinse the beaker several times and add rinsings to the funnel.
   NOTE: Control the filtration rate to keep the liquid level in the funnel near the top during rinsing. Do not wash the walls or add 2-propanol to the funnel when the liquid level is lower than 4 cm above the filter. Leave the vacuum on after filtration for sufficient time to produce a dry filter.
8. Remove the filter with forceps and attach it to the sample holder for XRD analysis.

CALIBRATION AND QUALITY CONTROL:

9. Prepare and analyze working standard filters:
   a. Prepare two suspensions of chrysotile asbestos in 2-propanol by weighing 10 mg and 100 mg of the dry powder to the nearest 0.01 mg. Quantitatively transfer each to a 1 L glass-stoppered bottle using 1.00 L 2-propanol.
      NOTE: Depending on the particle size of the standard, it may need to be ground and wet sieved (step 3). Dry the standards in a 110 °C oven for 4 h or more. Store in a desiccator.
   b. Suspend the powder in the 2-propanol with an ultrasonic probe or bath for 20 min. Immediately move the flask to a magnetic stirrer with thermally-insulated top and add a stirring bar to the suspension. Cool the solution to room temperature before withdrawing aliquots.
   c. Mount a filter on the filtration apparatus. Place several mL 2-propanol on the filter surface. Turn off the stirrer and shake vigorously by hand. Within a few seconds of setting the bottle down, remove the lid and withdraw an aliquot from the center of the 10 mg/L or 100 mg/L suspension. Do not adjust the volume in the pipet by expelling part of the suspension. If more than the desired aliquot is withdrawn, return all of the suspension to the bottle, rinse and dry the pipet, and take a new aliquot. Transfer the aliquot from the pipet to the filter. Keep the tip of the pipet near the surface but not submerged in the delivered suspension.
   d. Rinse the pipet with several mL 2-propanol, draining the rinse into the funnel. Repeat the rinse several more times. Prepare working standard filters, in triplicate, by this technique, at e.g., 0 µg, 20 µg, 30 µg, 50 µg, 100 µg, 200 µg, and 500 µg.
   e. Apply vacuum and rapidly filter the suspension. Leave vacuum on until filter is dry. Do not wash down the sides of the funnel after the deposit is in place since this will rearrange the material on the filter. Transfer the filter to the sample holder.
   f. Analyze by XRD (step 12). The XRD intensities (step 12.d) are designated I_x^o and are then normalized (step 12.e) to obtain $\hat{I}_x^o$. The intensities for standards greater than 200 µg should be corrected for matrix absorption (steps 12.f and 13).
   g. Prepare a calibration graph by plotting $\hat{I}_x^o$, as a function of the deposited asbestos mass, W_A, µg, of each standard.
      NOTE: Poor repeatability (relative standard deviation greater than 10% above 40 µg chrysotile) indicates that new standards should be made. The data should lie along a straight line. It is preferable to use a weighted least squares with $1/\sigma^2$ weighing, where σ^2 is the variance of the data at a given loading.
   h. Determine the slope, *m*, of the calibration curve in counts per microgram. The intercept on the abscissa should be 0 µg ± 5 µg.
      NOTE: A large intercept indicates an error in determining the background, i.e., an incorrect baseline has been calculated or interference by another phase.
10. Select six silver membrane filters as media blanks (for determination of sample self-absorption, step 13) randomly from the same box of filters to be used for depositing the samples. Mount each of the media blanks on the filtration apparatus and apply vacuum to draw 5 mL to 10 mL of 2-propanol through the filter. Remove, let dry, and mount on sample holders. Determine the net normalized count for the silver peak, $\hat{I}_{Ag}^o$, for each media blank (step 12). Obtain an average value, $\overline{B}_{Ag}$, for the normalized silver peak intensities of the six media blanks.

MEASUREMENT:

11. Obtain a qualitative X-ray diffraction scan (e.g., 10 degrees to 80 degrees 2-theta) of the sample to determine the presence of chrysotile and interferences. The expected diffraction peaks are as follows:

	Peak (2-Theta Degrees)	
Mineral	**Primary**	**Secondary**
Chrysotile	12.08	24.38
Silver	38.12	44.28

12. Mount the filter (sample, standard, or blank) in the XRD instrument and:
    a. Determine the net intensity, I_r, of the reference specimen before each filter is scanned. Select a convenient normalization scale factor, N, which is approximately equivalent to the net count for the reference specimen peak, and use this value of N for all analyses.
    b. Measure the diffraction peak area of a chrysotile peak that is free of interference. Scan times should be long, e.g., 15 min.
    c. Measure the background on each side of the peak for one-half the time used for peak scanning. The sum of these two counts is the average background. Determine the position of the background for each sample.
    d. Calculate the net intensity, I_x (the difference between the peak integrated count and the total background count).
    e. Calculate and record the normalized intensity, $\hat{I}_x$, for the sample peak on each sample and standard:

$$\hat{I}_x = \frac{I_x}{I_r} N.$$

    NOTE: Normalizing to the reference specimen intensity compensates for long-term drift in X-ray tube intensity. If intensity measurements are stable, the reference specimen may be run less frequently; net intensities should be normalized to the most recently measured reference intensity.
    f. Determine the net count, I_{Ag}, of an interference-free silver peak on the sample filter following the same procedure. Use a short scan time for the silver peak (for example, 5% of scan time for analyte peaks) throughout the method. Normalize I_{Ag} (step 12.e) to obtain $\hat{I}_{Ag}$.
    g. Scan each field blank over the same 2-theta range used for the analyte and silver peaks. These analyses serve only to verify that contamination of the filters has not occurred. The analyte peak should be absent. The normalized intensity of the silver peak should match that of the media blanks.

CALCULATIONS:

13. Calculate the percentage, C, of chrysotile in the bulk dust sample:

$$C = \frac{(\hat{I}_x \times \mathrm{f}(T) - b) \times 100}{m \times W_S}, \%,$$

where: $\hat{I}_x$ = normalized asbestos peak intensity for sample peak,
b = intercept of calibration graph ($\hat{I}_x^{\circ}$ vs. W_A),
m = slope of calibration graph (counts per µg),
$\mathrm{f}(T) = \frac{-R\ln(T)}{1-T^R}$ = absorption correction factor (see Tables 1a and 1b),
$R = \sin(\theta_{Ag}) / \sin(\theta_x)$,

T = $\hat{I}_{Ag} / \overline{B}_{Ag}$ = transmittance of sample,

$\hat{I}_{Ag}$ = normalized silver peak intensity from sample,

$\overline{B}_{Ag}$ = average normalized silver peak intensity from media blanks (average of six values), and

W_S = mass, µg, of deposited sample.

NOTE: For a more detailed discussion of the absorption correction procedure, see references 5, 6, 7, and 8.

EVALUATION OF METHOD:

This method is based on the work of B.A. Lange in developing P&CAM 309 [1,2]. Samples in the range of 1% to 100% chrysotile in talc were studied to establish the feasibility of an XRD method for airborne asbestos. Analytical precision was as follows:

% Chrysotile in Talc	$\overline{S}_r$ (%)
100	6.9
10	4.7
7	9.8
5	8.2
3	10.1
1	12.5

This work also showed that bias of results after absorption corrections are made is negligible.

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METHOD REVISED BY:

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Table 1a. Absorption correction factor as a function of transmittance (1.00 to 0.70) for chrysotile primary and secondary peak combinations with silver primary peak

	Absorption Correction Factor	
Transmittance	Primary Peak	Secondary Peak
1.00	1.0000	1.0000
0.99	1.0157	1.0078
0.98	1.0317	1.0157
0.97	1.0480	1.0237
0.96	1.0647	1.0319
0.95	1.0817	1.0402
0.94	1.0991	1.0486
0.93	1.1168	1.0572
0.92	1.1350	1.0659
0.91	1.1535	1.0747
0.90	1.1724	1.0837
0.89	1.1917	1.0928
0.88	1.2114	1.1021
0.87	1.2316	1.1115
0.86	1.2522	1.1212
0.85	1.2733	1.1309
0.84	1.2948	1.1409
0.83	1.3168	1.1510
0.82	1.3394	1.1613
0.81	1.3624	1.1718
0.80	1.3859	1.1825
0.79	1.4100	1.1933
0.78	1.4346	1.2044
0.77	1.4598	1.2157
0.76	1.4856	1.2272
0.75	1.5120	1.2389
0.74	1.5390	1.2508
0.73	1.5666	1.2630
0.72	1.5949	1.2754
0.71	1.6239	1.2881
0.70	1.6536	1.3010

Table 1b. Absorption correction factor as a function of transmittance (0.69 to 0.39) for chrysotile primary and secondary peak combinations with silver primary peak

	Absorption Correction Factor	
Transmittance	Primary Peak	Secondary Peak
0.69	1.6839	1.3142
0.68	1.7151	1.3277
0.67	1.7470	1.3414
0.66	1.7797	1.3555
0.65	1.8132	1.3698
0.64	1.8475	1.3845
0.63	1.8827	1.3995
0.62	1.9188	1.4148
0.61	1.9558	1.4305
0.60	1.9938	1.4465
0.59	2.0328	1.4629
0.58	2.0728	1.4797
0.57	2.1139	1.4969
0.56	2.1560	1.5145
0.55	2.1993	1.5325
0.54	2.2438	1.5510
0.53	2.2895	1.5700
0.52	2.3365	1.5895
0.51	2.3848	1.6095
0.50	2.4344	1.6300
0.49	2.4855	1.6510
0.48	2.5380	1.6727
0.47	2.5921	1.6950
0.46	2.6478	1.7179
0.45	2.7051	1.7414
0.44	2.7642	1.7657
0.43	2.8251	1.7907
0.42	2.8879	1.8165
0.41	2.9526	1.8431
0.40	3.0195	1.8705
0.39	3.0885	1.8989

METHAMPHETAMINE and Illicit Drugs, Precursors and Adulterants on Wipes by Liquid-Liquid Extraction

9106

FORMULA: Table 1 | MW: Table 1 | CAS: Table 1 | RTECS: Table 1

METHOD: 9106, Issue 1 | **EVALUATION: Partial** | **Issue 1: 17 October 2011**

OSHA: none for surfaces
NIOSH: none for surfaces
Other OELs and guidelines: [1, 2, 3]

PROPERTIES: Table 2

SYNONYMS: Table 3

SAMPLING

SAMPLER:	Wipe
SAMPLE AREA:	100 cm^2 or 1000 cm^2
SHIPMENT:	Preferably ship refrigerated, <6 °C
SAMPLE STABILITY:	30 days at <6 °C (See Table 4)
FIELD BLANKS:	2 to 10 blanks per sample set

MEASUREMENT ACCURACY

LEVEL STUDIED:	3 µg/sample on smooth surfaces
BIAS:	Table 10a and 10b
OVERALL PRECISION ($\hat{S}_{rT}$):	Table 7a and 7b [4]
ACCURACY:	Table 7a and 7b [4]

MEASUREMENT

TECHNIQUE:	GAS CHROMATOGRAPHY/MASS SPECTROMETRY
ANALYTES:	Table 1
DESORPTION:	0.1 M sulfuric acid
CLEANUP/ EXTRACTION:	Hexane cleanup followed by methylene chloride extraction
DERIVATIZATION:	Chlorodifluoroacetic anhydride
INJECTION:	2 µL, splitless
TEMPERATURE	
- Injection:	265 °C
- Detector:	285 °C
- Column:	90 °C (2 min), 310 °C (10 °C/min), hold for 11 min
MASS SPECTROMETER:	Scan mode (29 – 470 AMU), 2 scan per sec, Selected ion monitoring (SIM) mode Table 5
CARRIER GAS:	Helium, 1.5 mL/min
COLUMN:	Capillary, fused silica, 30 m × 0.32 mm ID; 0.5 µm film phenyl arylene polymer
CALIBRATION:	Standards from spiked wipes with internal standard, See Table 6
RANGE:	Table 7a and 7b [4]
ESTIMATED LOD:	Table 4
PRECISION ($\bar{S}_r$):	Table 7a and 7b [4]

APPLICABILITY: For methamphetamine, the range is 0.05 to 60 µg/sample (sample = 100 cm^2 or 1000 cm^2). This method was developed for the analysis of selected drugs and precursors on surfaces in clandestine drug labs. [4, 5] Sampling methodology was tested using wipes on smooth, non-porous surfaces. The APPENDIX contains sampling information for other types of surfaces.

INTERFERENCES: No chromatographic interferences detected. Water, surfactants and polyols inhibit derivatization.

OTHER WIPE METHODS: NIOSH 9109 uses solid-phase extraction and gas chromatography/mass spectrometry (GC/MS) to measure multiple drugs [6]. NIOSH 9111 uses liquid chromatography/mass spectrometry (LC/MS) to measure methamphetamine [7].

REAGENTS:

NOTE: See APPENDIX A for special instructions on reagents.

1. Analytes listed in Table 1.*
2. Internal standards from those listed in Table 8.
3. Solvents, residue free analytical grades:
   a. Hexane *
   b. Isopropanol (IPA)*
   c. Methanol *
   d. Methylene chloride (CH_2Cl_2) *
   e. Toluene *
   f. Acetone*
4. Concentrated sulfuric and hydrochloric acids (AR or trace metals analysis grades).*
5. Sodium hydroxide, A.C.S. grade.*
6. Anhydrous granular sodium sulfate, AR grade.
7. Anhydrous granular potassium carbonate, AR grade.
8. Bromothymol Blue, ≥95%, A.C.S., phenolphthalein, A.C.S.; crystal violet (Gentian Violet), ≥95%, A.C.S.
9. Purified gases: helium for carrier gas, nitrogen for drying.
10. Chlorodifluoroacetic anhydride, 98%* derivatizing agent. Moisture sensitive!
11. 4,4'-Dibromooctafluorobiphenyl, 99%, instrument internal standard (IIS).
12. Deionized water (ASTM type II).

SOLUTIONS:

NOTE: See APPENDIX A for special instructions on solutions.

1. Prepare solutions of analytes of interest. Calculate concentrations as the free base. Keep refrigerated (<6 °C). Protect solutions from light.
   a. Stock solutions are prepared at about 1-2 mg/mL in methanol.
   b. Analyte spiking solutions are prepared by diluting the stock solutions to about 200 µg/mL each in methanol.
2. Prepare internal standard spiking solution in methanol at about 200 µg/mL. (Note: Add about 2 milligrams of crystal violet per 20 mL of internal standard spiking solution to help indicate which samples have been spiked.)
3. Desorption solution: 0.1 M H_2SO_4 (sulfuric acid.) Add 22 mL conc. sulfuric acid to 4 L deionized water.
4. Bromothymol blue and phenolphthalein pH indicator solution: 1 mg/mL each in 4:1 isopropanol: deionized water.
5. Sodium hydroxide*, 10 M: Dissolve 40 grams sodium hydroxide in enough deionized water to make 100 mL. Do not store in glass-stoppered bottle.
6. Hydrochloric acid, 0.3 M, in methanol: Dilute 2.5 mL conc. hydrochloric acid in about 80 mL methanol; dilute to 100 mL with methanol.
7. Crystal violet indicator: 2-3 mg/mL in isopropanol.
8. Reconstitution solvent: 10% acetone in toluene with 4 µg/mL of 4,4'-dibromooctafluorobiphenyl (optional).*

* See SPECIAL PRECAUTIONS

EQUIPMENT:

NOTE: See APPENDIX B for special instructions on equipment.

1. Wipe, (7.6 cm × 7.6 cm) 12-ply or equivalent.
2. Sample storage and shipping container: 50-mL polypropylene centrifuge tubes with PTFE-lined caps.
3. Extraction tubes and vials:
   a. Glass test tubes, 25-mL (20 × 120 mm), with PTFE-lined caps;
   b. Glass test tubes, 14-mL (16 × 100 mm), with PTFE- lined caps, (ASTM Specification E982 [5], or equivalent, suitable for repeated autoclaving);
   c. Amber GC autosampler vials (2-mL) and caps.
4. Gas chromatograph/mass spectrometer detector, with column and integrator, see p. 9106-1.
5. Liquid Transfer:
   a. Syringes: 10-, 25-, 100-, and 500-µL sizes.
   b. Mechanical pipette with disposable tips or repeating dispenser: 0.5-, 2.5-, and 10-mL sizes.
   c. Repeating dispenser: 1- to 5-mL.
   d. Three repeating dispensers: 10 to 20-mL each.
6. Volumetric flasks: 10-, 100-, and 250-mL.
7. Forceps.
8. Gloves, latex or nitrile. Avoid vinyl gloves (see 9106-3, Sampling step 1, NOTE 2).
9. Scoop for solid reagents.
10. Empty drying columns: 1 cm i.d. × 12-15 cm length polypropylene plastic columns having a fritted polyethylene disc or equivalent (e.g. 10-mL pipette tip with small wad of silanized glass wool packed into the tip).
11. Nitrogen blow-down apparatus with water bath capable of maintaining 35 °C.
12. Vortex mixer.
13. Rotating mixer capable of 10-30 rpm.
14. Aspirator flask: 1-L, with aspirator tubing and a 12.5 cm long 16 gauge needle.
15. Centrifuge: capable of up to 4000 x g and of holding 25-mL glass test tubes.
16. Oven capable of 70 to 90 °C ± 2 °C.
17. Test tube racks, heat resistant to 90 °C.
18. Pasteur pipettes.
19. pH paper.
20. Template: 10 cm × 10 cm or 31.7 cm × 31.7 cm opening, made of relatively rigid disposable cardstock or sheet of PTFE.
21. Ice or other cold media for shipping.

SPECIAL PRECAUTIONS: The solvents are flammable and have adverse health effects. Phenethylamines target the nervous system at very low concentrations and are easily absorbed through the skin. Avoid breathing vapors. Avoid skin contact. Work should be performed in a hood with adequate ventilation. Analysts must wear proper eye and hand protection (e.g. latex gloves) to prevent absorption of even small amounts through the skin. Dissolving sodium hydroxide and concentrated hydrochloric or sulfuric acid in water is highly exothermic. Goggles must be worn. The derivatization reagents react violently with water.

Caution must also be exercised in the collecting, handling, and analysis of samples. Clandestine drug labs may produce unknown and seriously toxic by-products. For example, in the manufacture of designer drugs (e.g., MPPP, a homolog of Alphaprodine), at least one very neurotoxic by-product, 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine (MPTP), has been identified that specifically and irreversibly causes Parkinson's disease [8,9].

SAMPLING:

See APPENDIX C for special instructions on sampling.

1. Using a new pair of gloves, remove a gauze wipe from its protective package. Moisten the wipe with approximately 3 to 4 mL of methanol (or isopropanol).
   NOTE 1: Apply no more solvent than that needed to moisten approximately the central 80% of the area of the gauze wipe. Excess solvent may cause sample loss due to dripping from the wipe.
   NOTE 2: Do not use vinyl gloves due to the potential for leaching of phthalate plasticizers and contamination of the samples.
2. Place the template over the area to be sampled (may tape in place along outside edge of template). Wipe the surface to be sampled with firm pressure, using vertical S-strokes. Fold the exposed side of the pad in and wipe the area with horizontal S-strokes. Fold the pad once more and wipe the area again with vertical S strokes.
3. Fold the pad, exposed side in, and place in shipping container and seal with cap.
   NOTE: Keep samples refrigerated (<6 ^{o}C). While methamphetamine and several related amines are stable on the recommended wipe media for at least 7 days at room temperature, refrigeration is recommended as soon as possible (see Table 4).
4. Either clean the template before use for the next sample or use a new disposable template.
5. Label each sample clearly with a unique sample identifier.
6. Prepare a minimum of two field blanks with one field blank for every ten samples.
   NOTE: In addition, include at least 3 media blanks for the analytical laboratory to use for their purposes. The wipes used for the media blanks should be from the same lot as the field samples.

SAMPLE PREPARATION:

See APPENDIX D for special instructions on sample preparation.

7. Desorption from media:
   a. Remove cap from shipping container.
      NOTE: Sample wipe should fit loosely in the container. If not, transfer sample to a larger container.
   b. Spike 60 µL of internal standard spiking solution onto each wipe sample.
   c. Add 30 mL desorption solution (0.1 M sulfuric acid).
      NOTE: If the samples were transferred to a larger container, rinse the original shipping container with the desorption solution, shake, and decant the rinsate into the larger container.
   d. Cap securely and mix contents by inverting the tubes end over end on a rotary mixer or equivalent at 10-30 rpm for at least one hour.

e. Check the pH which should be about ≤ 4. Adjust the pH with diluted (2.5 to 3 M) sulfuric acid drop-wise, mixing the contents by shaking or inversion a few times after each addition of acid before checking the pH.
f. After mixing, transfer 10 mL of supernatant to a 25-mL glass centrifuge tube.
NOTE: If cleanup is to be performed on a subsequent day, store samples in a refrigerator. Analytes are stable in the desorption solution for at least one week refrigerated.

8. Cleanup: Potential contamination from oils, triglycerides, plasticizers and other hydrocarbons are reduced through a hexane back-extraction step.
a. To each 10-mL aliquot of acid desorbate, add 10 mL of hexane, cap and mix on a rotary mixer for one hour. Allow to stand for 15-30 minutes for the phases to separate. If an emulsion forms, centrifuge the tubes at 1500-2000 rpm for a few minutes. If the emulsion persists, add about 0.5 mL of acetonitrile to the surface of the emulsion and gently mix the layers at the interface of the emulsion. Centrifuge again if necessary.
b. Aspirate the (upper) organic layer to waste. Exercise care to not remove any of the aqueous layer.
9. Extraction of analytes into methylene chloride:
a. Add 1-2 drops (20-50 µL) of the mixed pH indicator (phenolphthalein + bromothymol blue) solution to each sample. The color of the samples should be yellow, which indicates that the samples are sufficiently acidic for desorption of the analytes from the wipe samples.
b. Add 0.5 mL of 10 M sodium hydroxide to each sample. The color of the samples should turn brilliant purple or magenta, confirming that the pH is greater than 9-9.5 (necessary for the extraction of the amines into methylene chloride). If the color remains yellow, or only turns green or light blue, check the pH with pH paper to confirm that it is greater than 9.5. If it is not, add another 0.5 mL of 10 M sodium hydroxide, mix, and check the pH again.
NOTE: The color of the solution will gradually fade from purple to deep blue within about 20-30 minutes. This is due to the known tendency of phenolphthalein to fade at high pH.
c. Add 10 mL of methylene chloride to each sample. Cap and mix on a rotary mixer for one hour. Allow to stand for 15 to 30 minutes. If an emulsion forms, centrifuge as described above (step 8a).
d. Aspirate the aqueous (upper) layer to waste as described above, being careful to not remove any of the lower methylene chloride layer.
10. Removal of water from the methylene chloride extract:
a. Prepare potassium carbonate-sodium sulfate drying columns.
Note: See APPENDIX E for preparation of drying columns.
b. Rinse the packed columns with about 6 mL of methylene chloride. Dry columns afterwards by forcing dry nitrogen or clean air through the top for 10-20 seconds.
c. Arrange 14-mL collection tubes (16 × 100 mm test tube) in test tube racks. Add 6 µL of crystal violet solution and 100 µL of 0.3 M hydrochloric acid in methanol to each collection tube.
NOTE: Crystal violet is not critical but helps later on as a visualizing aid for monitoring the progress of drying. Hydrochloric acid is critical to prevent loss of the amphetamines during evaporative concentration.
d. Position the drying columns over the collection tubes.
e. Transfer (decant) the methylene chloride layer into the drying column reservoir. After the last of the sample passes into the bed of the column, rinse the drying column twice with 1 mL of methylene chloride each time and combine with sample eluate.
11. Derivatization:
See APPENDIX F for special instructions on derivitization.
a. Evaporate the methylene chloride eluates in a nitrogen blow-down apparatus with the water bath set at 35 °C. Rinse the tips of the evaporation needles thoroughly with methanol or acetone between samples to prevent cross-contamination. When the samples are dry, remove and cap the tubes immediately.

NOTE: The dark color of the crystal violet helps make the residue more visible when it is dried. If at least 0.1 mL of isopropanol was present in the eluates, the crystal violet will also go through a series of color changes that helps in monitoring the drying process.

b. To each dried sample, add 100 µL of chlorodifluoroacetic anhydride and recap tubes. Mix the contents by vortexing briefly.
   NOTE 1: It is recommended that the tubes be kept capped and to only uncap about 5 at a time for the addition of the derivatizing reagent. Do not leave the acid anhydride bottle open between taking aliquots since the reagent is moisture sensitive.
   NOTE 2: If incomplete derivatization is routinely experienced, increase volume of reagent to 150 or 200 µL. The color of the crystal violet will turn yellow or yellow-green with the addition of chlorodifluoroacetic anhydride.
c. Heat in an oven at 70-75 °C for 20-30 minutes.
d. After heating, allow the tubes to cool to room temperature. Remove caps and evaporate the contents to dryness under a stream of nitrogen at room temperature. As the solution concentrates it turns from a yellow or yellowish-green solution to a bluish-green just before going to dryness. At the point of dryness the color of the residue normally turns rapidly to blue or violet, depending upon the amount of coextractants (the more co-extractants, the more blue the color and the less likely a violet color will develop). Remove the tubes just as soon as the blue or violet color becomes apparent. Losses have been experienced if blowing is continued for more than 2 minutes beyond the blue or violet color stage.
   NOTE: If an oil-like residue or film persists, then the sample may have too many contaminants that were not removed at the cleanup step or were introduced subsequent to cleanup. In such a case, return to step 7f and perform the clean-up (step 8) on another 10-mL aliquot of the sample desorbate using methylene chloride as the cleanup solvent instead of hexane. Discard the (lower) organic layer to waste before proceeding to steps 9 through 11.
e. Reconstitute the dried residue with 1 mL of the reconstitution solvent. The reconstituted solution normally will become deep blue in color. Mix by vortexing briefly a couple of times. Transfer the solutions to 2-mL amber-colored GC vials containing 200 to 250 mg anhydrous sodium sulfate. Cap vials, label, and analyze by GC/MS (See MEASUREMENT, steps 15-17).
   NOTE: Derivatives of phenylpropanolamine (norephedrine) break down significantly over several days at room temperature. GC vials containing derivatives should be kept refrigerated until analysis.

CALIBRATION AND QUALITY CONTROL:

12. Determine retention times for the derivatives of the analytes of interest using the column and chromatographic conditions specified on page 9106-1. Table 9 gives typical retention times for various drugs, precursors, and adulterants.
13. Calibrate daily with at least six calibration standards plus a blank (CS0) selected from Table 6 to cover the analytical range.
    a. Prepare the analyte spiking solution as follows: Add known amounts of individual drug stock solutions to a volumetric flask and dilute to volume with methanol. A recommended final concentration for this solution is approximately 200 µg each per mL.
    b. Prepare calibration standards and media blanks in clean shipping containers (e.g. 50-mL polypropylene centrifuge tubes or equivalent).
       NOTE: Liquid standards (standards without added blank wipe media) may be prepared in lieu of media standards if cotton gauze was used for the samples.
    c. Add 3 mL methanol (or isopropanol, if isopropanol was used with the samples in the field) to each calibration standard and media blank.

d. Spike a known volume of analyte spiking solution into each calibration standard by spiking directly onto the media or into solution. Use the spiking volumes suggested in Table 6 to cover the desired range.
e. Process each of these through steps 7 through 11 (same as the field samples.)
f. Analyze these along with the field samples. (See MEASUREMENT, steps 15-17.)

14. Prepare matrix-spiked (QC) and matrix-spiked duplicate (QD) quality control samples [12].
    a. Cotton gauze from the same lot used for taking samples in the field should be provided to the analytical laboratory to prepare these matrix-spiked quality control samples.
    b. The quality control samples (QC and QD) must be prepared independently at concentrations within the analytical range. (See Table 6 for applicable concentration ranges.)
    c. One quality control media blank (QB) must be included with each QC and QD pair.
        i. Transfer clean gauze wipes to new shipping containers.
        ii. Add 3 mL of isopropanol (or methanol, if methanol was used in wiping) to each gauze wipe.
        iii. Spike QC and QD with a known amount of analyte as suggested in Table 6.
    d. Process each of these through steps 7 through 11 (same as the field samples).
    e. Analyze these along with the field samples. (See MEASUREMENT, steps 15-17.)

MEASUREMENT:

See APPENDIX G for special instructions on measurement.

15. Analyze the calibration standards, quality control samples, blanks, and samples by GC/MS.
    a. Set gas chromatograph according to manufacturer's recommendations and to conditions listed on page 9106-1.
    b. Set mass spectrometer conditions to manufacturer's specifications and those given on page 9106-1 for the scan mode or those in Table 5 for the SIM mode.
    c. Inject sample aliquot with autosampler or manually.
        NOTE: After the derivatives are prepared and just before analyzing any samples or standards, inject the highest concentrated standard several times in order to prime or deactivate the GC column and injection port. This will help minimize any drift in the instrument's response to target analytes relative to their internal standards.
    d. After analysis, the vials should be recapped promptly and refrigerated if further analysis is anticipated.
16. Using extracted ion current profiles for the primary (quantification) ions specific to each analyte, measure GC peak areas of analyte(s) and internal standard(s) and compute relative peak areas by dividing the peak area of the analyte by the area of the appropriate internal standard. Recommended primary (quantification) ions and internal standards are given in Tables 5, 7, and 8. Prepare calibration graph (relative peak area vs. µg analyte per sample).
17. Samples from initial investigations of clandestine laboratories are likely to include highly contaminated samples. If sample results exceed the upper range of the calibration curve, the sample in the GC vial may be diluted and reanalyzed or a smaller aliquot of the initial acid desorbate diluted, re-extracted, derivatized, and analyzed. Refer to APPENDIX H for instructions and limitations on making dilutions.

CALCULATIONS:

18. Determine the mass (in µg/sample) of respective analyte found in the wipe samples, and in the media blank from the calibration graph.
19. Calculate final concentration, C, of analyte in µg/sample:

$$C = c\frac{V_1}{V_2}\frac{V_3}{V_4} - b\frac{V_5}{V_2}$$

Where: c = concentration in sample (in µg/sample determined from the calibration curve).

$\frac{V_1}{V_2}$ = volume correction factor (needed only when the volume of internal standard spiking solution used for spiking the samples – such as for composite samples requiring larger desorption solution volumes – is different from that used for spiking the calibration standards). (See Table 6, footnote 4.)

V_1 = volume in µL of internal standard spiking solution used to spike samples.
V_2 = volume in µL of internal standard spiking solution used to spike the standards.

$\frac{V_3}{V_4}$ = dilution factor, if applicable

V_3 = 10 mL (volume of desorbate taken for cleanup in step 8).
V_4 = volume in mL of desorbate actually taken for cleanup and diluted to 10 mL with blank desorbing solution containing internal standard.
b = concentration in media blank (in µg/sample determined from the calibration curve).
$\frac{V_5}{V_2}$ = volume correction factor for the media blank (needed only if the volume of internal standard spiking solution used for spiking the media blank is different from that used for spiking the calibration standards.)
V_5 = volume in µL of internal standard spiking solution used to spike media blank.

20. Report concentration, C′, in µg per total area wiped (in cm^2) as follows:

$$C' = \frac{C}{A}$$

Where: C = µg/sample (step 19).
A = Total area wiped in cm^2 per sample.

NOTE: For example, if the sample was a composite sample and the area was 400 cm^2, report results as µg/400 cm^2 and not averaged to µg/100 cm^2. In general, if the area wiped was greater than or less than 100 cm^2, do not convert value to µg/100 cm^2. To avoid confusion, report separately both µg/sample (C) and the total area wiped in cm^2 per sample (A) for both discrete and composite samples.

EVALUATION OF METHOD:

This method was evaluated for those analytes listed in Tables 7a and 7b over a range of approximately 0.1 µg/sample to 30 µg/sample. These concentration levels represent approximately the 1 through 300 times the limit of quantitation (LOQ) level for most of the analytes [9]. Results are reported in the Backup Data Report for NIOSH 9106 [4].

The limits of detection (LOD and LOQ) were determined by preparing a series of liquid standards in desorption solution, processing them through the liquid-liquid extraction procedure of NIOSH 9106, and analyzing in both the scan and SIM modes. The LODs were estimated using the procedure of Burkart [12]. An LOD of 0.05 µg/sample for methamphetamine on wipes was achieved in either scan or SIM mode. The LOD was set at 0.05 µg/sample because that was the level of the lowest calibration standard for the LOD study. Lower LODs (e.g. 0.02 µg/sample) have been achieved in practice by including calibration standards at lower concentration levels. The cleanliness and performance of the mass spectrometer must be maintained such that at 0.1 µg/sample, a signal of at least 5 to 10 times the baseline noise is achievable. This is more easily accomplished in the SIM mode with the mass spectrometer.

Six different wipe media were evaluated. These were 3″×3″ 12-ply cotton gauze, 4″×4″ AlphaWipes® (TX® 1004), 4″×4″ 4-ply NU GAUZE®, 4″×4″ 4-ply MIRASORB®, 4″×4″ 6-ply SOF-WICK®, and 4″×4″ 4-ply TOPPER® sponges. Results are given in the Backup Data Report [1]. No synthetic media performed

better than cotton gauze. Some media (TOPPER® and SOF-WICK®) did not perform well, possibly due to co-extracted nonionic (polyethoxyethylene type) surfactants that are not removed using hexane and incompletely removed using methylene chloride in the cleanup step.

Precision and accuracy were determined by analyzing 6 replicates at each of 6 concentration levels (nominally 0.1, 0.3, 1, 3, 10, and 30 µg/sample). Results are presented in Tables 7a and 7b for cotton gauze. The best precision and accuracies were dependent upon the use of carefully chosen internal standards, especially where there is steric hindrance of the amine (e.g. having *N*-ethyl and *N*-propyl groups).

Long term sample storage stability was determined for periods up to 30 days under refrigeration (4 °C ± 2 °C) and for up to 7 days at room temperature (22-24 °C). Results are given in Table 4. The precision and accuracy and long term storage stability evaluations were conducted using isopropanol as the wetting solvent. A second precision and accuracy study using methanol confirmed that methanol is an acceptable substitute for isopropanol.

Recovery of amphetamines from six different types of surfaces using cotton gauze was evaluated (see Tables 10a and 10b). The practice of serial wiping (wiping the same surface area a second time with a second gauze wipe and combining both wipes as a single sample) was evaluated. Four solvents for wetting the gauze were tested (distilled water, 5% distilled white vinegar, isopropanol, and methanol). Six replicate samples were made on a latex painted wall. Recoveries and precisions are given in Table 10a. The recoveries with 5% distilled white vinegar were better than for distilled water, but not as good as for isopropanol. Methanol is superior to isopropanol. Recoveries with isopropanol are greatly improved with a repeat (serial) wipe (11% improvement compared to only about 6% improvement with methanol). The study and results are reported in the Backup Data Report for NIOSH 9109 [13]. Additional research on surface sample recovery and solvent effectiveness has been reported by Serrano et al. [15] and VanDyke et al. [16].

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Table 1. Formula and registry numbers of analytes.

Compound (alphabetically)	MW[1] (Daltons) Free base	HCl salt	Hemisulfate salt	Structural Formula As free base	CAS #[2]	RTECS[6]
(DL)-Amphetamine	135.21	171.67	184.25	$C_6H_5{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH_2$	300-62-9[3] 60-13-9[5]	SH9450000 SI1750000
(D)-Amphetamine[7]	135.21	171.67	184.25	$C_6H_5{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH_2$	51-64-9[3] 51-63-8[5]	SI1400000
(L)-Amphetamine	135.21	171.67	184.25	$C_6H_5{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH_2$	156-34-3[3]	SH9050000
Caffeine	194.19			$(CH_3)_3{\cdot}[C_5HN_4O_2]$	58-08-2[3]	EV6475000
(DL)-Ephedrine	165.24	201.70	214.28	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	90-81-3[3] 134-71-4[4]	
(L)-Ephedrine[8]	165.24	201.70	214.28	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3)NH{\cdot}CH_3$	299-42-3[3] 50-98-6[4] 134-72-5[5]	KB0700000 KB1750000 KB2625000
(D)-Ephedrine	165.24	201.70	214.28	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3)NH{\cdot}CH_3$	321-98-2[3] 24221-86-1[4]	KB0600000 KB1925000
(±)-MDEA	207.27	243.73		$CH_2O_2C_6H_3{\cdot}CH_2{\cdot}CH(CH_3)NH{\cdot}C_2H_5$	82801-81-8[3] 116261-63-2[4]	
(±)-MDMA	193.24	229.71		$CH_2O_2C_6H_3{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	42542-10-9[3] 92279-84-0[4]	SH5700000
(+)-MDMA[7]	193.24	229.71		$CH_2O_2C_6H_3{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	64057-70-1[4]	SH5700000
(DL)-Methamphetamine	149.24	185.70	198.28	$C_6H_5{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	4846-07-5[3]	
(D)-Methamphetamine[7]	149.24	185.70	198.28	$C_6H_5{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	537-46-2[3] 51-57-0[4]	SH4910000 SH5455000
(L)-Methamphetamine	149.24	185.70	198.28	$C_6H_5{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	33817-09-3[3]	SH4905000
Phencyclidine	243.39	279.85		$C_6H_5{\cdot}C[C_5H_{10}]{\cdot}N[C_5H_{10}]$	77-10-1[3] 956-90-1[4]	TN2272600 TN2272600
Phentermine	149.24	185.70		$C_6H_5{\cdot}CH_2{\cdot}C(CH_3)_2{\cdot}NH_2$	122-09-8[3] 1197-21-3[4]	SH4950000
(DL)-Norephedrine	151.21	187.67	200.25	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NH_2$	14838-15-4[3] 154-41-6[4]	RC2625000 DN4200000
1R,2S (-)-Norephedrine	151.21	187.67	200.25	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NH_2$	492-41-1[3]	RC2275000
1S,2R (+)-Norephedrine	151.21	187.67	200.25	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NH_2$	37577-28-9[3]	
1S,2S (+)-Norephedrine	151.21	187.67	200.25	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NH_2$	36393-56-3 2153-98-2[4] 492-39-7[4]	RC9275000
(D)-Pseudoephedrine[8,9]	165.24	201.70	214.28	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NHCH_3$	90-82-4[3] 345-78-8[4]	UL5800000 UL5950000
(L)-Pseudoephedrine[10]	165.24	201.70	214.28	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	321-97-1[3]	

(1) Molecular weights are calculated from the empirical formula using the 1987 IUPAC Atomic Weights of the Elements, Merck Index [9]. The molecular weight of the hemisulfate is ½ the weight of the 2:1 sulfate salt (2 moles amine + 1 mole H_2SO_4).
(2) CAS from various sources: Merck Index [14], NIOSH RTECS [17], MSDS sheets from Sigma/Aldrich [18], Cerilliant [19], and other sources [21].
(3) Free base form.
(4) Hydrochloride salt.
(5) 2:1 Sulfate salt (2 moles amine + 1 mole H_2SO_4.
(6) RTECS = NIOSH Registry of Toxic Effects of Chemical Substances [17].
(7) More active isomer.
(8) Naturally occurring isomer.
(9) The D form of pseudoephedrine is a decongestant.
(10) The L form of pseudoephedrine is a bronchodilator. Dehydroxylation forms the less active L-methamphetamine.

Table 2. Physical properties of analytes[1]

Compound (alphabetically)	CAS	m.p.(°C)	Vapor Pressure (mm Hg)	pK_a[4]	Log P[5]	Solubility in Water, g/100 mL
(DL)-Amphetamine	300-62-9	—	—	10.1 @ 20 °C	1.76	2.8 @ 25 °C
(D)-Amphetamine	51-64-9	<25	—	9.9	1.76	—
(D)-Amphetamine sulfate	51-63-8	>300	—	—	6.81	—
(L)-Amphetamine	156-34-3	—	0.201 @ 25 °C	10.1 @ 20 °C	1.76	2.8 @ 25 °C
Caffeine	58-08-2	238	15 @ 89 °C	10.4 @ 40 °C	-0.07	2.16 @ 25 °C
(DL)-Ephedrine	90-81-3	76.5	—	—	0.68	—
(L)-Ephedrine	299-42-3	34	0.00083 @ 25 °C	10.3 @ 0 °C	1.13	6.36 @ 30 °C
(L)-Ephedrine HCl	50-98-6	218	2.04E-10 @ 25 °C	pH 5.9 @ 1/200 dil.[3]	-2.45	25[6]
MDEA	82801-81-8	—	—	—	—	—
MDMA HCl	42542-10-9	148-149[2]	—	—	—	—
(D)-Methamphetamine	537-46-2	—	0.163 @ 25 °C	9.87 @ 25 °C	2.07	1.33 @ 25 °C
(D)-Methamphetamine HCl	51-57-0	170-175[2]	—	—	—	—
Phencyclidine	77-10-1	46.5	—	8.29	4.69	—
Phencyclidine HCl	956-90-1	233-235[2]	—	—	—	—
Phentermine	122-09-8	—	0.0961 @ 25 °C	—	1.90	1.86 @ 25 °C
Phentermine HCl	1197-21-3	198[2]	—	—	—	—
(±) Phenylpropanolamine	14838-15-4	—	0.000867 @ 25 °C	9.44 @ 20 °C	0.67	14.9 @ 25 °C
(±) Phenylpropanolamine HCl	154-41-6	194	—	—	-2.75	—
(L)-Norephedrine	492-41-1	51-53[3]	—	—	—	—
1S,2S (+)-Norephedrine	36393-56-3	77.5-78	0.000867 @ 25 °C	9.44 @ 20	0.83	14.9 @ 25
1S,2S (+)-Norephedrine HCl	492-39-7	—	—	pH 5.9-6.1 in aq. soln. [3]	0.22	2 @ 25
(D)-Pseudoephedrine	90-82-4	119	0.00083 @ 25 °C	10.3 @ 0 °C	0.89	10.6 @ 25 °C
(D)-Pseudoephedrine HCl	345-78-8	181-182[2]	—	pH 5.9 @ 1/200 dil.[3]	—	—

(1) Handbook of Physical Properties of Organic Chemicals unless otherwise noted [21].
(2) Merck Index [14].
(3) Sigma-Aldrich MSDS [18].
(4) Negative log of the acid dissociation constant for the amine in aqueous solution.
(5) Log P = octanol-water partition coefficient.
(6) Temperature not given in source.

Table 3. Synonyms of analytes

Generic names[1]	Trade and street names[2]	Additional names[3]
(DL)-Amphetamine; (±)-Amphetamine	Benzedrine; Phenedrine; Bennies	(±)-α-Methylbenzeneethanamine[4]; dl-α-Methylphenethylamine[4]; dl-1-Phenyl-2-aminopropane; (±)-Desoxynorephedrine
(D)-Amphetamine; (+)-Amphetamine	Dextroamphetamine; Dexedrine; dexies	(S)-α-Methylbenzeneethanamine[4]; d-α-Methylphenethylamine[4]; d-1-phenyl-2-aminopropane; d-β-Phenylisopropylamine
(L)-Amphetamine; (-)-Amphetamine	Levoamphetamine; component of Adderall	(R)-α-Methylbenzeneethanamine[4]; l-α-Methylphenethylamine[4]; l-1-phenyl-2-aminopropane; (-)-1-phenyl-2-aminopropane
Caffeine	Component (with ephedrine) of cloud 9 and herbal XTC	3,7-Dihydro-1,3,7-trimethyl-1H-purine-2,6-dione[4]; 1,3,7-Trimethylxanthine
(DL)-Ephedrine; (±)-Ephedrine	Ephedral; Racephedrine; Sanedrine	(R*,S*)-(±)-alpha-[2-(Methylamino)ethyl]benzenemethanol; DL-alpha-[1-(Methylamino)ethyl]benzyl alcohol; dl-Ephedrine
(L)-Ephedrine; (-)-Ephedrine; (1R,2S)-(-)-Ephedrine; l-Ephedrine	Primatene; Xenadrine; Ma Huang (Ephedra sinica and other species(5)); (with caffeine) cloud 9 and herbal ecstasy	(R-(R*,S*))-α-(1-Methylaminoethyl)benzenemethanol; L-erythro-2-(Methylamino)-1-phenylpropan-1-ol; (1R,2S)-(-)-2-Methylamino-1-phenyl-1-propanol; (-)-alpha-(1-Methylamino-ethyl)-benzyl alcohol; (-)-1-hydroxy-2-methylamino-1-phenylpropane; L-(-)-Ephedrine
(D)-Ephedrine		(1S,2R)-(+)-2-Methylamino-1-phenyl-1-propanol; (+)-Ephedrine
MDEA	MDE; Eve	(±)-3,4-Methylenedioxy-N-ethylamphetamine; N-ethyl-alpha-methyl-1,3-benzodioxole-5-ethanamine
MDMA	Adam, ecstasy, X, XTC	N,α-Dimethyl-3,4-1,3-benzodioxole-5-ethanamine; 3,4-Methylenedioxymethamphetamine
(DL)-Methamphetamine; (±)-Methamphetamine		N,α-Dimethylbenzeneethanamine[4]; N,α-Dimethylphenethylamine; dl-Desoxyephedrine; N-methyl-β-phenylisopropylamine
(D)-Methamphetamine; (+)-Methamphetamine; d-Methamphetamine	Methedrine; Desoxyn; chalk; crank; crystal; glass; ice; meth, speed; upper	(S)-N,α-Dimethylbenzeneethanamine; (S)-(+)-N,α-Dimethyl-phenethylamine[4]; d-1-Phenyl-2-methylaminopropane; d-Desoxyephedrine; d-N-methyl-β-phenyl-isopropylamine
(L)-Methamphetamine; (-)-Methamphetamine	Component in decongestant vapor inhaler (Vick's brand)	(R)-(-)-N,α-Dimethylphenethylamine; (-)-Deoxyephedrine; (-)-2-(Methylamino)-1-phenylpropane
Phencyclidine	Sernylan; Sernyl; angel dust; PCP; peace pill	1-(1-Phenylcyclohexyl) piperidine[4]
Phentermine	Fastin; Normephentermine	α,α-Dimethylbenzeneethanamine[4]; α,α-Dimethylphenethylamine[4]; 1,1-Dimethyl-2-phenylethylamine; α-Benzylisopropylamine
(DL)-Norephedrine; (±)-Norephedrine	(±)-Phenylpropanolamine; Obestat; Phenedrine;	(R*,S*)-(±)-α-(1-Aminoethyl)benzenemethanol[4]; -(±)-α-(1-Amino-ethyl)benzyl alcohol[4]; (±)-2-Amino-1-phenyl-1-propanol
(L)-Norephedrine; (-)-Norephedrine	Natural form found in Ephedra sinica and other species[5]	(1R,2S)- 2-Amino-1-phenyl-1-propanol; (1R,2S)-Norephedrine; l-erythro-2-Amino-1-phenylpropan-1-ol
(D)-Norephedrine; (+)-Norephedrine	Metabolite of cathinone in urine of Khat users.	(1S,2R)- 2-Amino-1-phenyl-1-propanol; (1S,2R)-Norephedrine; d-erythro-2-Amino-1-phenylpropan-1-ol
(+)-Norpseudoephedrine; Cathine	Amorphan; Adiposettin; Reduform; found naturally in Khat plant	(R*,R*)-α-(1-Aminoethyl)benzenemethanol[4]; d-threo-α-2-Amino-1-hydroxy-1-phenylpropane; 1S,2S-(+)-Norpseudoephedrine
L-(+)-Pseudoephedrine; (+)-Pseudoephedrine; d-Pseudoephedrine	Afrinol; Novafed; Sinufed; Sudafed; natural form found in Ephedra sinica and other species[5]	(S-(R*,R*))- α-[1-(Methylamino)ethyl]benzenemethanol; (1S,2S)-(+)-2-Methylamino-1-phenylpropanol; d-(alpha-(1-Methylamino)-ethyl)benzyl alcohol; (1S,2S)-(+)-Pseudoephedrine; d-threo-2-Methylamino-1-phenylpropan-1-ol; (+)-ψ-Ephedrine
D-(-)-Pseudoephedrine; (-)-Pseudoephedrine		(1R,2R)-(-)-Pseudoephedrine; (-)-ψ-Ephedrine; l-threo-2-Methylamino-1-phenylpropan-1-ol; (+)-ψ-Ephedrine

(1) Common or generic names. Salts forms are not given for simplicity.

(2) Trade and street names are exemplary, not exhaustive. Street names change over time and by locality. Salts and free base forms are not distinguished.

(3) Other names from Merck Index [14], NIOSH Registry of Toxic Effects of Chemical Substances [17], and MSDS sheets [19] and other reference materials [20]. NOTE: For amphetamine and methamphetamine the prefixes R-, D-, d-, and (+)- , although they mean different things, are essentially synonymous for the dextrorotatory stereoisomer and S-, L-, l-, and (-) are essentially synonymous for the levorotary stereoisomer. Many other synonyms exist.

(4) Uninverted CAS name as given in Merck Index [14].

(5) Extracts of Ephedra species contain various amounts of (+)-Norephedrine, (-)-N-methylephedrine, and (+)-N-methylpseudoephedrine. (+)-Norephedrine is reduced to amphetamine and N-methylephedrine and N-methylpseudoephedrine reduce to N,N-dimethylamphetamine [23, 24]. The presence of these latter two compounds in methamphetamine samples indicate that Ephedra spp. extracts may have been used in the synthesis [25].

Table 4. Limit of detection (LOD), method detection limit (MDL), and sample storage stability on cotton gauze. [1]

Compound	Int. std.[2]	Estimated LOD[3]		Estimated MDL[4]		Storage Stability[5]	
		Scan Mode (µg/sample)	SIM Mode (µg/sample)	Scan Mode (µg/sample)	SIM Mode (µg/sample)	30 days 4 °C	7 days 22 °C
(D)-Amphetamine	D11-Amp	0.07	0.05	0.04	0.02	100.5	94.5
	D14-Met	0.06	0.06	0.03	0.03	99.7	87.9
Caffeine	D11-Amp	1	0.2	0.4 [6]	0.02	99.3	98.8
	D14-Met	1	0.2	0.4 [6]	0.03	98.5	91.9
(L)-Ephedrine	D11-Amp	0.09	0.1	0.02	0.01	95.6	97.2
	D14-Met	0.08	0.09	0.01	0.06	94.8	90.5
MDEA	N-PAmp	0.05	0.07	0.1	0.02	98.9	102.1
MDMA	D11-Amp	0.05	0.06	0.04	0.02	99.7	111.1
	D14-Met	0.05	0.07	0.03	0.02	98.9	103.2
(D)-Methamphetamine	D11-Amp	0.07	0.05	0.03	0.02	98.7	100.6
	D14-Met	0.05	0.05	0.03	0.02	98.0	93.5
Phencyclidine	D11-Amp	0.3	0.06	0.03	0.02	103.7	105.2
	D14-Met	0.3	0.07	0.03	0.02	102.9	97.7
Phentermine	D11-Amp	0.06	0.05	0.02	0.02	102.0	101.5
	D14-Met	0.05	0.05	0.02	0.02	101.1	94.3
		0.06	0.05	0.01			
(±)-Norephedrine[7]	D11-Amp	0.2	[8]	0.1 [9]	[8]	94.3	92.7
	D14-Met	0.2		0.2 [10]	[8]	93.6	86.2
Pseudoephedrine	D11-Amp	0.08	0.07	0.03	0.02	100.4	97.9
	D14-Met	0.07	0.09	0.05	0.03	99.6	91.1
	NMPhen	0.06	0.09	0.05	0.02	-	-

(1) Backup Data Report [4].

(2) Internal standards: D11-Amp = Amphetamine-D_{11}, D14-Met = Methamphetamine-D_{14}, NMPhen = N-Methyl phenethylamine, N-PAmp = N-Propyl amphetamine.

(3) LODs vary according to individual GC columns, instrument conditions and cleanliness, media interferences, and internal standards used. The lowest calibration standard for these determinations was 0.05 µg/sample. Lower LODs are achievable with lower concentration calibration standards and operation of the mass spectrometer in the SIM mode. LODs were calculated on liquid standards using the procedure of Burkart [12].

(4) MDLs are provided as an alternate expression of sensitivity. These MDLs are calculated as the standard deviation of six replicates on spiked media analyzed at the 0.1 µg/sample level (except as noted) times the Student's t value for 6 replicates (3.365). (Normally 7 replicates are used.)

(5) Cotton gauze samples were spiked at 3 µg/sample per analyte. Six samples were analyzed immediately after preparation. Six samples were stored at room temperature (about 22 °C) for 7 days and then analyzed. Eighteen samples were stored at +4 °C (±2 °C). Of the 18 samples stored at +4 °C, six each were analyzed at 7 and 21 days and three each were analyzed at 14 and 30 days. (Backup Data Report [4].) Apparent recoveries vary according to internal standard used.

(6) The 0.3 µg/sample level was undetectable in the scan mode. MDLs were calculated from the 1 µg/sample level.

(7) (±)-Norephedrine = (±)-phenylpropanolamine.

(8) (±)-Norephedrine was not evaluated in the SIM mode due to breakdown of derivative with room temperature storage for one week.

(9) MDL calculated from the 0.3 µg/sample level. (Recoveries were >120% at the 0.1 µg/sample level.)

(10) MDL calculated from the 1 µg/sample level. (Recoveries were >120% at the 0.1 and 0.3 µg/sample levels.)

Table 5. Example of mass spectrometer operation parameters for selected ion monitoring mode.(1)

Chlorodifluoroacetyl derivatives	Scan window(2)	Acquisition ions (*m/z*) per group(3)							
Acquisition Group 1	10.5 to 13.0	104	118	128	156	160	170	172	177
Acquisition Group 2	13.0 to 15.2	104	156	158	170	172	198	296	
Acquisition Group 3	15.2 to 18.0	109	135	162	170	184	194	200	242

GC Peak No.(4)	Target Analytes and Internal Standards:(5)	Retention Time(6) (min)	Primary Ion (*m/z*)(7) (Quantification Ion)	Secondary ion and approximate relative abundance(8) (relative to the Primary Ion)
	Acquisition Group 1			
2	Amphetamine-D_{11} (I$)(9)	11.07	160	128 85%
3	Amphetamine	11.15	156	118 85%
5	Phentermine	11.34	170	172 33%
8	n-Methyl phenethylamine (I$)(9)	12.20	156	104 95%
9	Methamphetamine-D_{14} (I$)(9)	12.51	177	128 32%
10	Methamphetamine	12.61	170	118 32%
	Acquisition Group 2:			
18	Phenylpropanolamine	13.27	156	246 25%
20	Dibromooctafluorobiphenyl(10)	13.63	296	456 115%
21	N-n-Propylamphetamine (I$)(9)	13.8	198	156 75%
25	Ephedrine	14.27	170	172 33%
28	Pseudoephedrine	14.74	170	172 33%
	Acquisition Group 3:			
32	Caffeine	15.66	194	109 50%
40	Phencyclidine	16.41	200	242 35%
41	MDMA	16.48	170	162 95%
43	MDEA	16.87	184	162 75%

(1) In this example, 10 analytes and 5 internal standards are grouped into 3 acquisition groups having no more than 8 primary and secondary ions per acquisition group. For 6 analytes and internal standards or less, one acquisition group may be sufficient.

(2) Scan window is in minutes. Actual times are dependant upon GC column and instrument conditions.

(3) Ions (*m/z*) in bold numbers are suggested primary (quantification) ions. For best signal to noise ratio, do not exceed 10 ions per acquisition group. Dwell times per ion (*m/z*) is 50 milliseconds.

(4) GC peak numbers are those in Figure 1 and Table 9.

(5) The list of analytes and internal standards shown is an example. Analyte(s) and internal standard(s) must be selected according to analytical objectives.

(6) Retention times are dependant upon GC column and instrument conditions.

(7) The better ions for quantification are usually the base peak or those with masses >100 *m/z* and relative abundances >50% of the base peak. These minimize interference from co-eluting hydrocarbons. The suggested primary ions are not necessarily the base peaks in the mass spectra of the analytes, especially if the base peaks are ions common to aromatics (e.g. *m/z* 91) and paraffinic or olefinic hydrocarbons (e.g. *m/z* 42, 57, and 58). Suggested ions for other analytes and internal standards are given in Tables 8 and 9.

(8) Secondary ions may be used for quantification if the primary ion encounters interference. Secondary ions improve qualitative identification for SIM analyses. The relative abundances given are approximate (±10 to 20%) and depend upon specific instrument tuning and conditions. They are relative to the primary ion and not necessarily to the base peak in the mass spectrum of each analyte. The relative abundance of secondary ions for each analyte needs to be determined from a mass spectrum acquired on the instrument to be used.

(9) (I$) = internal standard. Internal standards must be paired with the appropriate analytes. Tables 7a and 7b give precision and accuracy data for various pairings. Other potentially useful internal standards are given in Table 8. Highly deuterated analogs of the target analytes are preferred, where available.

(10) Dibromooctafluorobiphenyl is an optional secondary internal standard useful for monitoring autosampler performance and instrument tuning. A shift in the mass axes or the relative abundance of *m/z* 296 to that of *m/z* 456 throughout an analytical sequence will help signal degraded tuning.

Table 6. Suggested spiking schedule for calibration standards and quality control samples

	Add the following to clean shipping containers (e.g. 50-mL polypropylene centrifuge tubes) in the following order.						
Calibration Standards[10]	Number of Wipes[1,2]	Volume[2] of Isopropanol or Methanol[3]	Volume[2] of Internal Standard Spiking Solution[4,5]	Volume of Target Analyte Spiking Solution[5,6]	Volume of Spiking Solution diluted 1/20[5,7]	Volume[2] of Desorption Solution[8]	Resulting µg/sample as Free Base[9]
CS0	0	3 mL	60 µL		0.0 µL	30 mL	0.00
CS1	0	3 mL	60 µL		2 µL	30 mL	0.02
CS2	0	3 mL	60 µL		5 µL	30 mL	0.05
CS3	0	3 mL	60 µL		10 µL	30 mL	0.1
CS4	0	3 mL	60 µL		20 µL	30 mL	0.2
CS5	0	3 mL	60 µL		60 µL	30 mL	0.6
CS6	0	3 mL	60 µL	10 µL		30 mL	2.0
CS7	0	3 mL	60 µL	30 µL		30 mL	6.0
CS8	0	3 mL	60 µL	100 µL		30 mL	20
CS9	0	3 mL	60 µL	300 µL		30 mL	60
CS10	0	3 mL	60 µL	1000 µL		30 mL	200
Quality Control Samples[11]							
QB (media blank)	1	3 mL	60 µL	0.0 µL		30 mL	0.0
QC (matrix spike)	1	3 mL	60 µL	3-300 µL	or 20-60 µL	30 mL	0.2-60
QD (matrix spike duplicate)	1	3 mL	60 µL	3-300 µL	or 20-60 µL	30 mL	0.2-60

(1) Gauze wipes may be added to the calibration standards but are not necessary if cotton gauze is used. Blank gauze wipes must always be added to the quality control samples, QB, QC, and QD.

(2) a.) If a sample consists of 2 gauze wipes, the volume of desorption solution must be increased to 40 mL to accommodate the second wipe. The shipping container should be a 50-mL polypropylene centrifuge tube or equivalent to accommodate the extra volume of desorption solution for 2 wipes. It is not critical to know the exact volume of desorption solution and wetting alcohol used per sample. It only needs to be enough to cover the samples and to permit free percolation through the samples. See step 7.
b.) If a set of samples consists predominantly of 2 gauze wipes, the QB, QC, and QD should also consist of 2 wipes and treated as per the samples. The volume of isopropanol (or methanol) added to the QC samples should be increased to 4 mL for two gauze wipes to simulate samples containing two gauze wipes.

(3) If methanol was used for wipe sampling, it should also be used in the calibration standards, blanks, and QCs instead of isopropanol.

(4) Concentration of internal standards in the internal standard spiking solution is approximately 200 µg/mL as the free base. It is critical to know the exact volume of internal standard spiking solution that is added to the calibration standards, samples, blanks, and quality control samples. The volume spiked into the samples may vary with sample size but the volume spiked into each of the calibration standards must not vary. See step 7b.

(5) For quality control samples, spike onto wipe media within the shipping container. For liquid calibration standards (in lieu of media calibration standards), spike into the isopropanol (or methanol).

(6) Concentration of analytes in the target analyte spiking solution is approximately 200 µg/mL as the free base.

(7) Concentration of analytes in the diluted spiking solution for this table is approximately 10.0 µg/mL as the free base and can be prepared by diluting 100 µL of the target analyte spiking solution to 2 mL in methanol.

(8) Desorption solution is 0.1 M sulfuric acid in deionized water.

(9) This is µg per total sample irrespective of the total desorption solution volume or the area wiped.

(10) Select 6 calibration standards from the list to cover the analytical range plus the blank.

(11) Prepare one set of quality control samples for every 20 samples or less.

Table 7a. Precision and accuracy in scan mode.[1]

Compound	Internal Standard[2]	Range[3] µg/sample	Accuracy	Overall Precision $\hat{S}_{rT}$	Bias	
					Average	Range
(D)-Amphetamine	D11-Amp	0.1-30	17.1	0.0670	-0.0613	-0.1048 - -0.0170
	D14-Met	0.1-30	13.7	0.0610	+0.0338	-0.0151 - +0.1056
	NMPhen	0.1-30	12.5	0.0559	-0.0310	-0.0651 - +0.0177
Caffeine	D11-Amp	1.0-30	20.0	0.0708	-0.0832	- 0.1476 - -0.0542
	D14-Met	1.0-30	12.5	0.0636	-0.0014	- 0.0274 - +0.0381
	NMPhen	1.0-30	15.6	0.0796	-0.0040	-0.0789 - +0.1321
(L)-Ephedrine	D11-Amp	0.1-10	15.4	0.0627	+0.0510	-0.0148 - +0.1128
	D14-Met	0.3-10	17.8	0.0674	+0.0666	+0.0261 - +0.1660
	NMPhen	0.3-30	15.0	0.0707	+0.0293	-0.0259 - +0.0973
MDEA	N-PAmp	0.3-29	16.6	0.0817	-0.0224	-0.0656 - +0.0657
MDMA	D11-Amp	0.3-27	20.2	0.0778	-0.0739	-0.1011 - -0.0489
	D14-Met	0.3-27	16.6	0.0652	+0.0589	-0.0947 - +0.0036
	NMPhen	0.3-27	22.0	0.0722	-0.1017	-0.1486 - -0.0315
(D)-Methamphetamine	D11-Amp	0.1-30	14.7	0.0631	-0.0435	-0.0657 - -0.0060
	D14-Met	0.1-30	12.5	0.0546	-0.0348	-0.1144 - +0.0188
	NMPhen	0.1-10[5]	14.9	0.0503	-0.0665	-0.1179 - +0.0110
Phencyclidine	D11-Amp	0.1-10	18.2	0.0690	-0.0683	-0.1257 - -0.0136
	D14-Met	0.3-3	13.4	0.0465	-0.0577	-0.0662 - -0.0493
	NMPhen	0.3-10	16.8	0.0609	-0.0682	-0.1137 - +0.0091
Phentermine	D11-Amp	0.1-30	15.2	0.0486	-0.0720	-0.1010 - +0.0291
	D14-Met	0.1-30	10.7	0.0509	+0.0190	-0.0395 - +0.0671
	NMPhen	0.1-30	9.6	0.0420	-0.0269	-0.0612 - +0.0340
(±)-Norephedrine[4]	D11-Amp	1-30	6.5	0.0328	+0.0061	-0.0070 - +0.0248
Pseudoephedrine	D11-Amp	0.3-30	17.2	0.0571	-0.0783	-0.1273 - -0.0560
	D14-Met	0.3-30	14.9	0.0649	-0.0422	-0.0888 - +0.0395
	NMPhen	0.3-30	18.7	0.0488	-0.1068	-0.1505 - -0.0422

(1) Backup Data Report [4]. Values are for chlorodifluoroacetyl derivatives and analysis by GC-MS in scan mode. Each sample consisted of a pair of 3" x 3" 12-ply cotton gauze pads. There were 6 replicate samples per concentration level and six concentration levels evaluated from approximately 0.1 to 30 µg/sample.

(2) Internal Standards Deuterated: Non-deuterated:
D11-Amp = Amphetamine-D_{11} NMPhen = N-Methyl phenethylamine
D14-Met = Methamphetamine-D_{14} N-PAmp = N-Propyl amphetamine

(3) Range used for calculation of precision, accuracy, and bias. The entire range studied for all analytes was approximately 0.1 to 30 µg/sample (1xLOQ to 300xLOQ).

(4) (±)-Norephedrine = (±)-phenylpropanolamine.

(5) One or more higher level concentrations were omitted from the computations due to inlier CVs (<0.0200.)

Table 7b. Precision and accuracy in SIM mode.[1]

Compound	Internal Standard[2]	Range[3] µg/ sample	Accuracy[4]	Overall[4] Precision $\hat{S}_{rT}$	Bias	
					Average	Range
(D)-Amphetamine	D11-Amp	0.1-30	14.3	0.0412	-0.0750	-0.1153 - -0.0351
	D14-Met	0.1-30	10.1	0.0508	-0.0074	-0.0500 - +0.0389
	NMPhen	0.1-30	13.3	0.0439	-0.0606	-0.1117 - -0.0318
Caffeine	D11-Amp	0.1-30	21.3	0.0578	-0.1182	-0.1949 - -0.0697
	D14-Met	0.1-30	14.4	0.0534	-0.0558	-0.1061 - -0.0170
	NMPhen	0.3-30	19.8	0.0387	-0.1338	-0.1775 - -0.0820
(L)-Ephedrine	D11-Amp	0.3-30	9.1	0.0421	-0.0199	-0.0423 - +0.0157
	D14-Met	0.3-30	20.5	0.0503	0.1226	+0.0637 - +0.1883
	NMPhen	0.3-30	10.2	0.0449	+0.0260	-0.0075 - +0.0769
MDEA	N-PAmp	0.3-29	10.3	0.0264	-0.0597	-0.0879 - -0.0095
MDMA	D11-Amp	0.1-27	16.2	0.0503	-0.0750	-0.1423 - -0.0292
	D14-Met	0.1-0.9[5]	15.4	0.0503[6]	-0.0712	-0.1247 - +0.0032
	NMPhen	0.1-27	15.4	0.0496	-0.0722	-0.1136- -0.0108
(D)-Methamphetamine	D11-Amp	0.1-10[5]	16.5	0.0379	-0.1030	-0.1414 - -0.0660
	D14-Met	0.1-30	9.2	0.0351	-0.0343	-0.0767 - +0.0006
	NMPhen	0.1-30	13.6	0.0322	-0.0827	-0.1221 - -0.0403
Phencyclidine	D11-Amp	0.1-10[5]	17.7	0.0428	-0.1068	-0.1303 - -0.0586
	D14-Met	0.1-3	11.3	0.0450	-0.0393	-0.0683 - -0.0205
	NMPhen	0.1-3[5]	16.1	0.0449	-0.0871	-0.1279 - -0.0383
Phentermine	D11-Amp	0.1-30	12.8	0.0394	-0.0637	-0.0982 - -0.0433
	D14-Met	0.1-30	9.8	0.0495	-0.0051	-0.0375 - +0.0556
	NMPhen	0.1-30	11.0	0.0394	-0.0451	-0.0766 - -0.0163
Pseudoephedrine	D11-Amp	0.3-30	17.3	0.0402	-0.1073	-0.1496 - -0.0514
	D14-Met	0.3-30	11.7	0.0519	-0.0294	-0.0559 - +0.0532
	NMPhen	0.3-30	17.0	0.0450	-0.0956	-0.1197 - -0.0576

(1) Backup Data Report [4]. Values are for chlorodifluoroacetyl derivatives and analysis by GC-MS in SIM mode (see Table 5 for MS conditions). Each sample consisted of a pair of 3″ × 3″ (7.5 cm x 7.5 cm) 12-ply cotton gauze pads. There were 6 replicate samples per concentration level and six concentration levels evaluated from approximately 0.1 to 30 µg/sample. Norephedrine (phenylpropanolamine) was not evaluated in the SIM mode due to breakdown at room temperature storage for several days prior to analysis.

(2) Internal Standards,
Deuterated:
D11-Amp = Amphetamine-D_{11}
D14-Met = Methamphetamine-D_{14}
Non-deuterated:
NMPhen = N-Methyl phenethylamine
N-PAmp = N-Propyl amphetamine

(3) Range used for calculation of precision, accuracy, and bias. The entire range studied for all analytes was approximately 0.1 to 30 µg/sample (1×LOQ to 300×LOQ).

(4) NIOSH [1995]. NIOSH Technical Report: Guidelines for Air Sampling and Analytical Method Development and Evaluation. By Kennedy ER, Fischbach TJ, Song R, Eller PM, Shulman SA. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 95-117.

(5) One or more higher level concentrations were omitted from the computations due to inlier CVs (<0.0200).

(6) The overall precision, $\hat{S}_{rT}$, is an estimate due to inlier precisions (<0.02) at several higher concentration levels.

Table 8a. Recommended internal standards and best application[1]

COMPOUND NAME	CAS	MW as free base	Quant. Ion	Secondary Ion	COMMENTS
(±)-Amphetamine-D_{11}	Not available	146.12	160	128	Preferred analog for amphetamine
(±)-Amphetamine-D_8	145225-00-9	143.15	126[3]	159[3]	Alternate for amphetamine-D_{11}
(±)-Amphetamine-D_6	Not available	141.16	160	123	Alternate for amphetamine-D_{11}
(±)-Methamphetamine-D_{14}	Not available	163.12	177	128	Preferred methamphetamine analog
(±)-Methamphetamine-D_{11}	152477-88-8	160.15	176	126	Alternate for methamphetamine-D_{14}
(±)-Methamphetamine-D_9	Not available	158.16	177	123	Alternate for methamphetamine-D_{14}
N-Methylphenethylamine	589-08-2	135.23	156	104	Alternate for methamphetamine-D_{14}
Phencyclidine-D_5	60124-86-9	248.35	205	247	Use only for phencyclidine.
MDEA-D_6[2]	160227-44-1	213.22	190	165	Use only for MDEA.
N-Propylamphetamine[2]	Not available	177.29	198	156	Alternate for MDEA-D_6

(1) Care must be exercised in the selection of internal standards for each analyte because of differences in derivatization efficiencies due to structural differences.
   a. Deuterated analogs of each target analyte may be acceptable as internal standards if they are isotopically pure enough and their ions do not interfere with the quantification ions (usually base peaks) of the target analyte, especially at the limit of detection for the target analyte. Conversely it is also important that ions in the target analyte, especially at high concentrations, do not interfere with the quantification ion (usually base peaks) of any deuterated analog used as the internal standard.
   b. The more highly deuterated an analog, the more it will chromatographically separate from the target analyte, reducing interference from common ions.
   c. Phentermine and mephentermine have been used as internal standards. Such use is not advised in this method because of their reported occasional use as adulterants in certain illicit drugs such as MDMA.

(2) N-Propylamphetamine and MDEA-D_6 are only applicable to MDEA and other hindered amines (e.g. fenfluramine and MBDB) due to similar steric hindrance at the nitrogen (N-ethyl or N-propyl substitution) which affects derivatization efficiency.

(3) It is better to use m/z 126 because at high concentration levels unlabelled amphetamine contributes significant interference to m/z 159 of amphetamine-D_8.

Table 8b. Recommended best application of internal standards

	Recommended Deuterated Internal Standards				Recommended Alternate Non-deuterated Internal Standards[3]		
TARGET ANALYTE	Amphet-amine-D_{11}[2]	Metham-phetamine-D_{14}[2]	MDEA-D_6[1]	Phency-clidine-D_5	N-Methyl-phenethyl-amine	4-Phenyl-1-butyl-amine	N-Propyl-amphet-amine[1]
Amphetamine	X	X			X		
Caffeine		X			X		
Ephedrine	X	X			X	X	
MDEA			X				X
MDMA		X			X		
Methamphetamine	X	X			X		
Phencyclidine		X		X	X		
Phentermine	X				X		
(±)-Norephedrine[4]	X					X	
Pseudoephedrine		X			X		

(1) N-Propylamphetamine and MDEA-D_6 are only applicable to MDEA and other hindered amines (e.g. fenfluramine and MBDB) due to similar steric hindrance at the nitrogen (N-ethyl or N-propyl substitution) which affects derivatization efficiency.

(2) The alternate deuterated compounds listed in part A above may be used. Avoid ring-labeled amphetamine-D_5 (CAS 65538-33-2) since the primary (quantification) ion is the same as for amphetamine and GC peaks overlap significantly. Also avoid methamphetamine-D_5 (CAS 60124-88-1) since GC peaks significantly overlap and secondary ions for the chlorodifluoroacetyl derivative are not baseline resolved.

(3) The listed non-deuterated compounds are effective as internal standards for the listed target analytes. Non-deuterated internal standards might not be permissible.

(4) (±)-Norephedrine is the same as (±)-phenylpropanolamine.

Table 9. Gas chromatographic retention times for chlorodifluoroacetyl derivatives of amphetamines, precursors, adulterants, and miscellaneous drugs of abuse.[1]

GC Peak No.[2]	Compound	Recommended Quantification (1′) and Confirmation(2′, 3′) Ions (*m/z*)[3] 1′	2′	3′	Form[4]	Retention Time in Minutes	Relative Retention Time[5]	Relative Retention Time[6]
1	Nicotine	84	133	162	parent	8.92	0.396	0.757
2	(DL)-Amphetamine-D_{11}(I$)[7]	160	128	162	derivative	10.26	0.800	0.870
3	(DL)-Amphetamine	156	118	158	derivative	10.34	0.807	0.877
4	Phenethylamine[8]	104	91	-	derivative	10.38	0.810	0.880
5	Phentermine[8]	170	172	132	derivative	10.52	0.821	0.892
6	N-Methyl pseudoephedrine[9]	134	162	75	derivative	10.54	0.822	0.894
7	N-Methyl pseudoephedrine[9]	72	-	-	parent	abt 11	0.86	0.93
8	N-Methyl phenethylamine (I$)[7]	156	104	158	derivative	11.37	0.887	0.964
9	(DL)-Methamphetamine-D_{14} (I$)[7]	177	98	179	derivative	11.70	0.913	0.992
10	(DL)-Methamphetamine	170	172	118	derivative	11.79	0.920	1.000
11	Fenfluramine[8]	184	186	159	derivative	11.83	0.923	1.003
12	S-(-)-Cathinone (from Khat plant)	105	77	132	derivative	11.99	0.935	1.017
13	Bupropion (Wellbutrin®, Zyban®)	44	100	111	parent	12.14	0.947	1.030
14	N-Ethyl amphetamine	184	186	118	derivative	12.22	0.953	1.036
15	Ecgonine, methyl ester	182	82	311	derivative	12.36	0.964	1.048
16	S-(-)-Methcathinone (“Cat”)	170	105	172	derivative	12.38	0.966	1.050
17	Norpseudoephedrine (Cathine)	156	158	246	bis-derivative	12.46	0.972	1.057
18	(±)-Norephedrine	156	158	246	bis-derivative	12.49	0.974	1.059
19	Aminorex	107	79	232	derivative (-CN)	12.70	0.991	1.077
20	Dibromooctafluorobiphenyl (I$)[7]	296	456	454	parent	12.82	1.000	1.087
21	N-Propyl amphetamine (I$)[7]	198	156	200	derivative	12.97	1.012	1.100
22	4-Methoxyamphetamine	121	148	78	derivative	13.22	1.031	1.121
23	4-Phenyl-1-butylamine (I$)[7]	176	104	-	derivative	13.27	1.035	1.126
24	1S,2R(+)-Ephedrine-D_3 (I$)[7]	173	175	85	derivative	13.44	1.048	1.140
25	(DL)-Ephedrine	170	172	260	bis-derivative	13.48	1.052	1.143
26	Acetaminophen[8]	108	221	263	derivative	13.67	1.066	1.159
27	Methyl phenidate (Ritalin®)	84	56	91	parent	13.81	1.077	1.171
28	Pseudoephedrine	170	172	260	bis-derivative	13.93	1.087	1.182
29	Meperidine (Demerol® etc.)	71	247	172	parent	13.99	1.091	1.187
30	Atropine	124	94	103	parent (-H_2O)	14.25	1.112	1.209
31	(±)-MDA	135	162	291	derivative	14.36	1.120	1.218
32	Caffeine[8]	194	109	67	parent	14.84	1.158	1.259
33	N,N-Dimethyltryptamine (DMT)	58	129	102	derivative	14.97	1.168	1.270
34	(±)-BDB	135	176	170	derivative	15.11	1.179	1.282
35	Ketamine (“special K”)[8,11]	180	182	209	parent	15.20	1.186	1.289
36	Lidocaine[8]	86	58	120	parent	15.28	1.192	1.296
37	Trifluoromethylphenyl piperazine[11]	200	145	172	derivative	15.46	1.206	1.318
38	Benzyl piperazine[11] (“Legal XTC”)	91	197	175	derivative	15.54	1.202	1.318
39	Phencyclidine-D_5 (I$)[7]	205	96	246	parent	15.59	1.216	1.322
40	Phencyclidine (PCP)	200	242	243	parent	15.62	1.218	1.325
41	MDMA[11]	170	162	135	derivative	15.66	1.221	1.328

Table 9 continued,

Table 9, continued. Gas chromatographic retention times for chlorodifluoroacetyl derivatives of amphetamines, precursors, adulterants, and miscellaneous drugs of abuse.[1]

GC Peak No.[2]	Compound	Recommended Quantification (1′) and Confirmation (2′, 3′) Ions (*m/z*)[3] 1′	2′	3′	Form[4]	Retention Time Minutes	Relative Retention Time[5]	Relative Retention Time[6]
42	MDEA-D_6 (I$)[7]	190	165	135	derivative	16.01	1.249	1.358
43	MDEA[11]	184	162	135	derivative	16.04	1.251	1.360
44	Phenylephrine[8]	156	158	374	tris-derivative	16.10	1.256	1.366
45	(±)-MBDB	184	176	135	derivative	16.29	1.271	1.382
46	Theophylline[8]	180	95	68	parent	16.34	1.275	1.386
47	Mescaline	181	194	179	derivative	16.43	1.282	1.394
48	Phenylephrine[8]	156	248	158	bis-derivative	16.65	1.299	1.412
49	Chlorpheniramine[8]	203	205	167	parent	16.73	1.305	1.419
50	Methyl phenidate	196	198	-	derivative	17.20	1.322	1.459
51	4-Bromo-2,5-DMPEA[10] (Nexus)	242	244	229	derivative	17.57	1.370	1.490
52	cis-(±)-4-Methylaminorex (“U4Euh”)	203	160	117	derivative	17.89	1.396	1.517
53	Dextromethorphan[8]	271	59	150	parent	18.09	1.411	1.534
54	Methaqualone	235	250	233	parent	18.27	1.425	1.550
55	Cocaine	82	182	303	parent	18.62	1.452	1.579
56	Atropine[8]	124	82	94	derivative	19.10	1.490	1.620
57	Diazepam (Valium® etc.)	256	283	284	parent	20.76	1.619	1.761
58	Hydrocodone (Lortab® etc.)	299	242	284	parent	20.91	1.631	1.774
59	Hydromorphone (Dilaudid®)	285	228	229	parent	21.04	1.641	1.785
60	Hydrocodone (Lortab® etc.)	411	354	298	derivative	21.13	1.648	1.792
61	Morphine	268	397	269	derivative	21.20	1.654	1.798
62	Codeine	282	411	283	derivative	21.28	1.660	1.805
63	Oxycodone (OxyContin®)	315	230	316	parent	21.57	1.682	1.830
64	Hydromorphone (Dilaudid®)	397	341	398	derivative	21.78	1.699	1.847
65	Flunitrazepam (Rohypnol®, roofies)[11]	312	285	286	parent	22.19	1.731	1.882
66	Morphine	380	382	509	bis-derivative	22.26	1.736	1.888
67	Fentanyl (Sublimaze® etc.)	245	146	189	parent	22.96	1.791	1.947

(1) Actual retention times may vary depending on individual GC column and GC conditions. Gas chromatographic conditions used are on p. 9106-1. The mass spectrometer was operated under the conditions given on p 9106-1 (or see the Backup Data Report [4].)

(2) GC peak numbers represent peaks as numbered in Figure 1.

(3) Use extracted ion chromatograms of the primary ions (1′) for quantifying peaks in either the scan mode or the SIM mode. Use the secondary and tertiary ions (2′ and 3′) for qualitative identification when necessary. These ions are selected for nearness to the primary ion to minimize false negatives from skewed spectra and from low mass interference from hydrocarbons.

(4) Not all forms are presented. Parent compounds are not presented that have irregular or overly broad GC peak shapes under the GC conditions used. Spectra for chlorodifluoroacetyl derivatives are given in the Backup Data Report [4]

(5) Retention time relative to 4,4′-dibromooctafluorobiphenyl.

(6) Retention time relative to the chlorodifluoroacetyl derivative of methamphetamine.

(7) I$ = Internal standard.

(8) Intentional or unintentional adulterants. For example, phentermine may be added to MDMA and caffeine added to methamphetamine. Chlorpheniramine is an unintentional adulterant when pseudoephedrine containing chlorpheniramine is used as a methamphetamine precursor.

(9) Presence of (+)-Norephedrine, N-methylpseudoephedrine and/or N-methylephedrine in pseudoephedrine or ephedrine indicates extracts of Ephedra species (spp.) as source. Presence of amphetamine and N,N-dimethylamphetamine in methamphetamine final product also indicates the same source.[22, 23, 24]

(10) 4-Bromo-2,5-dimethoxyphenethylamine

(11) Typical “club drugs” (piperazine analogs as ecstasy substitutes, ketamine and flunitrazepan as predatory drugs).

Table 10a. Recovery from latex-painted wall with various solvents; one gauze wipe compared with the sum of two gauze wipes[1,2]

	Water[3]			Isopropanol			Methanol		
	First Gauze Wipe		Plus Second Wipe[4]	First Gauze Wipe		Plus Second Wipe[4]	First Gauze Wipe		Plus Second Wipe[4]
Test Compound[5]	Percent	%RSD	Percent	Percent	%RSD	Percent	Percent	%RSD	Percent
Amphetamine	51	14	56	67	6.0	78	90	4.0	96
Cocaine	36	22	36	69	22	80	89	9.1	94
Ephedrine	48	23	52	76	7.4	85	91	4.4	96
MDMA	40	20	44	61	9.0	70	88	5.3	94
MDEA	45	22	50	69	12	80	90	11	97
Methamphetamine	46	16	50	64	7.4	75	87	3.5	94
Phencyclidine	27	26	30	64	9.6	73	86	5.2	91
Phentermine	53	9.2	58	78	6.6	91	95	2.9	101
Phenylpropanolamine	58	21	62	80	9.3	95	85	5.0	94
Pseudoephedrine	49	20	53	73	7.0	85	95	3.3	101

(1) Backup Data Report for NIOSH 9109 [13]. Area of each sample was 100 cm^2.
(2) Wall was an existing standard gypsum board wall painted with a latex based paint. Painted surface was at least one year old. There were six replicates for each solvent tested.
(3) Water was deionized water (ASTM type II). Note low recovery and high %RSD.
(4) For the serial wipe study, each 100-cm^2 area was wiped again with a fresh pre-wetted gauze wipe and the amount recovered was determined separately. In practice, a second (serial) wipe is included with the first gauze wipe; both gauze wipes constitute a single sample. The percent recoveries shown in the column represent the sum of the amounts recovered in both the first and second wipes.
(5) Each pre-measured area was spiked with 3 µg of each analyte in methanol and the methanol allowed to dry for several minutes prior to wipe sampling.

Table 10b. Recovery from various surfaces with various solvents; one gauze wipe compared with the sum of two gauze wipes[1]

		Isopropanol			Methanol		
		First Gauze Wipe		Plus Second Wipe[2]	First Gauze Wipe		Plus Second Wipe[2]
Surface Material[3]	Replicates	Percent	%RSD	Percent	Percent	%RSD	Percent
Enamel (lid of washing machine)	4[3]	58	5.7	68	81	2.4	87
Vinyl veneer on particle board	4[4]	60	5.2	68	81	4.8	89
Latex painted wall	6[3]	64	7.4	75	87	3.5	94
Refrigerator door	2[4]	65	2.9	76	91	4.0	92
Varnished hardwood panel	2[5]	72	5.4	76	82	3.7	86
Formica® countertop	4[4]	75	4.9	82	87	3.8	91

(1) Backup Data Report for NIOSH 9109 [13]. Area of each sample was 100 cm^2.
(2) For the serial wipe study, each 100-cm^2 area was wiped again with a fresh pre-wetted gauze wipe and the amount recovered was determined separately. In practice, a second (serial) wipe is included with the first gauze wipe; both gauze wipes constitute a single sample. The percent recoveries shown in the column represent the sum of the amounts recovered in both the first and second wipes.
(3) The Refrigerator door and the washing machine lid were from used appliances. The vinyl-veneered particle board (a book shelf), the Formica® countertop, and the varnished hardwood paneling were all purchased new. All surfaces of used and new materials were pre-cleaned with multiple rinses of methanol prior to spiking. Each pre-measured 100-cm^2 square was spiked with 3 µg methamphetamine.
(4) Samples were taken using the side-to-side and then top-to-bottom wiping technique.
(5) Half of the samples were wiped using the side-to-side wiping technique and half were wiped using the concentric squares wiping technique. There were no significant differences in recoveries. Percent recoveries and %RSDs are for both techniques combined.
(6) Samples were taken each time using only top-to-bottom wiping with the grain of the wood in an "N" pattern.

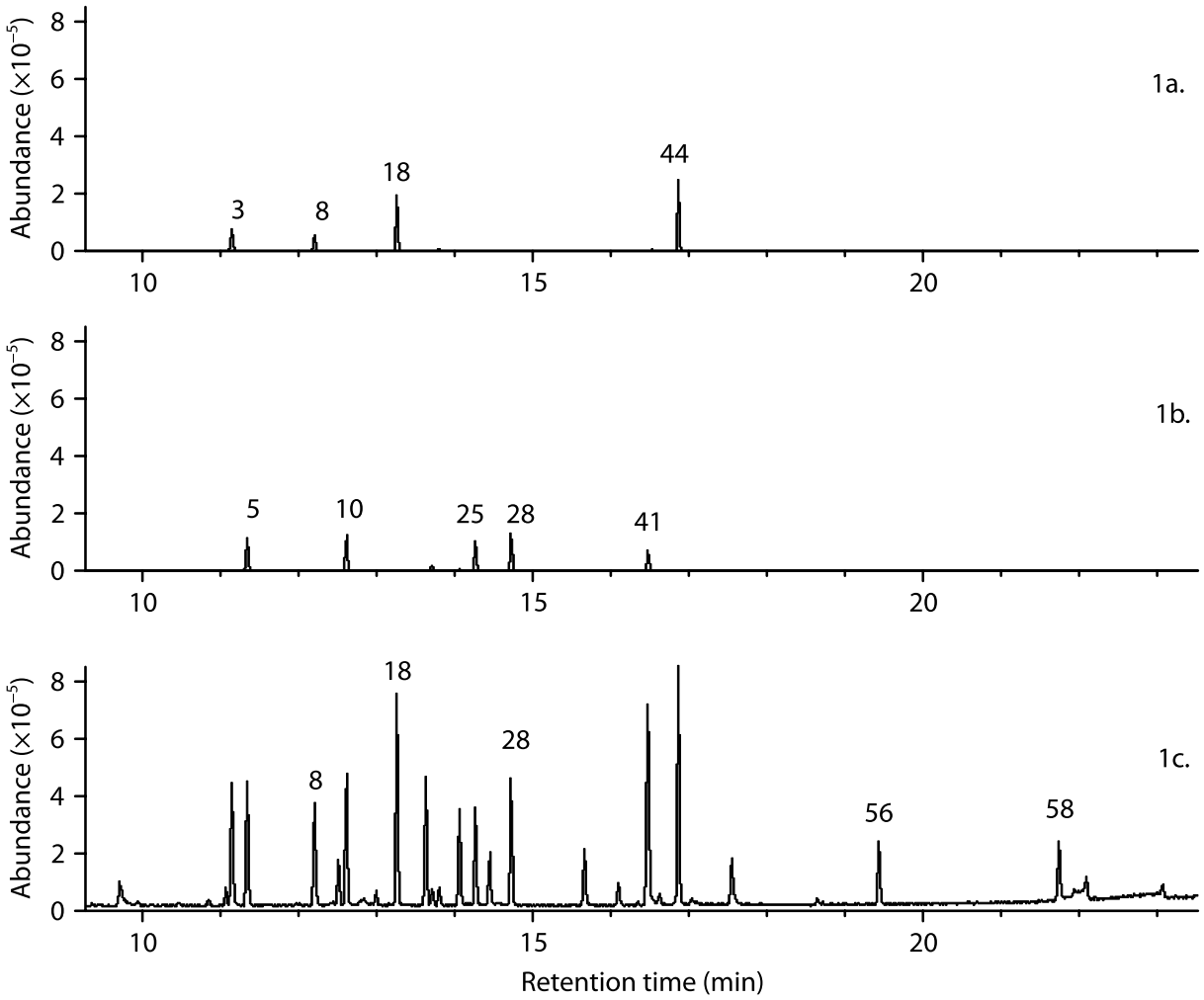

Figure 1. Typical chromatograms of chlorodifluoroacetyl derivatives by GC-MS in scan mode

Figure 1a. Extracted ion chromatogram for *m/z* 156 (155.70 to 156.70).
Figure 1b. Extracted ion chromatogram for *m/z* 170 (169.70 to 170.70).
Figure 1c. Total ion chromatogram (TIC).

GC Peak Identification: See Table 9 for identification of numbered GC peaks. (But note that retention times in Table 9 do not correspond to those in Figure 1 because a different 0.5 µm film phenyl arylene polymer capillary column was used.)
GC-MS Conditions: See p. 9106-1 for GC-MS conditions.

APPENDIX

A. REAGENTS and SOLUTIONS:

1. For derivatization, pentafluoropropionic anhydride (PFPA) may be substituted for chlorodifluoroacetic anhydride (CDFAA). Spectra, retention times, suggested quantification ions, and precision and accuracy data for PFPA derivatives are given in the Backup Data Report [4]. Spectra for CDFAA derivatives are also given in the Backup Data Report [4].
   NOTE: 100 µL of pentafluoropropionic anhydride (PFPA) may be substituted for chlorodifluoroacetic anhydride, but the samples must be heated to 90 °C for 20-30 minutes in step 11c.
2. The instrumental internal standard, 4,4'-dibromooctafluorobiphenyl is optional. It is useful for monitoring instrument tuning and autosampler performance.
3. Primary amines form Schiff bases and enamines with ketones and aldehydes. These may in turn form derivatives with the acylating reagents. The use of acetone must be avoided strictly prior to the analytes being derivatized. Glassware and equipment rinsed with acetone must be thoroughly dried. Toluene should be avoided for making up standard solutions because it usually contains benzaldehyde, an oxidation product of toluene. Condensation products have been observed between primary amines and benzaldehyde. The only solvents recommended for the preparation of stock solutions and dilutions thereof are methanol (preferably) and isopropanol.
4. The reconstitution solvent should not contain methanol or other alcohol since the derivatized alcohol groups in ephedrine type compounds are hydrolyzed over time. Toluene containing 10 percent acetone is recommended.

B. EQUIPMENT:

1. Wipe media: Besides cotton gauze, 4"×4" (10 cm x 10 cm) 4-ply MIRASORB® (Johnson and Johnson), and 4"×4" (10 cm x 10 cm) AlphaWipe® (TX® 1004, Texwipe Corp.) were acceptable wipe media and can be used in the absence of cotton gauze. MIRASORB®, a non-woven cotton/polyester blend, is discontinued but counterparts exist that claim to be of identical construction and fiber composition. AlphaWipe® is a hydrophilic, highly adsorbent, tightly knitted continuous filament polyester wipe. Precision and accuracy data for MIRASORB® and AlphaWipe® are given in the Backup Data Report [4].
2. Shipping containers: The 50-mL polypropylene centrifuge tubes with caps are preferred for one or two gauze wipes and are not as breakable as glass 40-mL VOA vials. The 40-mL VOA vials are acceptable for single gauze wipes. Larger containers (glass with a PTFE lined cap) should be used for combining more than two gauze wipes into a single sample. The size of the container for two or more wipes should be approximately 25 mL per gauze wipe (e.g. a minimum size of 100-mL for up to four gauze wipe samples). There needs to be enough extra headspace in the shipping container to allow the desorption solution to cover the gauze wipes and to percolate freely through the wipe sample(s) during mixing.
3. Each regulatory agency having legal jurisdiction over the contaminated site may require different but specific off-site preparation and on-site sampling procedures. It is important to consult local regulatory agencies or departments of health having legal jurisdiction over contaminated sites to determine specific sampling, quality control, analyses, and reporting requirements.

C. SAMPLING:

1. Follow specific requirements of surface area to be wiped (usually 100 cm^2 or 1000 cm^2) and action threshold (or maximum allowable residual level) set by the state or specified by the client. Uptake rates depend upon the wipe sampling method used, so the specific wipe technique used must be specified, and any deviations from the required wipe sampling requirements noted.
   NOTE: To ensure that samples have not been tampered with, the use of custody seals and a chain-of-custody form is strongly recommended.
2. Prepare a rigid template from disposable cardstock or a sheet of PTFE having either a 10 cm × 10 cm or 32 cm × 32 cm square-cut hole. The template must be able to retain its shape during wiping to ensure that the areas wiped were either 100 cm^2 or 1000 cm^2. Secure the template(s) to the area(s)

to be wiped (e.g. with tape along outside edge of template). If a single-use disposable template is not used, clean the template between samples to avoid cross-contamination, and provide the laboratory with a blank wipe of the cleaned template between samples to determine that no cross-contamination has occurred.

3. A template might not always be applicable, as in curved or odd-shaped areas such as around burners on stove tops or a fan blade. In such cases sample an area as close to either 100 cm^2 or 1000 cm^2 as feasible and provide the measurement to the regulatory agency and to the analytical laboratory for proper reporting. Tape can be used to delineate the sampling area.
4. It is recommended to provide extra wipe media from the same lot for required media blanks, field equipment blanks, samples, and quality-control samples.
5. Gauze in sterile packaging is recommended to minimize the chance for cross-contamination, which can more easily occur with open bulk packaged cotton gauze.
6. To prevent contamination in the field, another alternative is to pre-wet and insert the gauze wipes into the sample containers off-site. This avoids any possibility of the bottle of methanol or isopropanol becoming contaminated on-site with methamphetamine (or other analytes). If the wipes were prepared off-site, then remove pre-wetted gauze wipe from sample container, opening only one sample container at a time. In either case, squeeze out and discard any excess solvent from the gauze wipe. Use fresh latex or nitrile gloves for each separate sample and blank. Do not use vinyl gloves due to the potential for leaching of phthalate plasticizers and contamination of the samples.
7. Wipe techniques
   a. Concentric Squares Wiping Technique (particularly suitable for smooth and non-porous surfaces): Fold the pre-wetted gauze in half and then fold in half again. Using firm pressure wipe the area within the template. Start at one of the inside corners of the template and wipe in concentric squares, progressing toward the center. End with a scooping motion. Without allowing the gauze to touch any other surface, reverse the last fold so that the exposed side of the gauze is facing inward and using a fresh surface of the gauze, wipe the same area in the same manner as before. Roll or fold the gauze again and insert into the shipping container.
      Note: Wiping in concentric squares is described by OSHA [25]. It is especially suitable for large (e.g. 1000 cm^2) areas.
   b. Side-to-side Wiping (or Blotting) Technique (particularly suitable for rough, porous, and/or soiled surfaces): Fold the pre-wetted gauze in half and then fold in half again. Using firm pressure wipe or blot the area within the template with at least five overlapping side-to-side horizontal passes (see NOTE) beginning at the top and progressing to the bottom in a "Z" pattern. End with a scooping motion. If blotting, blot at least five times on each horizontal pass (see NOTE). Without allowing the gauze to touch any other surface, reverse the last fold so that the exposed side of the gauze is facing inward. Using a fresh surface of the gauze, wipe or blot the area again with at least five overlapping top-to-bottom vertical passes beginning at the left side and progressing to the right in an "N" pattern. If blotting, blot at least five times on each vertical pass. Roll or fold the gauze again and insert into the shipping container. Blotting is suggested in areas so soiled or rough that the threads of the gauze media are continually snagged.
      NOTE: On areas larger than 100 cm^2, more than five passes and blots will be needed.
   c. Repeat or Serial Wiping: If isopropanol is used for wiping, a serial or repeat wipe sample of the same area with a fresh gauze wipe will improve sampling efficiency. (See recoveries for second wipe in Tables 10a and 10b.) For serial wiping, repeat the wiping procedure described above (APPENDIX steps 7a or 7b) with a fresh gauze wipe. Place the second gauze wipe into the same shipping container as the first gauze. The 50-mL polypropylene centrifuge tubes are large enough to contain up to two gauze wipes.
      NOTE: If the area to be wiped remains substantially wet from the first gauze, the second gauze wipe might be used in the dry state to soak up the residual solvent from the first gauze wipe.
8. Composite sampling: Composite samples are allowed by some regulatory agencies. Their use for quantitative purposes may be subject to the permission and guidance of regulatory agencies. Refer

to guidelines of regulatory agency for directions on composite sampling. A basic default guideline for composite sampling is as follows: Do not mix inconsistent samples; that is, areas wiped must be equal in area, sampled areas must have the same high or low probability of contamination, and sampled areas must relate to a specific target appliance or site and not to several appliances or incongruous sites combined.

NOTE: Composite samples cannot meet specific action-threshold requirements for discrete sampling locations. Nor do composite samples consisting of four wipes, for example, improve the sensitivity by decreasing the LOD four fold; instead it raises the LOD by a factor related to the extra volume of desorption solution that is required to desorb a larger number of wipes. The following example illustrates these two points. Assume that the action level was 0.1 µg/100 cm^2. If the analysis gave an LOD of 0.06 µg/sample for a single wipe or discrete sample covering an area of 100 cm^2, then the LOD for the analysis could be expressed as 0.06 µg/100 cm^2, which is low enough to be able to determine whether any discrete sample is at or exceeds the action level. Now if a composite of four wipes was taken, each with an area of 100 cm^2 for a total area wiped of 400 cm^2, the LOD for that composite sample is not 0.06 µg/400 cm^2 nor is it 0.015 µg/100 cm^2; it is actually several times larger than 0.06 µg/400 cm^2. First of all it increases relative to the ratio of the volume of desorption solution used to desorb the sample compared to that used for the calibration standards. Secondly it has nothing to do with the area that was wiped, because the LOD for the calibration curve is determined in terms of µg per sample, independent of the area. To explain the first point, assume approximately 90 mL was used (for ease in calculation) to desorb the four wipes and 30 mL (the normal amount for a single wipe) was used to desorb each calibration standard. The calculation of the LOD for the four composited samples would be µg/sample × (desorption volume for 4 wipes)/(desorption volume for the calibration standards), or 0.06 µg/sample × (90 mL/30 mL), or 0.18 µg/sample for the composited sample. Since the area wiped for the composite sample was 400 cm^2, the LOD for that sample could be expressed as 0.18 µg/400 cm^2. Regarding the second point, this value, 0.18 µg/400 cm^2, cannot be construed or mathematically reduced to 0.045 µg/100 cm^2 because it cannot be known whether three of the four wipes were blank and the fourth wipe just under the value of 0.18 µg. Hence, the effective LOD per individual wipe has to be regarded not only as 0.18 µg/400 cm^2 but also as 0.18 µg/100 cm^2 because any value determined for entire 400 cm^2 might have come from just one of those 100 cm^2 areas. Thus, for composite samples, the LOD must be expressed in terms of the entire area wiped and not extrapolated to some portion thereof. In this example, an LOD of 0.18 µg/100 cm^2 is above the action threshold of 0.1 µg/100 cm^2, meaning that this composite sample cannot satisfy the requirement that residual levels be below 0.1 µg/100 cm^2. It remains for the regulatory agency and not the laboratory to determine how to apply results for composite samples to the established action levels. The same consideration that is given above for the LOD applies to results that are greater than the LOD. To avoid confusion in reporting concentrations for composite samples, it is recommended that the sample concentration (in µg/sample, whatever the sample size) and the total area wiped (in cm^2) be reported separately. For example, a result of 0.4 µg/sample for a sample consisting of four separate wipes of 100 cm^2 each (for a total area wiped of 400 cm^2), is to be reported as 0.4 µg/400 cm^2 and not averaged to 0.1 µg/100 cm^2. This manner of reporting may be required by some regulatory agencies.

9. For quality assurance purposes, regulatory agencies may require duplicate samples to be taken in the field. If such is the case, an area contiguous with and adjacent to the first area, if possible, should be wiped as described under SAMPLING. Do not re-wipe the previously wiped area. This sample is a blind sample and should not be identifiable by the analytical laboratory as a duplicate of any other sample. These are distinct from the laboratory duplicates of a single sample described in step 14 of the method. Field duplicates are useful for evaluating the consistency of sampling technique, assuming uniformity of contamination on adjacent sampling sites. Laboratory duplicates are useful for evaluating consistency of sample preparation and instrumental analysis.

D. DESORPTION FROM MEDIA:

1. An internal standard spiking solution volume of 60 µL was selected for ease in scaling from 60 µL per 30 mL to 80 µL per 40 mL of desorption solution. In either case the rate of 2 µL internal standard spiking solution per mL desorption solution was used. However, any convenient volume of internal standard spiking solution (e.g. 50 µL) that can be delivered reproducibly is acceptable. Whatever volume is chosen, there must be no variation in the volume of the internal standard spiking solution used in preparing each of the calibration standards. If spiking Strategy A is used (see APPENDIX D3), it is critical to know the exact volume of internal standard spiking solution that is applied to each sample (V_1), the media blanks (V_5), and the calibration standards (V_2), since these volumes are used for internal standard spiking solution volume corrections in step 19.
2. It is not necessary to know the exact volume of desorption solution added to each sample or the volume of residual wetting alcohol because differences in the volumes are normalized through the use of internal standards added prior to desorption.
3. Alternate strategy for spiking internal standards (spiking strategy B below): By using the exact same volume of internal standard spiking solution in all samples, blanks, QC samples, and calibration standards, regardless of the volume of desorption solution added or residual wetting alcohol, the volume corrections in step 19, (V_1/V_2 and V_5/V_2) drop out of the equation. However, the internal standard GC peak areas must still be measurable in samples where larger volumes of desorption solution are used (such as for composite samples). Because of the increased dilution of the internal standard in larger samples, this approach should be limited to desorption solution volumes of about 120 mL or less.

   NOTE: There are two separate strategies for handling larger samples requiring larger volumes of desorption solvent. These are outlined below as strategies A and B.

Number of Wipes	Size of Shipping Container (mL)	Volume of Internal Standard Spiking Solution (µL)		Volume of Desorption Solution (mL) (Strategies A and B)
		Strategy A	Strategy B	
1	40-50	60	60	30
2	50	80	60	40
4 (e.g., Composite)	100-120	160	60	80
		Apply volume correction factors at step 19.	Do not apply volume correction factors at step 19.	

   With either strategy, if two gauze wipes were included in the samples, then use 40 mL of desorption solution. If four gauze wipes were included in the samples, then use 80 mL of desorption solution.

   a. In strategy A, the volume of internal standard spiking solution is kept at a constant ratio of 2 µL per mL of desorption solution added. This enables larger samples to be desorbed without diminishing the area of the GC peak for the internal standard. However, a volume correction factor (V_1/V_2) is needed in the final calculations in step 19. Therefore, the exact volume of internal standard added to each of the samples relative to that added to the calibration standards must be known.
   b. In strategy B, the volume of internal standard spiking solution is kept constant for all samples and calibration standards, but need not be exactly 60 µL. This enables the final calculations to be made in step 19 without a volume correction factor. However, the area of the GC peak for the

internal standard will vary with sample desorption volume and the internal standard must be concentrated enough to be measurable where larger volumes of desorption solution are used.

E. DRYING COLUMN PREPARATION

Using 1 cm i.d. × 12-15 cm long polypropylene columns having a fritted polyethylene disc or equivalent (see EQUIPMENT), add 1 gram (~0.8 cc) of anhydrous potassium carbonate (the bed dimension will be about 1.0 cm dia. × 1 cm long). Add 1 gram (~0.8 cc) anhydrous sodium sulfate on top of the potassium carbonate. Remove any particles clinging electrostatically to the outside surfaces.

NOTE: Particles of the drying salts must not get into the collection tube, either through the frits or glass wool plugs, or from particles clinging electrostatically to the outside of the columns. Salts appear to inhibit derivatization efficiency.

F. DERIVATIZATION:

If isopropanol was used as the wetting solvent for the wipes, some of it will be co-extracted into the methylene chloride. In the presence of trace isopropanol, the crystal violet will go through a series of color changes as the extracts are evaporated to dryness. However, if methanol was used as the wetting solvent, the color of the crystal violet will remain blue to blue-violet at all stages of drying. Yet even with methanol, the same color changes can be afforded by adding 0.1 mL of isopropanol to the extracts prior to evaporation. Recoveries of analyte will not be affected in the absence of isopropanol, however, as long as the residues are dry before proceeding to step 11b.

With the presence of a small amount of added or co-extracted isopropanol, as each sample concentrates, the color of the solution will go from a blue or violet color rapidly through green to a yellow color as the residue approaches dryness, which is indicative of increasing hydrogen ion concentration in the residual alcohol. Upon continued blowing with nitrogen, the color of the residue turns back to a green or blue hue just at the point of dryness, which is indicative of the loss of excess hydrogen chloride and/or alcohol. At this stage the samples are dry and may be removed. Continued blowing beyond this point may turn the dried residue to a deep blue-violet or violet color. Losses of analyte have not been experienced even after blowing for five additional minutes beyond the violet stage as long as the hydrochloric acid had been added. Color changes will not be as dramatic or will not develop if too much crystal violet is used.

As the samples become concentrated, the tubes may be raised up in the water bath so that only the very bottoms of the tubes touch the surface of the water. This makes it easier to observe the color changes. The tubes may be raised out of the water bath, but blow-down times are lengthened.

Prolonged heating at high temperatures during derivatization with the acidic conditions of the acid anhydride derivatizing agents promotes mutual isomerization between the ephedrine diastereomers (ephedrine and pseudoephedrine). Dehydration of the ephedrine compounds (ephedrine, norephedrine, and pseudoephedrine) also occurs to some extent to yield β-amino-β-methyl styrenes. Heating during derivatization for longer than one hour is especially not recommended. Thirty minutes is sufficient.

NOTE: The color of the solution will gradually fade from purple to deep blue within about 20-30 minutes. This is due to the known tendency of phenolphthalein to fade at high pH. It has also been observed that in certain bulk samples, unknown constituents will cause the color of phenolphthalein to fade rapidly so that a purple color cannot be obtained at a pH >9, leaving only the blue color of the bromothymol blue. A quick check with pH paper can confirm that the pH is 9 or greater.

G. MEASUREMENT:

Recoveries for the laboratory control matrix spike samples (QC and QD) must meet the guidelines of the specific regulatory agency involved, if applicable (80-120% is a reasonable target in the absence of specific guidance).

NOTE: The QC samples (QC and QD) in this method may be referred to in some guidance documents as matrix spike and matrix spike duplicate samples (MS/MSD), but serve the same purpose. Analyze and report field-equipment blanks as samples. Do not subtract their values from any other sample.

Recoveries of Continuing Calibration Verification (CCV) standards must meet guidelines of regulatory agency (80-120% is a reasonable target in the absence of specific guidance). The CCV standards may be referred to in some guidance documents as "QC samples," but such "QCs" are equivalent to liquid standards (not matrix spiked samples) and serve the same purpose of the CCVs in this method.

With the GC/MS it is possible to achieve the lower limit of 0.05 µg or less per sample for methamphetamine in either the scan mode or SIM mode. The scan mode is essential where the identification of unknowns is an analytical objective. If lower limits of detection are desired or difficult to obtain in the scan mode, or for routine target compound only analyses, the instrument may be operated in the SIM mode.

H. MAKING DILUTIONS:

If the samples exceed the upper calibration range for the analysis, one of the following procedures may be used to estimate the high level concentrations.

1. Dilution Procedure A (dilution of the derivatized sample by reconstitution solvent):
   This option may be used only if the analytes in the sample were completely derivatized (see NOTE below). If derivatization was complete, transfer an aliquot of the sample from the GC vial (e.g. 0.2 mL for a 1:5 dilution) to a clean GC vial and dilute with reconstitution solvent (e.g. 0.8 mL for a 1:5 dilution), cap vial, mix, and reanalyze. However, dilution also dilutes the internal standard, and this procedure is useful only if the GC peak area for the internal standard is sufficiently measurable and the calibration curve is reasonably linear. Dilutions probably should not exceed a factor of 10. If this approach is used it is not necessary to enter a dilution factor in step 19 (V_3/ V_4) since both internal standard and analyte are diluted equally. The accuracy of this dilution procedure depends upon the linearity of the calibration curve in the extrapolated region beyond the upper end of the calibration curve.
   NOTE: Determination of Incomplete Derivatization: Incomplete derivatization can be caused by water, glycols, a large excess of analyte, or other contaminants that interfere with or compete for the derivatization reagent. If any one of the following symptoms appears, use Dilution Procedure B described below.

a. An "oily" film (i.e., apparently viscous liquid) or unusual residue (e.g. grit) remains after being blown-down under nitrogen after derivatization (step 11d). This may be due to the presence of water, glycols, detergents, salts, or other contaminants. Incomplete derivatization has been observed with such residues.
b. A very large (off scale) GC peak for any one of the derivatives (e.g. pseudoephedrine, a precursor for methamphetamine) indicates the possibility of incomplete derivatization for other analytes (e.g. methamphetamine) due to competition for the derivatization reagent.
c. A smaller than usual GC peak area for the internal standard (<50% of the average) in undiluted samples suggests that something was competing for or inhibiting the derivatizing reagent. Such inhibition or competition for the internal standard will be experienced by the target analyte as well.
d. Incomplete derivatization can be confirmed by the obvious presence of a GC peak for an underivatized target analyte. Underivatized analytes are not always detectable. Ephedrines usually do not show up on DB-5 capillary columns in this method, but GC peaks for underivatized secondary amines (e.g. methamphetamine) and for high levels of underivatized primary amines

(e.g. amphetamine) can be detected, usually as irregularly shaped GC peaks, depending upon GC column conditions.

e. The problem of incomplete derivatization can be minimized by the use of an isotopic (e.g. deuterated) analog for each of the target analytes as the internal standard for that compound. This allows quantification in spite of incomplete derivatization.

2. Dilution Procedure B (dilution of a smaller aliquot of the original desorbate): If the sample was not completely derivatized or if large dilutions are needed (e.g. greater than about 1:5), the following procedure can be used. See NOTE in part 1 above. The procedure may also be used if derivatization was determined to be complete.

a. Dilute an aliquot of the original aqueous acid desorbate of the wipe sample to 10 mL with desorption solution from a simulated sample blank, and re-extract. Add both the aliquot to be diluted and the diluting solution from the simulated blank directly to a clean 25-mL glass centrifuge tube (step 7f) and proceed to step 8. For example, to make a 1:10 dilution, transfer 1 mL of original desorbate to the 25-mL tube and dilute with 9 mL from a simulated sample blank.

b. The simulated sample blank should be prepared identically to the sample being diluted, using the same volumes of internal standard spiking solution and desorption solution that were used with the sample in the original desorption. For example, if the original sample was desorbed with 40 mL desorption solution with 80 µL of added internal standard spiking solution, then prepare the simulated blank in the same way. The volume of wetting alcohol is estimated (e.g. about 3 mL per 3"×3" (7.5 cm x 7.5 cm) 12-ply cotton gauze wipe). Include a dilution factor (V_3/V_4) in the calculations in step 19 (e.g. V_3/V_4 = 10 mL divided by the volume in mL of original desorbate diluted to 10 mL with solution from the simulated blank). The dilution factor in the above example is 10 mL/ 1 mL or 10.

c. Correct for differences in internal standard spiking solution volumes in step 19 (if applicable) using for V_1 the volume of internal standard spiking solution which was added to the original undiluted sample.

NOTE: This dilution procedure gives quantitative results only if the residual volume of methanol (or isopropanol) used for wetting the sample wipes was exactly the same as the volume used in preparing the calibration standards (normally about 3 mL, see Table 6). Deviations of a few milliliters in residual wetting alcohol will not affect the results for undiluted samples, but will amount to an error of a few percent in the final results of samples that are diluted.

d. The potential error due to differences in residual wetting solvent can be estimated for specific volumes of desorption solution and wetting alcohol. Assume the sample wipes and calibration standards are both desorbed in 30 mL of desorption solution and 3 mL of alcohol is added to the calibration standards. The potential error in volume (and final results) in the samples is approximately ±3 % (inversely proportional) per mL difference in the residual alcohol in the samples (i.e., ±1 mL difference in 33 mL). For 40 mL of desorption solution and 4 mL of alcohol added to the calibration standards, the error is ±2 % for every mL difference (i.e., ±1 mL difference in 44 mL). However, since the volume of residual wetting alcohol is not known and cannot be determined once the sample wipe has been desorbed, the actual error cannot be determined. However, the maximum possible error can be calculated. Since the maximum amount of alcohol that a recommended wipe can hold is about 6 mL when saturated (dripping wet), there can only be a deviation of plus or minus 3 mL from the 3 mL alcohol added to the calibration standards. Therefore, the maximum error in a result due to differences in the volume of residual alcohol in a cotton gauze sample compared to the standards can only be three times the error for a 1 mL difference in volume. Since the error for ±1 mL is ±3.03%, the maximum error for ±3 mL is three times larger, or ±9.1%. In practice, the error will be less than this because it is unlikely that the gauze samples will be completely dry or completely saturated after squeezing out the excess alcohol and wiping a surface. The practical amount of alcohol that remains in the wipes when the excess is squeezed out is between 1 and 2 mL. This translates into an error that is between +3%

and +6% in the final results for diluted samples. Undiluted samples will not be affected. This error is within the overall accuracy for the method for methamphetamine.

3. Dilution Procedure C (dilution of desorbates from dried samples):
   Dilution errors for over-range samples may be corrected by knowing the exact amount of residual alcohol in the samples. The volume (or weight) of residual solvent in each gauze wipe might be determined by the difference between a wet weight and dry weight. Better yet, the error might be eliminated for diluted samples by adding, after the samples are dried (without taking any weight), the same known volume of wetting alcohol that is added to the calibration standards (i.e., 3 mL). Thereafter, if any samples need dilution, there will be no dilution errors due to differences in residual alcohol, because all samples and standards will have the same volume of alcohol and total volume of desorption solution.

   However, air drying of the samples is not recommended because of the possible loss of methamphetamine due to its volatility when it is not in the salt form, which form cannot be assured in field samples. Also, manipulating the samples for weighing and drying might introduce contamination. Drying is not recommended as a procedure for analytes having a vapor pressure high enough to be lost in the process, or that tend to form azeotropes with alcohols; this is especially important when the critical action levels for remedial cleanup are at the lower end of the method calibration range. Drying is not an option if the samples have already been desorbed.

METHAMPHETAMINE and Illicit Drugs, Precursors, and Adulterants on Wipes by Solid Phase Extraction

9109

FORMULA: Table 1 MW: Table 1 CAS: Table 1 RTECS: Table 1

METHOD: 9109, Issue 1 **EVALUATION: Partial** **Issue 1: 17 October 2011**

OSHA: none for surfaces
NIOSH: none for surfaces
Other OELs and guidelines: [1, 2, 3]

PROPERTIES: Table 2

SYNONYMS: Table 3

SAMPLING

SAMPLER: Wipe

SAMPLE AREA: 100 cm^2 or 1000 cm^2

SHIPMENT: Ship refrigerated preferably, <6 °C

SAMPLE STABILITY: At least 30 days at <6 °C (See Table 4)

FIELD BLANKS: 2 to 10 blanks per sample set

MEASUREMENT ACCURACY

LEVEL STUDIED: 3.0 µg/sample

BIAS: Table 9 [4]

OVERALL PRECISION ($\hat{S}_{rT}$): Surface recovery not performed

ACCURACY: Table 7a and 7b [4]

MEASUREMENT

TECHNIQUE: GAS CHROMATOGRAPHY/MASS SPECTROMETRY

ANALYTES: Table 1

DESORPTION: 0.1 M sulfuric acid

CLEANUP/ EXTRACTION: Solid phase extraction

DERIVATIZATION: MSTFA and MBHFBA

INJECTION VOLUME: 2 µL Splitless

TEMPERATURE
Injection: 255 °C.
Detector: 285 °C
Column: 90 °C (2 min), to 310 °C (10 °C/ min), hold 6 min

MASS SPECTROMETER: Scan mode (29 – 470 AMU), 2 scan/sec or selected ion monitoring (SIM) mode (Table 5)

CARRIER GAS: Helium, 1.5 mL/min

COLUMN: Capillary, fused silica, 30 m x 0.32 mm i.d., 0.5 µm U.S. Pharmacopeia (USP) G27 film

CALIBRATION: Standards from spiked wipes with internal standard, See Table 6

RANGE: Table 7a and 7b [4].

ESTIMATED LOD: Table 4

PRECISION ($\bar{S}_r$): Table 7a and 7b [4]

APPLICABILITY: For methamphetamine the range is 0.05 to 60 µg/sample (sample = 100 cm^2 or 1000 cm^2). This method was developed for the analysis of selected drugs and precursors on surfaces in clandestine drug labs [5]. Sampling methodology was tested using wipes on smooth, non-porous surfaces. The APPENDIX contains sampling information for other types of surfaces.

INTERFERENCES: No chromatographic interferences detected. Water, surfactants and polyols inhibit derivatization.

OTHER WIPE METHODS: NIOSH 9106 uses liquid-liquid extraction and gas chromatography/mass spectrometry (GC/MS) to measure multiple drugs [6]. NIOSH 9111 uses liquid chromatography/mass spectrometry (LC/MS) to measure methamphet-amine [7].

REAGENTS:

NOTE: See APPENDIX A for special instructions on reagents.

1. Analytes listed in Table 1*
2. Internal standards from those listed in Table 8a
3. Solvents, residue free analytical grades
   a. Isopropanol (IPA)*
   b. Methanol*
   c. Methylene chloride (CH_2Cl_2)*
   d. Acetonitrile*
4. Concentrated sulfuric and hydrochloric acids (Analytical Reagent [AR] or trace metals analysis grades)*
5. Ammonium hydroxide (NH_4OH), 28-30%, A.C.S. grade*
6. Bromothymol blue, ≥95%, A.C.S.; crystal violet (Gentian Violet), ≥95%, A.C.S.
7. Purified gases: helium for carrier gas, nitrogen for drying
8. MSTFA (N-methyl-N-trimethylsilyl-trifluoro-acetamide) derivatizing agent*
9. MBHFBA (N-methyl-N,N-bisheptafluorobutyramide) derivatizing agent*
10. 4,4'-Dibromooctafluorobiphenyl, 99%
11. Deionized water (ASTM type II)

SOLUTIONS:

NOTE: See APPENDIX A for special instructions on solutions.

1. Prepare solutions of analytes of interest (Table 1). Calculate concentrations as the free base. Keep solutions refrigerated (<6 °C). Protect solutions from light.
   a. Stock solutions are prepared at about 1-2 mg/mL in methanol.
   b. Analyte spiking solutions are prepared by diluting the stock solutions to about 200 µg/mL each in methanol.
2. Prepare internal standard spiking solution in methanol at about 200 µg/mL.
   NOTE: Add about 2 mg of crystal violet per 20 mL of internal standard spiking solution to help indicate which samples have been spiked.
3. Desorption solution: 0.1 M sulfuric acid. Add 22 mL conc. sulfuric acid to 4 liters deionized water.
4. Bromothymol blue pH indicator solution: 1 mg/mL in 4:1 isopropanol:deionized water.
5. Crystal violet indicator: 2-3 mg/mL in isopropanol.
6. Solid phase extraction (SPE) wash solution: Aqueous 0.1 M hydrochloric acid: Dilute 8.3 mL concentrated hydrochloric acid in about 800 mL water, dilute to 1 liter with ASTM Type II water.
7. SPE elution solution: 80:20:2 CH_2Cl_2:IPA:NH_4OH v/v. Prepare fresh daily.
8. 0.3 M hydrochloric acid in methanol: Dilute 2.5 mL conc. hydrochloric acid in about 80 mL methanol; dilute to 100 mL with methanol.
9. Derivatization diluent solvent: acetonitrile containing 4 µg/mL of 4,4'-dibromo-octafluorobiphenyl (optional).

* See SPECIAL PRECAUTIONS

EQUIPMENT:

NOTE: See APPENDIX B for special instructions on equipment.

1. Wipe, cotton gauze, (7.6 cm × 7.6 cm) 12-ply or equivalent.
2. Sample storage and shipping container: 50-mL polypropylene centrifuge tubes with polytetrafluoroethylene (PTFE)-lined caps or equivalent.
3. Gas chromatograph/mass spectrometer detector, with column and integrator, See p. 9109-1.
4. Solid phase extraction (SPE) mixed phase cation exchange hydrophilic extraction columns (See Appendix E)
5. Collection tubes and GC vials:
   a. Glass test tubes (13 mm x 100 mm) with PTFE-lined caps
   b. GC autosampler vials, 2-mL Limited-volume, 300-500 µL (amber vials recommended), and caps.
6. Volumetric flasks: 10-, 100-, and 250-mL.
7. Reagent bottle, 4-L .
8. Liquid Transfer:
   a. Syringes: 10-, 25-, and 100-µL.
   b. Mechanical pipette with disposable tips, 5-mL.
   c. Repeating dispensers: 1 to 5-mL.
   d. Syringe or repeating dispenser: 100-µL.
   e. Syringes: 250-µL.
9. Forceps.
10. Gloves: latex or nitrile. Avoid vinyl gloves (see 9109-3, Sampling, step 1, NOTE 2).
11. Rotating mixer capable of 10-30 rpm.
12. Vacuum manifold box with 12 to 36 vacuum ports, and adjustable flow rates.
13. Nitrogen blow-down apparatus with water bath capable of maintaining 35 °C.
14. Vortex mixer.
15. Pasteur pipettes.
16. pH paper.
17. Template: 10 cm x 10 cm (or 1 foot x 1 foot) opening made of relatively rigid disposable cardstock or sheet of PTFE.
18. Ice or other cold media for shipping.

SPECIAL PRECAUTIONS: The solvents are flammable and have associated adverse health effects. Phenethylamines target the nervous system at very low concentrations and are easily absorbed through the skin. Avoid breathing vapors. Avoid skin contact. Work should be performed in a hood with adequate ventilation. Analysts must wear proper eye and hand protection (e.g., latex gloves) to prevent absorption of even small amounts of amines through the skin as well as for protection from the solvents and other reagents. Dissolving concentrated hydrochloric or sulfuric acid in water is highly exothermic. Goggles must be worn. The derivatization reagents react violently with water.

Caution must also be exercised in the handling and analysis of samples. Clandestine drug labs may produce unknown and seriously toxic by-products. For example, in the manufacture of designer drugs (e.g., MPPP, a homolog of Alphaprodine), at least one very neurotoxic by-product, 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine (MPTP), has been identified that specifically and irreversibly causes Parkinson's disease [8,9].

SAMPLING:

See APPENDIX C for special instructions on sampling.

1. Using a new pair of gloves, remove a gauze wipe from its protective package. Moisten the wipe with approximately 3 to 4 mL of methanol (or isopropanol).
   NOTE 1: Apply no more solvent than that needed to moisten approximately the central 80% of the area of the gauze wipe. Excess solvent may cause sample loss due to dripping from the wipe.
   NOTE 2: Do not use vinyl gloves due to the potential for leaching of phthalate plasticizers and contamination of the samples.
2. Place the template over the area to be sampled (may tape in place along outside edge of template). Wipe the surface to be sampled with firm pressure, using vertical S-strokes. Fold the exposed side of the pad in and wipe the area with horizontal S-strokes. Fold the pad once more and wipe the area again with vertical S-strokes.
3. Fold the pad, exposed side in, and place in shipping container and seal with cap.
   NOTE: Keep samples refrigerated (<6 ºC). While methamphetamine and several related amines are stable on the recommended wipe media for at least 7 days at room temperature, refrigeration is recommended as soon as possible (see Table 4).
4. Either clean the template before use for the next sample or use a new disposable template.
5. Label each sample clearly with a unique sample identifier.
6. Prepare a minimum of two field blanks with one field blank for every ten samples.
   NOTE: In addition, include at least 3 media blanks for the analytical laboratory to use for their purposes. The wipes used for the media blanks should be from the same lot as the field samples.

SAMPLE PREPARATION:

See APPENDIX D for special instructions on sample preparation.

7. Desorption from media:
   a. Remove cap from shipping container.
      NOTE: Sample wipe should fit loosely in the container. If not, transfer sample to a larger container.
   b. Spike 60 µL of internal standard spiking solution onto each wipe sample.
   c. Add 30 mL desorption solution (0.1 M sulfuric acid).
      NOTE: If the samples were transferred to a larger container, rinse the original shipping container with the desorption solution, shake, and decant the rinsate into the larger container. Cap securely and mix contents by inverting the tubes end over end on a rotary mixer or equivalent at 10-30 rpm for at least one hour.

d. Check the pH which should be about ≤ 4. If needed, adjust the pH with diluted (2.5 to 3 M) sulfuric acid drop-wise, mixing the contents by shaking or inversion a few times after each addition of acid before checking the pH.
e. After mixing, transfer 10 mL of supernatant to a 25-mL glass centrifuge tube.
NOTE: If extraction is to be performed on a subsequent day, store samples in a refrigerator. Analytes are stable in the desorption solution for at least one week refrigerated.

8. Solid phase extraction procedure:
a. Column selection: Select one of the SPE columns listed in Appendix E. Each brand of column has a slightly different conditioning procedure and resistance to flow. Other brands of SPE columns may also work. Elution profiles of drugs to be analyzed need to be determined before use of columns other than those specified.
b. Setting up columns: Attach SPE columns to vacuum ports on the manifold. Attach vacuum line to vacuum pump capable of 25-30 psi vacuum.
c. Conditioning: Condition each column with 1 column volume (3 mL) of methanol followed by 1 column volume of Type II deionized water. For some brands the conditioning volume is 1/3 column volume. Check product literature.
d. Loading: Load each SPE column with 5 mL of the sample acid desorbate solution. Adjust vacuum so that the flow rate is about 1-2 mL/minute. The vacuum required to obtain that flow rate varies with brand of SPE column.
e. First wash: Wash each column with 1 column volume (3 mL) of 0.1 M aqueous hydrochloric acid. For some brands this volume may be decreased to 1 or 2 mL. Check product literature.
f. Second wash: Wash each column with 1 column volume of methanol. Add the methanol in 2 or 3 separate aliquots to ensure that the aqueous acid is flushed through. Discard all effluents.
g. Drying: Remove last traces of water in the SPE columns by pulling air through the columns under increased vacuum (e.g., 25 psi) for 5 minutes. Silica-based SPE columns or columns with high resistance to flow may require a longer time to reach dryness.
h. Elution: Position 13 x 100 mm collection tubes under each column. Elute analytes with 3 mL of elution solution (80:20:2 methylene chloride:isopropanol:concentrated ammonium hydroxide v/v, freshly prepared). Adjust vacuum so that the flow rate is 1 mL/minute or less. For some brands this flow rate may occur without applied vacuum. Most of the analytes (e.g., amphetamine, ephedrine, methamphetamine, etc.) are eluted in the first milliliter.

9. Evaporation: To each collection tube containing eluate, add about 5 µL crystal violet solution and 100 µL of 0.3 M hydrochloric acid in methanol. The samples are evaporated to dryness under gently blowing nitrogen at 25-35 °C. The samples should be removed from the evaporation bath within a few minutes after dryness. A mixed whitish and purple residue will remain. The purple color of the crystal violet helps to make the residue more visible when dried. The color of the crystal violet remains a constant blue to blue-violet during concentration and drying.

10. Derivatization: (Perform under the hood.) Add 100 µL of acetonitrile containing the optional dibromooctafluorobiphenyl secondary internal standard. Add 25 µL MSTFA and 25 µL MBHFBA in that order. Cap tubes between additions to prevent atmospheric humidity from affecting the reagents. (See note below. Have no more than 5 or 6 tubes uncapped at a time.) Vortex each tube about 4-5 seconds. Using Pasteur pipettes, transfer each mixture to low-volume (300-500 µL) amber autosampler vials and cap vials.
NOTE 1: Some derivatization takes place at room temperature, especially trimethylsilylation. Derivatization is completed on-column after injection. No prior heating is required or recommended.
NOTE 2: The color of the reconstituted solution should be deep blue to violet. If the color turns light blue or turquoise upon standing, moisture may be present (the vials may not have been capped tightly enough). Such samples need to be reprocessed beginning at step 8 since the derivatives are not stable in the presence of moisture. If the vials are securely capped, the

solutions will be stable for several days at room temperature and at least a week refrigerated. Protect vials from light (amber vials recommended.)

11. Analyze samples, standards, blanks, and QCs by GC-MS. (See MEASUREMENT, steps 15-17 and p. 9109-1.)

CALIBRATION AND QUALITY CONTROL:

12. Determine retention times for the derivatives of the analytes of interest using the column and chromatographic conditions specified on page 9109-1. Table 10 gives typical retention times for various drugs, precursors, and adulterants. Figure 1 shows a typical chromatogram.
13. Calibrate daily with at least six calibration standards and a blank selected from Table 6 to cover the analytical range.
    a. Prepare the analyte spiking solution as follows: Add known amounts of individual drug stock solutions to a volumetric flask and dilute to volume with methanol. A recommended final concentration for this solution is approximately 200 µg each per mL.
    b. Prepare calibration standards and media blanks in clean shipping containers (e.g., 50-mL polypropylene centrifuge tubes or equivalent).
       NOTE: Liquid standards (standards without added blank wipe media) may be prepared in lieu of media standards if cotton gauze was used for the samples.
    c. Add 3 mL methanol (or isopropanol if isopropanol was used with the samples in the field) to each calibration standard and media blank.
       NOTE: If two gauze wipes were routinely used for every sample, increase methanol (or isopropanol) to 4 mL. See Table 6, footnote 2.
    d. Spike a known volume of analyte spiking solution into each calibration standard by spiking directly onto the media or into solution. Use the spiking volumes suggested in Table 6 to cover the desired range.
    e. Process each of these through the desorption, solid phase extraction (SPE), drying, and derivatization steps (steps 7 through 11) along with the field samples.
    f. Analyze these along with the field samples. (See MEASUREMENT, steps 15-17.)
14. Prepare matrix-spiked and matrix-spiked duplicate (QC and QD) quality control samples [10].
    a. Cotton gauze from the same lot used for taking samples in the field should be provided to the analytical laboratory to prepare these matrix-spiked quality control samples.
    b. The quality control samples (QC and QD) must be prepared independently at concentrations within the analytical range. (See Table 6 for applicable concentration ranges.)
    c. One quality control media blank (QB) must be included with each QC and QD pair.
    d. Spike QC and QD with a known amount of target analyte as suggested in Table 6.
       i. Transfer clean wipes to new shipping containers.
       ii. Add 3 mL of methanol (or isopropanol if isopropanol was used in wiping) to each wipe.
       iii. Spike QC and QD with a known amount of analyte as suggested in Table 6.
       NOTE: If two gauze wipes were used for the majority of samples in an analytical set, use two clean gauze wipes for each QB, QC, and QD, and increase isopropanol (or methanol) to 4 mL. See Table 6, footnote 2.
    e. Process quality control samples through the desorption, SPE, drying, and derivatization steps (steps 7 through 11) along with the calibration standards, blanks, and field samples.
    f. Analyze these along with the calibration standards, blanks, and field samples. (See MEASUREMENT, steps 15-17.)

MEASUREMENT:

See APPENDIX G for special instructions on measurement.

15. Analyze the calibration standards, quality control samples, blanks, a continuing calibration verification (CCV) standard consisting of one of the initial calibration standards, and samples by GC/MS.

Set gas chromatograph according to manufacturer's recommendations and to conditions listed on page 9109-1.

a. Set mass spectrometer conditions to manufacturer's specifications and those given on page 9109-1 for the scan mode or those in Table 5 for the SIM mode.
b. Inject sample volume with autosampler or manually.
   NOTE: After the derivatives are prepared and just before analyzing any samples or standards, inject the highest concentrated standard several times in order to prime or deactivate the GC column and injection port. This will help minimize any drift in the instrument's response to target analytes relative to their internal standards.
c. After analysis, the vials should be recapped promptly and refrigerated if further analysis is anticipated.

16. Using extracted ion current profiles for the primary (quantification) ions specific to each analyte, measure GC peak areas of analyte(s) and internal standard(s) and compute relative peak areas by dividing the peak area of the analyte by the area of the appropriate internal standard. Recommended primary (quantification) ions and internal standards are given in Tables 5, 7 and 8. Prepare calibration graph (relative peak area vs. µg analyte per sample).
17. Samples from initial investigations of clandestine laboratories are likely to include highly contaminated samples. If sample results exceed the upper range of the calibration curve, the sample in the GC vial may be diluted and reanalyzed or a smaller aliquot of the initial acid desorbate diluted, re-extracted, derivatized, and analyzed. Refer to APPENDIX H for instructions and limitations on making dilutions.

CALCULATIONS:

18. Determine the mass in µg/sample of respective analyte found in the wipe samples, and in the media blank from the calibration graph.
19. Calculate final concentration, C, of analyte in µg/sample:

$$C = c\frac{V_1}{V_2}\frac{V_3}{V_4} - b\frac{V_5}{V_2}$$

c = concentration in sample (in µg/sample determined from the calibration curve).

$\frac{V_1}{V_2}$ = volume correction factor (needed only when the volume of internal standard spiking solution used for spiking the samples - such as for composite samples requiring larger desorption solution volumes - is different from that used for spiking the calibration standards). (See Table 6, footnote 4).

V_1 = volume in µL of internal standard spiking solution used to spike samples.

V_2 = volume in µL of internal standard spiking solution used to spike the standards.

$\frac{V_3}{V_4}$ = dilution factor, if applicable.

V_3 = 5 mL (volume of desorbate normally taken for extraction in step 8d).

V_4 = volume in mL of desorbate actually taken for extraction and diluted to 5 mL with blank desorbing solution containing internal standard.

b = concentration in media blank (in µg/sample determined from the calibration curve).

$\frac{V_5}{V_2}$ = volume correction factor for the media blank (needed only if the volume of internal standard spiking solution used for spiking the media blank is different from that used for spiking the calibration standards).

V_5 = volume in µL of internal standard spiking solution used to spike media blank.

20. Report concentration, C′, in µg per total area wiped (in cm^2) as follows:

$$C' = \frac{C}{A}$$

C = µg/sample (step 19).
A = Total area wiped in cm^2 per sample.

NOTE: In general, if the area wiped was greater than or less than 100 cm^2, do not convert value to µg/100 cm^2 unless specifically required or allowed by agency having legal jurisdiction. For example, if the sample was a composite sample and the area was 400 cm^2, report results as µg/400 cm^2 and not averaged to µg/100 cm^2 since regulatory agencies might not allow averaging of composite results to 100 cm^2. To avoid confusion, report separately both µg/sample (C) and the total area wiped in cm^2 per sample (A) for both discrete and composite samples.

EVALUATION OF METHOD:

This method was developed according to the NIOSH sampling and analytical method development guidelines [11]. This method was evaluated for those analytes listed in Tables 7a and 7b over a range of approximately 0.1 µg/sample to 30 µg/sample for several types of sampling media. These concentration levels represent approximately the 1 through 300 times the limit of quantitation (LOQ) level for most of the analytes. Results are reported in the Backup Data Report [4].

The limits of detection (LOD and LOQ) were determined by preparing a series of liquid standards in desorption solution, processing by the SPE of NIOSH 9109, and analyzing in the scan mode. The LODs were estimated using the procedure of Burkart [12]. An LOD of 0.1 µg/sample for methamphetamine on wipes was achieved in the scan mode. The LOD was set at 0.1 µg/sample because that was the level of the lowest calibration standard in the LOD/LOQ study. Lower LODs (e.g., 0.02 µg/sample) have been achieved in practice by including calibration standards at lower concentration levels. The cleanliness and performance of the mass spectrometer must be maintained such that at 0.1 µg/sample a signal of at least 5 to 10 times the baseline noise is achievable. This is more easily accomplished in the SIM mode.

Six different wipe media were evaluated. These were 3″x3″ (7.5 cm x 7.5 cm) 12-ply cotton gauze, 4″x4″ (10 cm x 10 cm) AlphaWipe® (TX 1004), 4″x4″ (10 cm x 10 cm) 4-ply NU GAUZE®, 4″x4″ (10 cm x 10 cm) 4-ply MIRASORB®, 4″x4″ (10 cm x 10 cm) 6-ply SOF-WICK®, and 4″x4″ (10 cm x 10 cm) 4-ply TOPPER® sponges. Results are given in the Backup Data Report [4]. No synthetic media performed better than cotton gauze. Some media (NU GAUZE® and SOF-WICK®) gave inconsistent results.

Precision and accuracy were determined by analyzing 6 replicates at each of 6 concentration levels (nominally 0.1, 0.3, 1, 3, 10, and 30 µg/sample). Results are presented in Table 7a for cotton gauze and 7b for AlphaWipe®. The best precision and accuracies were dependent upon the use of carefully chosen internal standards, especially with steric hindrance of the amine (e.g., having N-ethyl and N-propyl groups). Long term sample storage stability was determined for periods up to 30 days under refrigeration (<6 °C) and for up to 7 days at room temperature (22-24 °C). Results are given in Table 4.

Chlorodifluoroacetic anhydride (CDFAA) and pentafluoro propionic anhydride (PFPA) were evaluated as derivatizing agents for the SPE eluates. These were not effective, probably due to the high level of ammonium chloride residues in the SPE column eluates. They were most effective with the liquid-liquid extraction procedure of NIOSH 9106 [6].

For SPE, the mixed silanization-acylation reagent, MSTFA and MBHFBA [13-15], proved very effective. The derivatization mixture is transferred directly to amber mini-GC vials and direct-injected without prior heating.

Recovery of amphetamines from six different types of surfaces using cotton gauze was evaluated (see Table 9a and 9b). The practice of serial wiping (wiping the same surface area a second time with a second gauze wipe and combining both wipes as a single sample) was evaluated. Four solvents for wetting the gauze were tested (distilled water, 5% distilled white vinegar, isopropanol, and methanol). Six replicates samples were taken on a latex painted wall. Recoveries and precisions are given in Table 9a and 9b. The recoveries with 5% distilled white vinegar were better than for distilled water, but not as good as for isopropanol. Methanol is superior to isopropanol. Recoveries with isopropanol are greatly improved with a repeat (serial) wipe (11% improvement compared to only about 6% improvement with methanol). The study and results are reported in the Backup Data Report for NIOSH 9109 [4]. Additional research on surface sample recovery and solvent effectiveness has been reported by Van Dyke et al [13] and Serrano et al. [16].

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METHOD DEVELOPMENT BY:

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Table 1. Formula and registry numbers of analytes

Compound (alphabetically)	MW[1] (Daltons) Free base	HCl salt	Hemisulfate salt	Structural Formula As free base	CAS #[2]	RTECS[6]
(DL)-Amphetamine	135.21	171.67	184.25	$C_6H_5{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH_2$	300-62-9[3] 60-13-9[5]	SH9450000 SI1750000
(D)-Amphetamine[7]	135.21	171.67	184.25	$C_6H_5{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH_2$	51-64-9[3] 51-63-8[5]	SI1400000
(L)-Amphetamine	135.21	171.67	184.25	$C_6H_5{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH_2$	156-34-3[3]	SH9050000
Caffeine	194.19			$(CH_3)_3{\cdot}[C_5HN_4O_2]$	58-08-2[3]	EV6475000
(DL)-Ephedrine	165.24	201.70	214.28	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	90-81-3[3] 134-71-4[4]	
(L)-Ephedrine[8]	165.24	201.70	214.28	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3)NH{\cdot}CH_3$	299-42-3[3] 50-98-6[4] 134-72-5[5]	KB0700000 KB1750000 KB2625000
(D)-Ephedrine	165.24	201.70	214.28	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3)NH{\cdot}CH_3$	321-98-2[3] 24221-86-1[4]	KB0600000 KB1925000
(±)-MDEA	207.27	243.73		$CH_2O_2C_6H_3{\cdot}CH_2{\cdot}CH(CH_3)NH{\cdot}C_2H_5$	82801-81-8[3] 116261-63-2[4]	
(±)-MDMA	193.24	229.71		$CH_2O_2C_6H_3{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	42542-10-9[3] 92279-84-0[4]	SH5700000
(+)-MDMA[7]	193.24	229.71		$CH_2O_2C_6H_3{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	64057-70-1[4]	SH5700000
(DL)-Methamphetamine	149.24	185.70	198.28	$C_6H_5{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	4846-07-5[3]	
(D)-Methamphetamine[7]	149.24	185.70	198.28	$C_6H_5{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	537-46-2[3] 51-57-0[4]	SH4910000 SH5455000
(L)-Methamphetamine	149.24	185.70	198.28	$C_6H_5{\cdot}CH_2{\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	33817-09-3[3]	SH4905000
Phencyclidine	243.39	279.85		$C_6H_5{\cdot}C[C_5H_{10}]{\cdot}N[C_5H_{10}]$	77-10-1[3] 956-90-1[4]	TN2272600 TN2272600
Phentermine	149.24	185.70		$C_6H_5{\cdot}CH_2{\cdot}C(CH_3)_2{\cdot}NH_2$	122-09-8[3] 1197-21-3[4]	SH4950000
(DL)-Norephedrine	151.21	187.67	200.25	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NH_2$	14838-15-4[3] 154-41-6[4]	RC2625000 DN4200000
1R,2S (-)-Norephedrine	151.21	187.67	200.25	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NH_2$	492-41-1[3]	RC2275000
1S,2R (+)-Norephedrine	151.21	187.67	200.25	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NH_2$	37577-28-9[3]	
1S,2S (+)-Norephedrine	151.21	187.67	200.25	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NH_2$	36393-56-3 2153-98-2[4] 492-39-7[4]	RC9275000
(D)-Pseudoephedrine[8,9]	165.24	201.70	214.28	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NHCH_3$	90-82-4[3] 345-78-8[4]	UL5800000 UL5950000
(L)-Pseudoephedrine[10]	165.24	201.70	214.28	$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}NH{\cdot}CH_3$	321-97-1[3]	

(1) Molecular weights are calculated from the empirical formula using the 1987 IUPAC Atomic Weights of the Elements, Merck Index [17]. The molecular weight of the hemisulfate is ½ the weight of the 2:1 sulfate salt (2 moles amine + 1 mole H_2SO_4).
(2) CAS from various sources: Merck Index [17], NIOSH RTECS [18], MSDS sheets from Sigma/Aldrich [19], Cerilliant [20], and other sources [21].
(3) Free base form.
(4) Hydrochloride salt.
(5) 2:1 Sulfate salt (2 moles amine + 1 mole H_2SO_4.
(6) RTECS = NIOSH Registry of Toxic Effects of Chemical Substances [18].
(7) More active isomer.
(8) Naturally occurring isomer.
(9) The D form of pseudoephedrine is a decongestant.
(10) The L form of pseudoephedrine is a bronchodilator. Dehydroxylation forms the less active L-methamphetamine.

Table 2. Physical properties of analytes[1]

Compound (alphabetically)	CAS	m.p. (°C)	Vapor Pressure (mm Hg)	pK_a[4]	Log P[5]	Solubility in Water, g/100mL
(DL)-Amphetamine	300-62-9	—	—	10.1 @ 20 °C	1.76	2.8 @ 25 °C
(D)-Amphetamine	51-64-9	<25	—	9.9[6]	1.76	—
(D)-Amphetamine sulfate	51-63-8	>300	—	—	6.81	—
(L)-Amphetamine	156-34-3	—	0.201 @ 25 °C	10.1 @ 20 °C	1.76	2.8 @ 25 °C
Caffeine	58-08-2	238	15 @ 89 °C	10.4 @ 40 °C	-0.07	2.16 @ 25 °C
(DL)-Ephedrine	90-81-3	76.5	—	—	0.68	—
(L)-Ephedrine	299-42-3	34	0.00083 @ 25 °C	10.3 @ 0 °C	1.13	63.6 @ 30 °C
(L)-Ephedrine HCl	50-98-6	218	$2.04E^{-10}$ @ 25 °C	pH 5.9 @ 1/200 dil.[3]	-2.45	25[6]
MDEA	82801-81-8	—	—	—	—	—
MDMA HCl	42542-10-9	148-149[2]	—	—	—	—
(D)-Methamphetamine	537-46-2	—	0.163 @ 25 °C	9.87 @ 25 °C	2.07	1.33 @ 25 °C
(D)-Methamphetamine HCl	51-57-0	170-175[2]	—	—	—	—
Phencyclidine	77-10-1	46.5	—	8.29[6]	4.69	—
Phencyclidine HCl	956-90-1	233-235[2]	—	—	—	—
Phentermine	122-09-8	—	0.0961 @ 25°C	—	1.90	1.86 @ 25 °C
Phentermine HCl	1197-21-3	198[2]	—	—	—	—
(±) Phenylpropanolamine	14838-15-4	—	0.000867 @ 25 °C	9.44 @ 20 °C	0.67	14.9 @ 25 °C
(±) Phenylpropanolamine HCl	154-41-6	194	—	—	-2.75	—
(L)-Norephedrine	492-41-1	51-53[3]	—	—	—	—
1*S*,2*S* (+)-Norephedrine	36393-56-3	77.5-78	0.000867 @ 25 °C	9.44 @ 20 °C	0.83	14.9 @ 25 °C
1*S*,2*S* (+)-Norephedrine HCl	492-39-7	—	—	pH 5.9-6.1 in aq. soln.[3]	0.22	2 @ 25 °C
(D)-Pseudoephedrine	90-82-4	119	0.00083 @ 25 °C	10.3 @ 0 °C	0.89	10.6 @ 25 °C
(D)-Pseudoephedrine HCl	345-78-8	181-182[2]	—	pH 5.9 @ 1/200 dil.[3]	—	—

(1) Handbook of Physical Properties of Organic Chemicals unless otherwise noted [21].
(2) Merck Index [17].
(3) Sigma-Aldrich MSDS [19].
(4) Negative log of the acid dissociation constant for the amine in aqueous solution.
(5) Log P = octanol-water partition coefficient.
(6) Temperature not given in source.

Table 3. Synonyms of analytes

Generic names[1]	Trade and street names[2]	Additional names[3]
(DL)-Amphetamine; (±)-Amphetamine	Benzedrine; Phenedrine; bennies	(±)-α-Methylbenzeneethanamine[4]; dl-α-Methylphenethylamine[4]; dl-1-Phenyl-2-aminopropane; (±)-Desoxynorephedrine
(D)-Amphetamine; (+)-Amphetamine	Dextroamphetamine; Dexedrine; dexies	(S)-α-Methylbenzeneethanamine[4]; d-α-Methylphenethylamine[4]; d-1-phenyl-2-aminopropane; d-β-Phenylisopropylamine
(L)-Amphetamine; (-)-Amphetamine	Levoamphetamine; component of Adderall	(R)-α-Methylbenzeneethanamine[4]; l-α-Methylphenethylamine[4]; l-1-phenyl-2-aminopropane; (-)-1-phenyl-2-aminopropane
Caffeine	Component (with ephedrine) of cloud 9 and herbal XTC	3,7-Dihydro-1,3,7-trimethyl-1H-purine-2,6-dione[4]; 1,3,7-Trimethylxanthine
(DL)-Ephedrine; (±)-Ephedrine	Ephedral; Racephedrine; Sanedrine	(*R**,*S**)-(±)-alpha-[2-(Methylamino)ethyl]benzenemethanol; DL-alpha-[1-(Methylamino)ethyl] benzyl alcohol; *dl*-Ephedrine
(L)-Ephedrine; (-)-Ephedrine; (1*R*,2*S*)-(-)-Ephedrine; *l*-Ephedrine	Primatene; Xenadrine; Ma Huang (Ephedra sinica and other species[5]); (with caffeine) cloud 9 and herbal ecstasy	(*R*-(*R**,*S**))-*α*-(1-Methylaminoethyl)benzenemethanol; L-erythro-2-(Methylamino)-1-phenylpropan-1-ol; (1*R*,2*S*)-(-)-2-Methylamino-1-phenyl-1-propanol; (-)-alpha-(1-Methylamino-ethyl)-benzyl alcohol; (-)-1-hydroxy-2-methylamino-1-phenylpropane; L-(-)-Ephedrine
(D)-Ephedrine		(1*S*,2*R*)-(+)-2-Methylamino-1-phenyl-1-propanol; (+)-Ephedrine
MDEA	MDE; Eve	(±)-3,4-Methylenedioxy-N-ethylamphetamine; *N*-ethyl-alpha-methyl-1,3-benzodioxole-5-ethanamine
MDMA	Adam, ecstasy	*N,α*-Dimethyl-3,4-1,3-benzodioxole-5-ethanamine; 3,4-Methylenedioxymethamphetamine
(DL)-Methamphetamine; (±)-Methamphetamine		*N,α*-Dimethylbenzeneethanamine[4]; *N,α*-Dimethylphenethylamine; *dl*-Desoxyephedrine; N-methyl-*β*-phenylisopropylamine
(D)-Methamphetamine; (+)-Methamphetamine; *d*-Methamphetamine	Methedrine; Desoxyn; chalk; crank; crystal; glass; ice; meth; speed; upper	(*S*)-*N,α*-Dimethylbenzeneethanamine; (*S*)-(+)-*N,α*-Dimethyl-phenethylamine[4]; *d*-1-Phenyl-2-methylaminopropane; *d*-Desoxyephedrine; *d*-N-methyl-*β*-phenyl-isopropylamine
(L)-Methamphetamine; (-)-Methamphetamine	Component in decongestant vapor inhaler (Vick's brand)	(*R*)-(-)-*N,α*-Dimethylphenethylamine; (-)-Deoxyephedrine; (-)-2-(Methylamino)-1-phenylpropane
Phencyclidine	Sernylan; Sernyl; angel dust; PCP; peace pill	1-(1-Phenylcyclohexyl) piperidine[4]
Phentermine	Fastin; Normephentermine	*α,α*-Dimethylbenzeneethanamine[4]; *α,*α-Dimethylphenethylamine[4]; 1,1-Dimethyl-2-phenylethylamine; *α*-Benzylisopropylamine
(DL)-Norephedrine; (±)-Norephedrine	(±)-Phenylpropanolamine; Obestat; Phenedrine;	(*R**,*S**)-(±)-*α*-(1-Aminoethyl)benzenemethanol[4]; -(±)-*α*-(1-Amino-ethyl)benzyl alcohol[4]; (±)-2-Amino-1-phenyl-1-propanol
(L)-Norephedrine; (-)-Norephedrine	Natural form found in Ephedra sinica and other species[5]	(1*R*,2*S*)- 2-Amino-1-phenyl-1-propanol; (1*R*,2*S*)-Norephedrine; *l*-erythro-2-Amino-1-phenylpropan-1-ol
(D)-Norephedrine; (+)-Norephedrine	Metabolite of cathinone in urine of Khat users.	(1*S*,2*R*)- 2-Amino-1-phenyl-1-propanol; (1*S*,2*R*)-Norephedrine; *d*-erythro-2-Amino-1-phenylpropan-1-ol
(+)-Norpseudoephedrine; Cathine	Amorphan; Adiposettin; Reduform; found naturally in Khat plant	(*R**,*R**)-*α*-(1-Aminoethyl)benzenemethanol[4]; *d*-threo-*α*-2-Amino-1-hydroxy-1-phenylpropane; 1*S*,2*S*-(+)-Norpseudoephedrine
L-(+)-Pseudoephedrine; (+)-Pseudoephedrine; *d*-Pseudoephedrine	Afrinol; Novafed; Sinufed; Sudafed; natural form found in Ephedra sinica and other species[5]	(*S*-(*R**,*R**))- *α*-[1-(Methylamino)ethyl]benzenemethanol; (1*S*,2*S*)-(+)-2-Methylamino-1-phenylpropanol; *d*-(alpha-(1-Methylamino)-ethyl)benzyl alcohol; (1*S*,2*S*)-(+)-Pseudoephedrine; *d*-threo-2-Methylamino-1-phenylpropan-1-ol; (+)-*ψ*-Ephedrine
D-(-)-Pseudoephedrine; (-)-Pseudoephedrine		(1*R*,2*R*)-(-)-Pseudoephedrine; (-)-*ψ*-Ephedrine; *l*-threo-2-Methylamino-1-phenylpropan-1-ol; (+)-*ψ*-Ephedrine

(1) Common or generic names. Salts forms are not given for simplicity.

(2) Trade and street names are exemplary, not exhaustive. Street names change over time and by locality. Salts and free base forms are not distinguished.

(3) Other names from Merck Index [17], NIOSH Registry of Toxic Effects of Chemical Substances [18], and MSDS sheets [19,20]. NOTE: For amphetamine and methamphetamine the prefixes R-, D-, d-, and (+)- , although they mean different things, are essentially synonymous for the dextrorotatory stereoisomer and S-, L-, l-, and (-)- are essentially synonymous for the levorotary stereoisomer. Many other synonyms exist.

(4) Uninverted CAS name as given in Merck Index [17].

(5) Extracts of Ephedra species contain various amounts of (+)-Norephedrine, (-)-N-methylephedrine, and (+)-N-methylpseudoephedrine. (+)-Norephedrine is reduced to amphetamine and N-methylephedrine and N-methylpseudoephedrine reduce to N,N-dimethylamphetamine [22, 23]. The presence of these latter two compounds in methamphetamine samples indicate that Ephedra spp. extracts may have been used in the synthesis [24].

Table 4. Limit of detection (LOD), method detection limit (MDL), and sample storage stability[1]

		Estimated LOD[3]		Estimated MDL[4]		Storage Stability[5]	
Compound	Int. std.[2]	µg/sample liq. stds[6]	µg/sample liq. stds[7]	µg/sample cotton gauze	µg/sample Synthetic Wipe	30 days 4 °C	7 days 22 °C
(D)-Amphetamine	D11-Amp	0.1	0.1	0.02		100.5	94.5
	D14-Met	0.1	0.05	0.02	0.02	99.7	87.9
	NMPhen	0.1		0.04		-	-
Cocaine	D11-Amp	0.6		0.2 [9]		99.3	98.8
	D14-Met	0.4		0.1 [9]	0.1 [9]	98.5	91.9
	NMPhen	0.4		0.1 [9]		-	-
(L)-Ephedrine	D11-Amp	0.2	0.2	0.02		95.6	97.2
	D14-Met	0.1	0.1	0.02	0.02	94.8	90.5
	NMPhen	0.1		0.02		-	-
MDEA	N-PAmp	0.1		0.06	0.1	98.9	102.1
MDMA	D11-Amp	0.1		0.02		99.7	111.1
	D14-Met	0.1		0.02	0.04	98.9	103.2
	NMPhen	0.1		0.03		-	-
(D)-Methamphetamine	D11-Amp	0.2	0.07	0.02		98.7	100.6
	D14-Met	0.1	0.05	0.02	0.02	98.0	93.5
	NMPhen	0.1		0.02		-	-
Phencyclidine	D11-Amp	0.6		0.1 [9]		103.7	105.2
	D14-Met	0.4		0.1 [9]	0.5[9]	102.9	97.7
	NMPhen	0.4		0.1 [9]		-	-
Phentermine	D11-Amp	0.2		0.03		102.0	101.5
	D14-Met	0.1		0.03	0.03	101.1	94.3
	NMPhen	0.1		0.04		-	-
(±)-Norephedrine[8]	D11-Amp	0.1	0.05	0.03		94.3	92.7
	D14-Met	0.1	0.05	0.03	0.03	93.6	86.2
	NMPhen	0.1		0.03		-	-
Pseudoephedrine	D11-Amp	0.2	0.2	0.02		100.4	97.9
	D14-Met	0.1	0.1	0.02	0.02	99.6	91.1
	NMPhen	0.1		0.02		-	-

(1) Backup Data Report [4].

(2) Internal standards: D11-Amp = Amphetamine-D_{11}, D14-Met = Methamphetamine-D_{14}, NMPhen = N-Methyl phenethylamine, N-PAmp = N-Propyl amphetamine.

(3) LODs vary according to individual GC columns, instrument conditions and cleanliness, media interferences, and internal standards used. LODs were calculated on liquid standards using the procedure of Burkart (LODs for linear calibration curves are calculated as 3 times the standard error of the lowest three standards analyzed in replicate divided by the slope of the calibration curve) [12].

(4) MDLs are provided to satisfy regulatory agencies requiring this expression of sensitivity. These MDLs are calculated as the standard deviation of six replicates on spiked media analyzed at the 0.1 µg/sample level (except as noted) times the Student's t value for 6 replicates (3.365). (Normally 7 replicates are required.)

(5) Cotton gauze samples were spiked at 3 µg/sample per analyte. Six samples were analyzed immediately after preparation. Six samples were stored at room temperature (about 22 °C) for 7 days and then analyzed. Eighteen samples were stored at >6 °C. Of the 18 samples stored at >6 °C, six each were analyzed at 7 and 21 days and three each were analyzed at 14 and 30 days (Backup Data Report [4].) Apparent recoveries vary according to internal standard used.

(6) These LODs are conservative since the lowest calibration standard for these determinations was 0.1 µg/sample. Lower LODs are achievable with lower concentration calibration standards and operation of the mass spectrometer in the SIM mode.

(7) Typical LODs for a five point calibration curve with single standards at each concentration level. The lowest calibration standard for these determinations was 0.05 µg/sample.

(8) (±)-Norephedrine = (±)-phenylpropanolamine.

(9) MDLs for cocaine and phencyclidine were determined from the 0.3 µg/sample level because the GC peaks for the 0.1 µg/sample level were un-measurable. Precisions at the 0.3 µg/sample level were such that the MDLs calculated to 0.1 µg/sample anyway. This value may be realistic since the 0.1 µg/sample level samples had been stored for one month prior to analysis which may have affected stability.

Table 5. Example of mass spectrometer operation parameters for selected ion monitoring mode[1]

Heptafluorobutyryl-trimethyl-silyl derivatives	Scan window[2]	Acquisition ions (*m/z*) per group[3]									
Acquisition Group 1	8.20 to 10.20	**104**	**118**	**128**	**132**	**210**	**213**	**240**	**244**	**254**	**261**
Acquisition Group 2	10.20 to 13.20	**179**	**240**	**254**	**282**	**296**	**456**				
Acquisition Group 3	13.20 to 19.00	**82**	**162**	**182**	**200**	**242**	**254**	**268**			

GC Peak No.[4]	Target Analytes and Internal Standards	Retention Time[6](min)	Primary Ion (*m/z*)[7] (Quantification Ion)	Secondary ion and approximate relative abundance[8](relative to the Primary Ion)
	Acquisition Group 1:			
13	Amphetamine-D_{11} (I$)[9]	8.46	244	128 70%
5	Amphetamine	8.54	240	118 70%
92	Phentermine	8.72	254	132 12%
81	N-Methyl phenethylamine (I$)[9]	8.54	240	104 100%
68	Methamphetamine-D_{14} (I$)[9]	9.86	261	213 30%
64	Methamphetamine	9.94	254	210 35%
	Acquisition Group 2:			
95	Phenylpropanolamine	10.49	179	240 18%
97	N-Propylamphetamine (I$)[9]	11.05	282	240 85%
36	Ephedrine	11.40	179	254 17%
98	Pseudoephedrine	11.68	179	254 15%
32	Dibromooctafluorobiphenyl[10]	12.82	296	456 100%
	Acquisition Group 3:			
59	MDMA	13.81	254	162 80%
57	MDEA	14.19	268	162 60%
86	Phencyclidine	15.62	200	242 35%
27	Cocaine	18.65	182	82 110%

(1) In this example, 10 analytes and 5 internal standards are grouped into 3 acquisition groups having no more than 10 primary and secondary ions per acquisition group. For 6 analytes and internal standards or less, one acquisition group may be sufficient.

(2) Scan window is in minutes. Actual times are dependent upon GC column and instrument conditions.

(3) Ions (*m/z*) in bold numbers are suggested primary (quantification) ions. For best signal to noise ratio, do not exceed 10 ions per acquisition group. Dwell time per ion (*m/z*) is 50 milliseconds.

(4) GC peak numbers are those in Figures 1 and 2 and Table 10.

(5) The list of analytes and internal standards shown is an example. Analyte(s) and internal standard(s) must be selected according to analytical objectives.

(6) Retention times are dependent upon GC column and instrument conditions.

(7) The better ions for quantification are usually the base peak or those with masses >100 *m/z* and relative abundances >50% of the base peak. These minimize interference from co-eluting hydrocarbons. The suggested primary ions are not necessarily the base peaks in the mass spectra of the analytes, especially if the base peaks are ions common to aromatics (e.g., *m/z* 91) and paraffinic or olefinic hydrocarbons (e.g., *m/z* 42, 57, and 58). Suggested ions for other analytes and internal standards are given in Table 10.

(8) Secondary ions may be used for quantification if the primary ion encounters interference. Secondary ions improve qualitative identification for SIM analyses. The relative abundances given are approximate (±10 to 20%) and depend upon specific instrument tuning and conditions. They are relative to the primary ion and not necessarily to the base peak in the mass spectrum of each analyte. The relative abundance of secondary ions for each analyte needs to be determined from a mass spectrum acquired on the instrument to be used.

(9) (I$) = internal standard. Internal standards must be paired with the appropriate analytes. Tables 7a and 7b give precision and accuracy data for various pairings. Other potentially useful internal standards are given in Tables 8a, 8b, and 10. Highly deuterated analogs of the target analytes are preferred, where available.

(10) Dibromooctafluorobiphenyl is an optional secondary internal standard useful for monitoring autosampler performance and instrument tuning. A shift in the mass axes or the relative abundance of *m/z* 296 to that of *m/z* 456 throughout an analytical sequence will help signal degraded tuning.

Table 6. Suggested spiking schedule for calibration standards and quality control samples

	Add the following to clean shipping containers (e.g., 50-mL polypropylene centrifuge tubes) in the following order.						
Name	Number of Wipes[1,2]	Volume[2] of Isopropanol or Methanol[3]	Volume[2] of Internal Standard Spiking Solution[4,5]	Volume of Target Analyte Spiking Solution[5,6]	Volume of Spiking Solution diluted 1/20[5,7]	Volume[2] of Desorption Solution[8]	Resulting µg/sample as Free Base[9]
Calibration Standards[10]							
CS0	0	3 mL	60 µL		0.0 µL	30 mL	0.00
CS1	0	3 mL	60 µL		2 µL	30 mL	0.02
CS2	0	3 mL	60 µL		5 µL	30 mL	0.05
CS3	0	3 mL	60 µL		10 µL	30 mL	0.1
CS4	0	3 mL	60 µL		20 µL	30 mL	0.2
CS5	0	3 mL	60 µL		60 µL	30 mL	0.6
CS6	0	3 mL	60 µL	10 µL		30 mL	2.0
CS7	0	3 mL	60 µL	30 µL		30 mL	6.0
CS8	0	3 mL	60 µL	100 µL		30 mL	20
CS9	0	3 mL	60 µL	300 µL		30 mL	60
CS10	0	3 mL	60 µL	1000 µL		30 mL	200
Quality Control Samples[11]							
QB (media blank)	1	3 mL	60 µL	0.0 µL		30 mL	0.0
QC (matrix spike)	1	3 mL	60 µL	3-300 µL	or 20-60 µL	30 mL	0.2-60
QD (matrix spike duplicate)	1	3 mL	60 µL	3-300 µL	or 20-60 µL	30 mL	0.2-60

(1) Gauze wipes may be added to the calibration standards but are not necessary if cotton gauze is used. Blank gauze wipes must always be added to the quality control samples, QB, QC, and QD.

(2) a. If a sample consists of 2 gauze wipes, the volume of desorption solution must be increased to 40 mL to accommodate the second wipe. The shipping container should be a 50-mL polypropylene centrifuge tube or equivalent to accommodate the extra volume of desorption solution for 2 wipes. It is not critical to know the exact volume of desorption solution and wetting alcohol used per sample. It only needs to be enough to cover the samples and to permit free percolation through the samples. See step 7.
b. If a set of samples consists predominantly of 2 gauze wipes, the QB, QC, and QD should also consist of 2 wipes and treated as per the samples. The volume of isopropanol (or methanol) added to the QC samples should be increased to 4 mL for 2 gauze wipes to simulate samples containing 2 gauze wipes.

(3) If methanol was used for wipe sampling, it should also be used in the calibration standards, blanks, and QCs instead of isopropanol.

(4) Concentration of internal standards in the internal standard spiking solution is approximately 200 µg/mL as the free base. It is critical to know the exact volume of internal standard spiking solution that is added to the calibration standards, samples, blanks, and quality control samples. The volume spiked into the samples may vary with sample size but the volume spiked into each of the calibration standards must not vary. See step 7b.

(5) For quality control samples, spike onto wipe media within the shipping container. For liquid calibration standards (in lieu of media calibration standards), spike into the isopropanol (or methanol).

(6) Concentration of analytes in the target analyte spiking solution is approximately 200 µg/mL as the free base.

(7) Concentration of analytes in the diluted spiking solution for this table is approximately 10.0 µg/mL as the free base and can be prepared by diluting 100 µL of the target analyte spiking solution to 2 mL in methanol.

(8) Desorption solution is 0.1 M sulfuric acid in deionized water.

(9) This is µg per total sample irrespective of the total desorption solution volume or the area wiped.

(10) Select 6 calibration standards from the list to cover the analytical range plus the blank.

(11) Prepare one set of quality control samples for every 20 samples or less.

Table 7a. Precision and accuracy in scan mode for cotton gauze[1]

Compound	Internal Standard[2]	Range[3] µg/sample	Accuracy	Overall Precision $\hat{S}_{rT}$	Bias	
					Average	Range
(D)-Amphetamine	D_{11}-Amp	0.1-30	8.1	0.0412	-0.0054	-0.0386 to +0.0428
	D_{14}-Met	0.1-30	10.3	0.0472	-0.0227	-0.0844 to +0.0199
	NMPhen	0.1-30	13.2	0.0662	-0.0120	-0.0931 to +0.0290
Cocaine	D_{11}-Amp	1.0-30	15.8	0.0469	+0.0810	+0.0416 to +0.1375
	D_{14}-Met	3-30	13.3	0.0422	+0.0631	+0.0003 to +0.1294
	NMPhen	0.3-30	20.2	0.0729	+0.0823	-0.0092 to +0.1359
(L)-Ephedrine	D_{11}-Amp	0.1-30	9.8	0.0499	-0.0052	-0.0608 to +0.0262
	D_{14}-Met	0.1-30	9.2	0.0397	-0.0266	-0.0463 to +0.0221
	NMPhen	0.1-30	11.2	0.0493	-0.0284	-0.0775 to +0.0302
MDEA	N-PAmp	0.3-29	12.4	0.0618	+0.0127	-0.0475 to +0.0869
MDMA	D_{11}-Amp	0.1-27	14.3	0.0568	+0.0497	+0.0104 to +0.1197
	D_{14}-Met	0.1-27	13.1	0.0558	+0.0389	-0.0189 to +0.0978
	NMPhen	0.3-27	11.9	0.0605	+0.0007	-0.0570 to +0.0360
(D)-Methamphetamine	D_{11}-Amp	0.1-10	9.2	0.0395	+0.0270	-0.0289 to +0.0923
	D_{14}-Met	0.1-30	5.9	0.0302	+0.0015	-0.0440 to +0.0592
	NMPhen	0.3-30	6.9	0.0334	+0.0113	-0.0534 to +0.0448
Phencyclidine	D_{11}-Amp	0.3-30	17.2	0.0639	+0.0670	+0.0059 to +0.1222
	D_{14}-Met	0.3-30	15.9	0.0648	+0.0521	-0.0386 to +0.1039
	NMPhen	0.3-30	16.0	0.0638	+0.0547	-0.0474 to +0.0886
Phentermine	D_{11}-Amp	0.1-30	10.1	0.0444	+0.0261	-0.0067 to +0.0912
	D_{14}-Met	0.1-30	10.4	0.0527	+0.0041	-0.0600 to +0.0674
	NMPhen	1.0-30	8.2	0.0400	+0.0121	-0.0378 to +0.0407
(±)-Norephedrine[4]	D_{11}-Amp	0.1-30	12.2	0.0571	+0.0241	+0.0500 to +0.0610
	D_{14}-Met	0.1-30	12.5	0.0638	-0.0005	-0.0674 to +0.0708
	NMPhen	0.1-30	13.3	0.0675	+0.0036	-0.0533 to +0.0476
Pseudoephedrine	D_{11}-Amp	0.1-30	10.0	0.0507	-0.0059	-0.0530 to +0.0441
	D_{14}-Met	0.1-30	12.3	0.0507	-0.0392	-0.0737 to +0.0301
	NMPhen	1.0-30	15.6	0.0716	-0.0350	-0.0813 to +0.0617

(1) Backup Data Report [4]. Values are for the heptafluorobutyryl and mixed heptafluorobutyryl-trimethylsilyl derivatives and analysis by GC-MS in scan mode. Each sample consisted of a pair of 3″ x 3″ 12-ply cotton gauze pads. There were 6 replicate samples per concentration level and six concentration levels evaluated from approximately 0.1 to 30 µg/sample.

(2) Internal Standards

Deuterated:
D_{11}-Amp = Amphetamine-D_{11}
D_{14}-Met = Methamphetamine-D_{14}

Non-deuterated:
NMPhen = N-Methyl phenethylamine
N-PAmp = N-Propyl amphetamine

(3) Range used for calculation of precision, accuracy, and bias. The entire range studied for all analytes was approximately 0.1 to 30 µg/sample (1xLOQ to 300xLOQ).

(4) (±)-Norephedrine = (±)-phenylpropanolamine.

Table 7b. Precision and accuracy in scan mode for synthetic wipe[1]

Compound	Internal Standard[2]	Range[3] µg/ sample	Accuracy	Overall Precision $\hat{S}_{rT}$	Bias	
					Average	Range
(D)-Amphetamine	D14-Met	0.1-30	17.2	0.0611	-0.0712	-0.1066 to -0.0468
Cocaine	D14-Met	0.3-30	17.7	0.0901	-0.0014	-0.0246 to +0.0252
(L)-Ephedrine	D14-Met	0.1-30	10.7	0.0432	-0.0362	-0.0638 to -0.0039
MDEA	N-PAmp	0.3-29	9.6	0.0425	-0.0240	-0.0453 to +0.0416
MDMA	D14-Met	0.3-27	11.4	0.0498	-0.0297	-0.0612 to +0.0095
(D)-Methamphetamine	D14-Met	0.1-30	8.7	0.0430	-0.0114	-0.0483 to +0.0625
Phencyclidine	D14-Met	0.3-30	13.0	0.0391	+0.0658	+0.0216 to +0.1418
Phentermine	D14-Met	0.3-30	10.4	0.0295	-0.0560	-0.0917 to -0.0266
(±)-Norephedrine[4]	D14-Met	0.1-30	12.6	0.0577	+0.0282	-0.0220 to +0.0937
Pseudoephedrine	D14-Met	0.1-30	13.5	0.0592	-0.0352	-0.1001 to -0.0020

(1) Backup Data Report [4]. Values are for the heptafluorobutyryl and mixed heptafluorobutyryl-trimethylsilyl and analysis by GC-MS in scan mode (see p 9109-1 for GC and MS conditions). Each sample consisted of a pair of 3" x 3" 12-ply cotton gauze pads. There were 6 replicate samples per concentration level and six concentration levels evaluated from approximately 0.1 to 30 µg/sample.
(2) Internal Standards: D14-Met = Methamphetamine-D_{14}, N-PAmp = N-Propyl amphetamine.
(3) Range used for calculation of precision, accuracy, and bias. The entire range studied for all analytes was approximately 0.1 to 30 µg/sample (1xLOQ to 300xLOQ).
(4) (±)-Norephedrine = (±)-phenylpropanolamine.

Table 8a. Recommended internal standards[1] and best application

COMPOUND NAME	CAS	MW as free base	Quant. Ion	Secondary Ion	COMMENTS
(±)-Amphetamine-D_{11}	not available	146.12	244	128	Preferred analog for amphetamine
(±)-Amphetamine-D_8	145225-00-9	143.15	243	126	Alternate for amphetamine-D_{11}
(±)-Amphetamine-D_6	not available	141.16	244	123	Alternate for amphetamine-D_{11}
(±)-Methamphetamine-D_{14}	not available	163.12	261	213	Preferred methamphetamine analog
(±)-Methamphetamine-D_{11}	152477-88-8	160.15	260	213	Alternate for methamphetamine-D_{14}
(±)-Methamphetamine-D_9	not available	158.16	261	213	Alternate for methamphetamine-D_{14}
N-Methylphenethylamine	589-08-2	135.23	240	104	Alternate for methamphetamine-D_{14}
Phencyclidine-D_5	60124-86-9	248.35	205	96	Use only for phencyclidine
MDEA-D_6[2]	160227-44-1	213.22	268	162	Use only for MDEA
N-Propylamphetamine[2]	not available	177.29	282	240	Alternate for MDEA-D_6

(1) Care must be exercised in the selection of internal standards for each analyte because of differences in derivatization efficiencies due to structural differences.
   a. Deuterated analogs of each target analyte may be acceptable as internal standards if they are isotopically pure enough and their ions do not interfere with the quantification ions (usually base peaks) of the target analyte, especially at the limit of detection for the target analyte. Conversely it is also important that ions in the target analyte, especially at high concentrations, do not interfere with the quantification ion (usually base peaks) of any deuterated analog used as the internal standard.
   b. The more highly deuterated an analog, the more it will chromatographically separate from the target analyte, reducing interference from common ions.
   c. Phentermine and mephentermine have been used as internal standards. Such use is not advised in this method because of their reported occasional use as adulterants in certain illicit drugs such as MDMA.
(2) N-Propylamphetamine and MDEA-D_6 are only applicable to MDEA and other hindered amines (e.g., fenfluramine and MBDB) due to similar steric hindrance at the nitrogen (N-ethyl or N-propyl substitution) which affects derivatization efficiency.

Table 8b. Recommended best application of internal standards[1]

	Recommended Deuterated Internal Standards				Recommended Alternate Non-deuterated Internal Standards[3]	
Target Analyte	Amphetamine-D_{11}[2]	Methamphetamine-D_{14}[2]	MDEA-D_6[1]	Phencyclidine-D_5	N-Methylphenethylamine	N-Propylamphetamine[1]
Amphetamine	X	X			X	
Cocaine	X	X			X	
Ephedrine	X	X			X	
MDEA			X			X
MDMA	X	X			X	
Methamphetamine	X	X			X	
Phencyclidine	X	X		X	X	
Phentermine	X	X			X	
(±)-Norephedrine[4]	X	X			X	
Pseudoephedrine	X	X			X	

(1) N-Propylamphetamine and MDEA-D_6 are only applicable to MDEA and other hindered amines (e.g., fenfluramine and MBDB) due to similar steric hindrance at the nitrogen (N-ethyl or N-propyl substitution) which affects derivatization efficiency.

(2) The alternate deuterated compounds listed in part A above may be used. Avoid ring-labeled amphetamine-D_5 (CAS 65538-33-2) since the primary (quantification) ion is the same as for amphetamine and GC peaks overlap significantly. Also avoid methamphetamine-D_5 (CAS 60124-88-1) since GC peaks significantly overlap.

(3) The listed non-deuterated compounds are acceptable as internal standards for the listed target analytes for the applicable ranges and limits of detection listed in Tables 7a and 7b respectively. Non-deuterated internal standards might not be permissible. Consult regulations of agency having legal jurisdiction.

(4) (±)-Norephedrine is the same as (±)-phenylpropanolamine.

Table 9a. Recovery from wall (latex painted) with various solvents; one wipe compared with the sum of two wipes[1,2]

	Water[3]			Isopropanol			Methanol		
	First Wipe		Plus Second Wipe[4]	First Wipe		Plus Second Wipe[4]	First Wipe		Plus Second Wipe[4]
Test Compounds[5]	Percent	%RSD	Percent	Percent	%RSD	Percent	Percent	%RSD	Percent
Amphetamine	51	14	56	67	6.0	78	90	4.0	96
Cocaine	36	22	36	69	22	80	89	9.1	94
Ephedrine	48	23	52	76	7.4	85	91	4.4	96
MDMA	40	20	44	61	9.0	70	88	5.3	94
MDEA	45	22	50	69	12	80	90	11	97
Methamphetamine	46	16	50	64	7.4	75	87	3.5	94
Phencyclidine	27	26	30	64	9.6	73	86	5.2	91
Phentermine	53	9.2	58	78	6.6	91	95	2.9	101
Phenylpropanolamine	58	21	62	80	9.3	95	85	5.0	94
Pseudoephedrine	49	20	53	73	7.0	85	95	3.3	101

(1) Backup Data Report for NIOSH 9109 [4]. Area of each sample was 100 cm^2.

(2) Wall was an existing standard gypsum board wall painted with a latex based paint. Painted surface was at least one year old. There were six replicates for each solvent tested.

(3) Water was deionized water (ASTM type II). Note low recovery and high %RSD.

(4) For the serial wipe study, each 100-cm^2 area was wiped again with a fresh pre-wetted gauze wipe and the amount recovered was determined separately. In practice, a second (serial) wipe is included with the first gauze wipe; both gauze wipes constitute a single sample. The percent recoveries shown in the column represent the sum of the amounts recovered in both the first and second wipes.

(5) Each pre-measured area was spiked with 3 µg of each analyte in methanol and the methanol allowed to dry for several minutes prior to wipe sampling.

Table 9b. Recovery of methamphetamine from various surfaces with various solvents; one wipe compared with the sum of two wipes[1]

		Isopropanol			Methanol		
		First Wipe		Plus Second Wipe[2]	First Wipe		Plus Second Wipe[2]
Surface Material[3]	Replicates	Percent	%RSD	Percent	Percent	%RSD	Percent
Enamel (lid of washing machine)	4[4]	58	5.7	68	81	2.4	87
Vinyl veneer on particle board	4[5]	60	5.2	68	81	4.8	89
Latex painted wall	6[4]	64	7.4	75	87	3.5	94
Refrigerator door	2[5]	65	2.9	76	91	4.0	92
Varnished hardwood panel	2[6]	72	5.4	76	82	3.7	86
Formica® countertop	4[5]	75	4.9	82	87	3.8	91

(1) Backup Data Report for NIOSH 9109 [4]. Area of each sample was 100 cm^2.

(2) For the serial wipe study, each 100-cm^2 area was wiped again with a fresh pre-wetted gauze wipe and the amount recovered was determined separately. In practice, a second (serial) wipe is included with the first gauze wipe; both gauze wipes constitute a single sample. The percent recoveries shown in the column represent the sum of the amounts recovered in both the first and second wipes.

(3) The refrigerator door and the washing machine lid were from used appliances. The vinyl-veneered particle board (a book shelf), the Formica® countertop, and the varnished hardwood paneling were all purchased new. All surfaces of used and new materials were pre-cleaned with multiple rinses of methanol prior to spiking. Each pre-measured 100-cm^2 square was spiked with 3 µg methamphetamine.

(4) Samples were taken using the side-to-side and then top-to-bottom wiping technique.

(5) Half of the samples were wiped using the side-to-side wiping technique and half were wiped using the concentric squares wiping technique. There were no significant differences in recoveries. Percent recoveries and %RSDs are for both techniques combined.

(6) Samples were taken each time using only top-to-bottom wiping with the grain of the wood in an "N" pattern.

TABLE 10. Gas chromatographic retention times for heptafluorobutyryl and trimethylsilyl derivatives of selected drugs of abuse, precursors, and potential adulterants[1]

GC Peak No.	Compound	Derivative Form[2]	Notes[3]	Retention Time Minutes[4]	Relative Retention Time		Ions (Significant *m/z*)[7]		
					(5)	(6)	1′	2′[7]	3′[7]
1	Acetaminophen[8]	N,N′- bis-TMS-	Pri.deriv.	12.30	0.9594	1.2374	206	280 [90]	295 [70]
2	Acetaminophen[8]	N-HFB-N′-TMS-	Minor peak	10.37	0.8089	1.0433	330	404 [80]	419 [30]
3	Aminorex	N,N′- bis-HFB-	Major peak	14.12	1.1014	1.4205	385	342 [30]	169 [40]
4	Aminorex	N-HFB-N′-TMS-	Major peak	16.59	1.2941	1.6690	261	146 [48]	128 [45]
5	Amphetamine	N-HFB-	Pri.deriv.	8.54	0.6661	0.8592	240	118 [70]	169 [20]
6	Amphetamine	N-HFB-N-TMS-	OS artifact	9.21	0.7184	0.9266	312	91 [50]	313 [10]
7	Amphetamine-D_5, ring labeled (I$)[9]	N-HFB-	Pri.deriv.	8.47	0.6607	0.8521	240	123 [85]	96 [55]
8	Amphetamine-D_5,ring labeled (I$)[9]	N-HFB-N-TMS-	OS artifact	9.17	0.7153	0.9225	312	96 [45]	73 [95]
9	Amphetamine-D_6 (I$)[9]	N-HFB-	Pri.deriv.	8.45	0.6591	0.8501	244	123 [70]	93 [45]
10	Amphetamine-D_6 (I$)[9]	N-HFB-N-TMS-	OS artifact	9.14	0.7129	0.9195	316	93 [40]	73 [75]
11	Amphetamine-D_8 (I$)[9]	N-HFB-	Pri.deriv.	8.46	0.6599	0.8511	243	126 [75]	96 [40]
12	Amphetamine-D_8 (I$)[9]	N-HFB-N-TMS-	OS artifact	9.16	0.7145	0.9215	315	96 [25]	73 [55]
13	Amphetamine-D_{11} (I$)[9]	N-HFB-	Pri.deriv.	8.46	0.6599	0.8511	244	128 [70]	98 [45]
14	Amphetamine-D_{11} (I$)[9]	N-HFB-N-TMS-	OS artifact	9.14	0.7129	0.9195	316	98 [60]	73 [70]
15	Atropine[8]	O-TMS-	Pri.deriv.	18.86	1.4711	1.8974	124	361 [9]	82 [17]
16	BDB	N-HFB-	Pri.deriv.	13.35	1.0413	1.3431	135	176 [50]	254 [12]
17	BDB	N-HFB-N-TMS-	OS artifact	13.65	1.0647	1.3732	326	135 [60]	73 [90]
18	Benzoyl ecgonine	O-TMS-		19.18	1.4961	1.9296	82	240 [45]	361 [25]
19	Benzyl piperazine[10] (“Legal XTC”)	N-HFB-	Pri.deriv.	13.73	1.0710	1.3813	91	372 [30]	281 [30]
20	4-Bromo-2,5-DMPEA[11] (Nexus)	N-HFB-	Pri.deriv.	15.79	1.2317	1.5885	242	244 [98]	229 [75]
21	4-Bromo-2,5-DMPEA[11] (Nexus)	N-HFB-N-TMS-	OS artifact	16.22	1.2652	1.6318	229	231 [98]	298 [85]
22	Bupropion (Wellbutrin®, Zyban®)	parent		12.15	0.9477	1.2223	44	100 [45]	111 [20]
23	Caffeine[8]	parent		14.89	1.1615	1.4980	194	109 [45]	67 [45]
24	S-(-)-Cathinone (from Khat plant)	N-HFB-	Pri.deriv.	10.21	0.7964	1.0272	105	77 [45]	240 [15]
25	S-(-)-Cathinone (from Khat plant)	N-HFB-N-TMS-	OS artifact	10.89	0.8495	1.0956	105	312 [68]	77 [55]
26	Chlorpheniramine[8]	parent		16.74	1.3058	1.6841	203	205 [32]	167 [22]
27	Cocaine	parent		18.65	1.4548	1.8763	82	182 [90]	303 [20]
28	Codeine	O-HFB-	Minor peak	19.59	1.5281	1.9708	282	283 [20]	
29	Codeine	O-TMS-	Pri.deriv.	20.72	1.6162	2.0845	371	343 [25]	234 [55]
30	Dextromethorphan[8]	parent		18.10	1.4119	1.8209	271	270 [62]	214 [40]
31	Diazepam (Valium® etc.)	parent		20.80	1.6225	2.0926	256	283 [90]	284 [75]
32	Dibromooctafluorobiphenyl (I$)[9]	parent		12.82	1.0000	1.2897	296	456 [100]	454 [50]
33	N,N-Dimethyltryptamine (DMT)	N-HFB-	Pri.deriv.	13.00	1.0140	1.3078	58	129 [15]	42 [15]
34	N,N-Dimethyltryptamine (DMT)	N-TMS-	Minor peak	15.02	1.1716	1.5111	58	73 [12]	202 [10]
35	Ecgonine, methyl ester	O-TMS-		11.72	0.9142	1.1791	82	96 [75]	83 [75]
36	Ephedrine	N-HFB-O-TMS-	Pri.deriv.	11.40	0.8892	1.1469	179	254 [17]	327 [10]
37	1S,2R(+)-Ephedrine-D_3 (I$)[9]	N-HFB-O-TMS-	Pri.deriv.	11.36	0.8861	1.1429	179	257 [20]	330 [10]
38	N-Ethyl amphetamine	N-HFB-	Pri.deriv.	10.33	0.8058	1.0392	268	240 [35]	118 [15]
39	Fenfluramine[8]	N-HFB-	Pri.deriv.	10.12	0.7894	1.0181	268	240 [35]	159 [22]
40	Fenfluramine-D_{10} (I$)[9]	N-HFB-	Pri.deriv.	10.01	0.7808	1.0070	277	245 [35]	160 [15]

Table 10 continued

TABLE 10 (continued). Gas chromatographic retention times for heptafluorobutyryl and trimethylsilyl derivatives of selected drugs of abuse, precursors, and potential adulterants[1]

GC Peak No.	Compound	Derivative Form[2]	Notes[3]	Retention Time Minutes[4]	Relative Retention Time		Ions (Significant *m/z*)[7]		
					[5]	[6]	1′	2′[7]	3′[7]
41	Fentanyl (Sublimaze® etc.)	parent		22.97	1.7917	2.3109	245	146 [60]	189 [33]
42	Flunitrazepam (Rohypnol®, roofies)[10]	parent		22.20	1.7317	2.2334	312	285 [95]	286 [90]
43	Hydrocodone (Lortab® etc.)	HFB-	Minor peak	19.47	1.5187	1.9588	495	438 [50]	298 [40]
44	Hydrocodone (Lortab® etc.)	TMS-	Minor peak	20.82	1.6240	2.0946	371	356 [50]	234 [55]
45	Hydrocodone (Lortab® etc.)	parent	Pri.deriv.	20.93	1.6326	2.1056	299	242 [50]	243 [35]
46	Hydromorphone (Dilaudid®)	O-HFB-O′-TMS-	Minor peak	19.85	1.5484	1.9970	308	267 [92]	358 [75]
47	Hydromorphone (Dilaudid®)	O,O′-bis-TMS-	Minor peak	20.98	1.6365	2.1107	414	429 [100]	234 [75]
48	Hydromorphone (Dilaudid®)	O-TMS-	Pri.deriv.	21.21	1.6544	2.1338	357	300 [55]	342 [28]
49	Ketamine (“special K”)[8][10]	parent	Major peak	15.24	1.1888	1.5332	180	182 [32]	209 [22]
50	Lidocaine[8]	N-TMS-	Major peak	13.69	1.0679	1.3773	86	220 [75]	73 [45]
51	Lidocaine[8]	parent	Major peak	15.28	1.1919	1.5372	86	58 [10]	91 [5]
52	LSD (MW-519, scanned only to 470)	HFB-	Pri.deriv.	24.61	1.9197	2.4759	417	221 [95]	418 [45]
53	MBDB	N-TMS-	Minor peak	14.30	1.1154	1.4386	144	73 [50]	135 [15]
54	MBDB	N-HFB-	Pri.deriv.	14.44	1.1264	1.4527	268	176 [75]	210 [50]
55	MDA	N-HFB-	Pri.deriv.	12.54	0.9782	1.2616	135	162 [55]	240 [12]
56	MDA	N-HFB-N-TMS-	OS artifact	12.88	1.0047	1.2958	312	73 [58]	135 [48]
57	MDEA[10]	N-HFB-	Pri.deriv.	14.19	1.1069	1.4276	268	162 [60]	240 [50]
58	MDEA-D6 (I$)[9]	N-HFB-	Pri.deriv.	14.13	1.1022	1.4215	274	165 [46]	244 [35]
59	MDMA[10]	N-HFB-	Pri.deriv.	13.81	1.0772	1.3893	254	162 [80]	135 [45]
60	Meperidine (Demerol® etc.)	parent		13.97	1.0897	1.4054	247	246 [55]	218 [50]
61	Mephentermine	N-HFB-	Pri.deriv.	10.38	0.8097	1.0443	268	210 [95]	
62	Mescaline	N-HFB-	Pri.deriv.	14.68	1.1451	1.4769	181	194 [45]	179 [30]
63	Mescaline	N-HFB-N-TMS-	OS artifact	15.26	1.1903	1.5352	181	73 [35]	
64	Methamphetamine	N-HFB-	Pri.deriv.	9.94	0.7754	1.0000	254	210 [35]	118 [22]
65	Methamphetamine-D5 (I$)[9]	N-HFB-	Pri.deriv.	9.86	0.7691	0.9920	258	213 [30]	92 [20]
66	Methamphetamine-D9 (I$)[9]	N-HFB-	Pri.deriv.	9.84	0.7676	0.9899	261	213 [30]	123 [18]
67	Methamphetamine-D11 (I$)[9]	N-HFB-	Pri.deriv.	9.84	0.7676	0.9899	260	213 [25]	126 [20]
68	Methamphetamine-D14 (I$)[9]	N-HFB-	Pri.deriv.	9.86	0.7691	0.9920	261	213 [30]	128 [20]
69	Methaqualone	parent		18.31	1.4282	1.8421	235	250 [30]	233 [28]
70	S-(-)-Methcathinone (“Cat”)	N-HFB-	Pri.deriv.	10.55	0.8229	1.0614	254	210 [35]	105 [100]
71	4-Methoxyamphetamine	N-HFB-	Pri.deriv.	11.40	0.8892	1.1469	121	148 [40]	240 [10]
72	4-Methoxyamphetamine	N-HFB-N-TMS-	OS artifact	11.87	0.9259	1.1942	312	121 [100]	73 [100]
73	cis-(±)-4-Methylaminorex (“U4Euh”)	N,N′-bis-HFB-	Minor peak	13.78	1.0749	1.3863	399	169 [70]	160 [75]
74	cis-(±)-4-Methylaminorex (“U4Euh”)	N-HFB-N′-TMS-	Pri.deriv.	16.78	1.3089	1.6881	275	160 [60]	117 [30]
75	(-)-N-Methylephedrine[11]	O-TMS-	Pri.deriv.	9.66	0.7535	0.9718	72	73 [13]	163 [5]
76	(+)-N-Methylephedrine[11]	O-TMS-	Pri.deriv.	9.71	0.7574	0.9769	72	73 [13]	163 [5]
77	N-Methylphenethylamine (I$)[9]	N-HFB-	Pri.deriv.	9.54	0.7441	0.9598	240	104 [100]	169 [40]
78	Methylphenidate (Ritalin®)	N-HFB-	Pri.deriv.	15.38	1.1997	1.5473	280	281 [10]	

Table 10 continued

TABLE 10 (continued). Gas chromatographic retention times for heptafluorobutyryl and trimethylsilyl derivatives of selected drugs of abuse, precursors, and potential adulterants[1]

GC Peak No.	Compound	Derivative Form[2]	Notes[3]	Retention Time Minutes[4]	Relative Retention Time		Ions (Significant *m/z*)[7]		
					[5]	[6]	1′	2′[7]	3′[7]
79	N-Methyl pseudoephedrine[12]	O-TMS-	Pri.deriv.	9.66	0.7535	0.9718	72	73 [13]	163 [5]
80	Morphine	O-HFB-O′-TMS-	Minor peak	19.97	1.5577	2.0091	340	324 [28]	341 [25]
81	Morphine	O,O′-bis-TMS-	Pri.deriv.	21.08	1.6443	2.1207	429	414 [50]	401 [35]
82	Nicotine	parent		8.86	0.6911	0.8913	84	133 [35]	162 [18]
83	Norpseudoephedrine (Cathine)	N-HFB-O-TMS-	Pri.deriv.	10.39	0.8105	1.0453	179	180 [18]	240 [18]
84	Norpseudoephedrine (Cathine)	N-HFB-N,O-bis-TMS-	OS artifact	11.26	0.8783	1.1328	179	180 [18]	312 [10]
85	Oxycodone (OxyContin®)	TMS-	Pri.deriv.	21.66	1.6895	2.1791	387	388 [30]	372 [30]
86	Phencyclidine (PCP)	parent	Major peak	15.62	1.2184	1.5714	200	242 [35]	243 [25]
87	Phencyclidine (PCP)	N-HFB-dehydro-	Artifact	19.85	1.5484	1.9970	91	159 [60]	280 [10]
88	Phencyclidine-D5 (I$)[9]	parent	Major peak	15.59	1.2161	1.5684	205	96 [42]	246 [25]
89	Phencyclidine-D5 (I$)[9]	N-HFB-dehydro-	Artifact	19.83	1.5468	1.9950	96	164 [65]	280 [10]
90	Phenethylamine[8]	N-HFB-	Pri.deriv.	8.58	0.6693	0.8632	104	91 [60]	169 [15]
91	Phenethylamine[8]	N-HFB-N-TMS-	Pri.deriv.	9.51	0.7418	0.9567	298	105 [40]	220 [10]
92	Phentermine[8]	N-HFB-	Pri.deriv.	8.72	0.6802	0.8773	254	132 [12]	214 [8]
93	4-Phenyl-1-butylamine (I$)[9]	N-HFB-	Pri.deriv.	11.47	0.8947	1.1539	91	104 [25]	176 [22]
94	Phenylephrine[8]	N-HFB-O,O′-bis-TMS-	Pri.deriv.	13.94	1.0874	1.4024	267	268 [25]	240 [12]
95	Phenylpropanolamine	N-HFB-O-TMS-	Pri.deriv.	10.49	0.8183	1.0553	179	180 [18]	240 [18]
96	Phenylpropanolamine	N-HFB-N,O-bis-TMS-	OS artifact	11.01	0.8588	1.1076	179	180 [18]	312 [10]
97	N-Propyl amphetamine (I$)[9]	N-HFB-	Pri.deriv.	11.05	0.8619	1.1117	282	240 [85]	118 [20]
98	Pseudoephedrine	N-HFB-O-TMS-	Pri.deriv.	11.68	0.9111	1.1751	179	254 [15]	73 [75]
99	Theophylline [8]	parent	Major peak	15.50	1.2090	1.5594	237	252 [57]	223 [14]
100	Trifluoromethylphenyl piperazine [10]	N-HFB-	Pri.deriv.	13.76	1.0733	1.3843	200	229 [70]	172 [73]

(1) Actual retention times may vary depending on individual GC column and GC conditions. Gas chromatographic and mass spectrometer conditions used as on p. 9109-1.

(2) Derivative form. HFB = heptafluorobutyryl derivative. TMS = trimethylsilyl derivative. N- = attachment to nitrogen atom. O- = attachment to oxygen atom. Not all forms are presented. Trifluoroacetyl derivatives are not presented. Underivatized compounds are identified as a "parent" compound. Parent compounds that have poor chromatographic peak shapes under the conditions used are not presented. Spectra for the derivatives are given in the Backup Data Report (Appendix-II) [4].

(3) Major and minor peaks are identified where two or more forms are possible. In some cases two major peaks may exist. Pri.deriv. = Primary derivative, a major peak. The major peak or the primary derivative should be used for quantitation. OS artifact = Oversilylation artifact [14]. Oversilylation artifacts occur where a primary amine is substituted with both a heptafluorobutyryl and a trimethylsilyl group. Under the specified conditions of extraction and derivatization these remain as minor components and are of little concern.

(4) Retention times are not the same as in Table 10 or Figures 1 and 2 in this method since these data were obtained on a different instrument. Relative retention times should be approximately the same.

(5) Retention time relative to 4,4′-dibromooctafluorobiphenyl.

(6) Retention time relative to the heptafluorobutyryl derivative of methamphetamine.

(7) Significant ions that can be used for quantification and qualitative identification are given. The base peaks are not necessarily included, especially if they are low mass (<100 AMU). Numbers in brackets indicate the approximate relative abundance of the secondary (2′) and tertiary (3′) ions relative to the primary (1′) ion and not necessarily to the base peak of each mass spectrum. Relative abundance varies with different tuning criteria and cleanliness of the mass spectrometer source. The 1′ or 2′ ions are recommended for quantification. All ions are selected as much as possible above *m/z* 100 to avoid interference from low mass co-eluting interferences. The 2′ and 3′ ions are selected as much as possible for nearness to the primary ion to minimize false negatives from skewing of spectra as the mass spectrometer source becomes contaminated with use. Ubiquitous ions (e.g., *m/z* 73, 91, and 169) are avoided as much as possible.

(8) Intentional or unintentional adulterants. For example, phentermine may be added to MDMA and caffeine added to methamphetamine intentionally. Chlorpheniramine is an unintentional adulterant when pseudoephedrine containing chlorpheniramine is used as a methamphetamine precursor.

(9) (I$) = Internal standard. The best results are obtained using internal standards that are deuterated analogs of the target analyte, or those that are chemically and structurally similar to the target analytes.

(10) Typical "club drugs" (piperazine analogs as ecstasy substitutes, ketamine and flunitrazepan as predatory drugs).

(11) 4-Bromo-2,5-DMPEA = 4-Bromo-2,5-dimethoxyphenethylamine (Nexus).

(12) Presence of (+)-norephedrine, N-methylpseudoephedrine and/or N-methylephedrine in pseudoephedrine or ephedrine indicates extracts of Ephedra spp. as source of methamphetamine precursor. Presence of amphetamine and N,N-dimethylamphetamine in methamphetamine final product also suggests the same source [22, 23, 24].

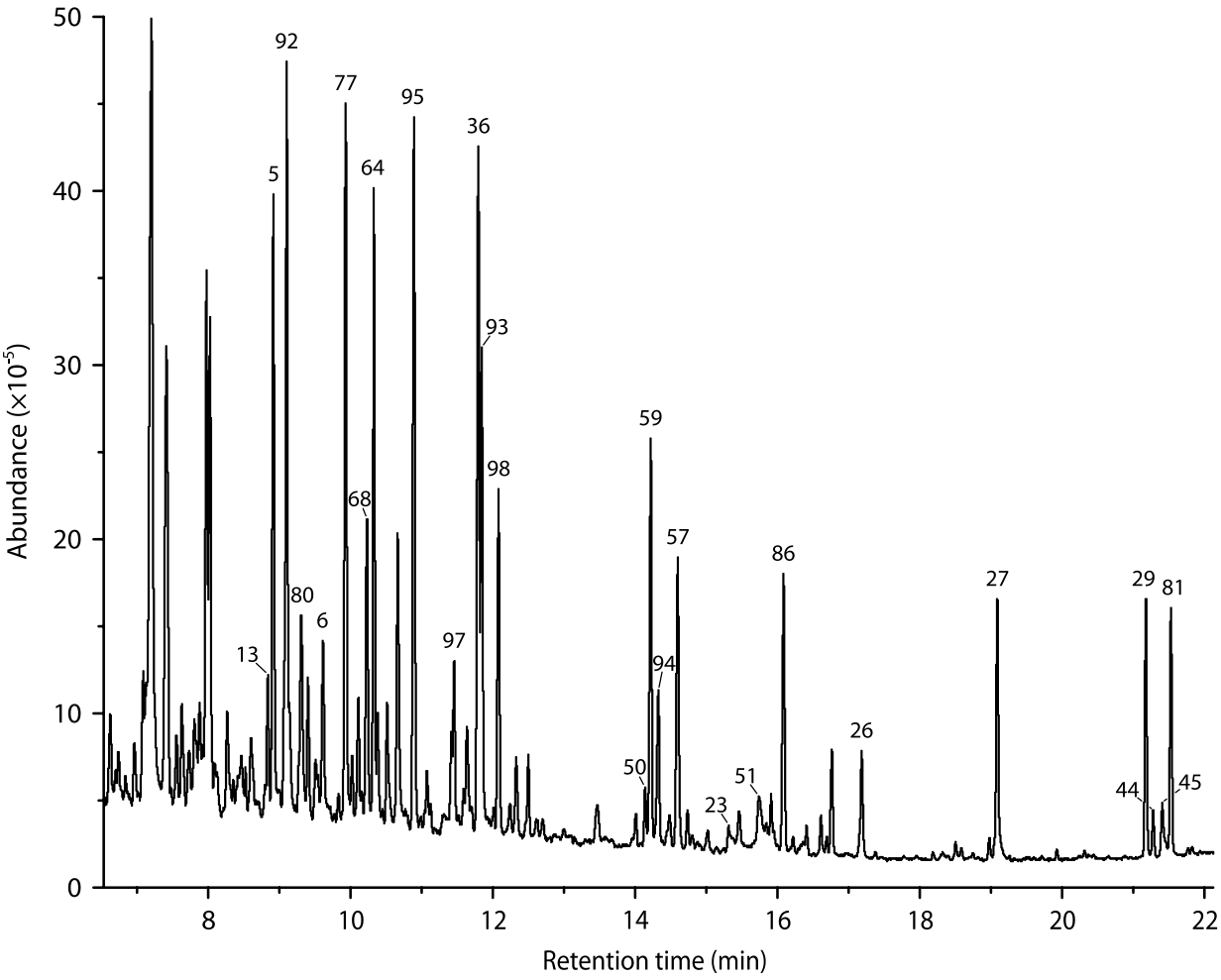

Figure 1. Typical chromatogram of mixed heptafluorobutyryl and trimethylsilyl derivatives by GC-MS in scan mode (time in minutes)

GC Peak Identification: See Table 10 for identification of numbered GC peaks. (But note that retention times in Table 10 do not correspond to those in Figure 1 because a different U.S. Pharmacopeia (USP) G27 column and instrument was used.)

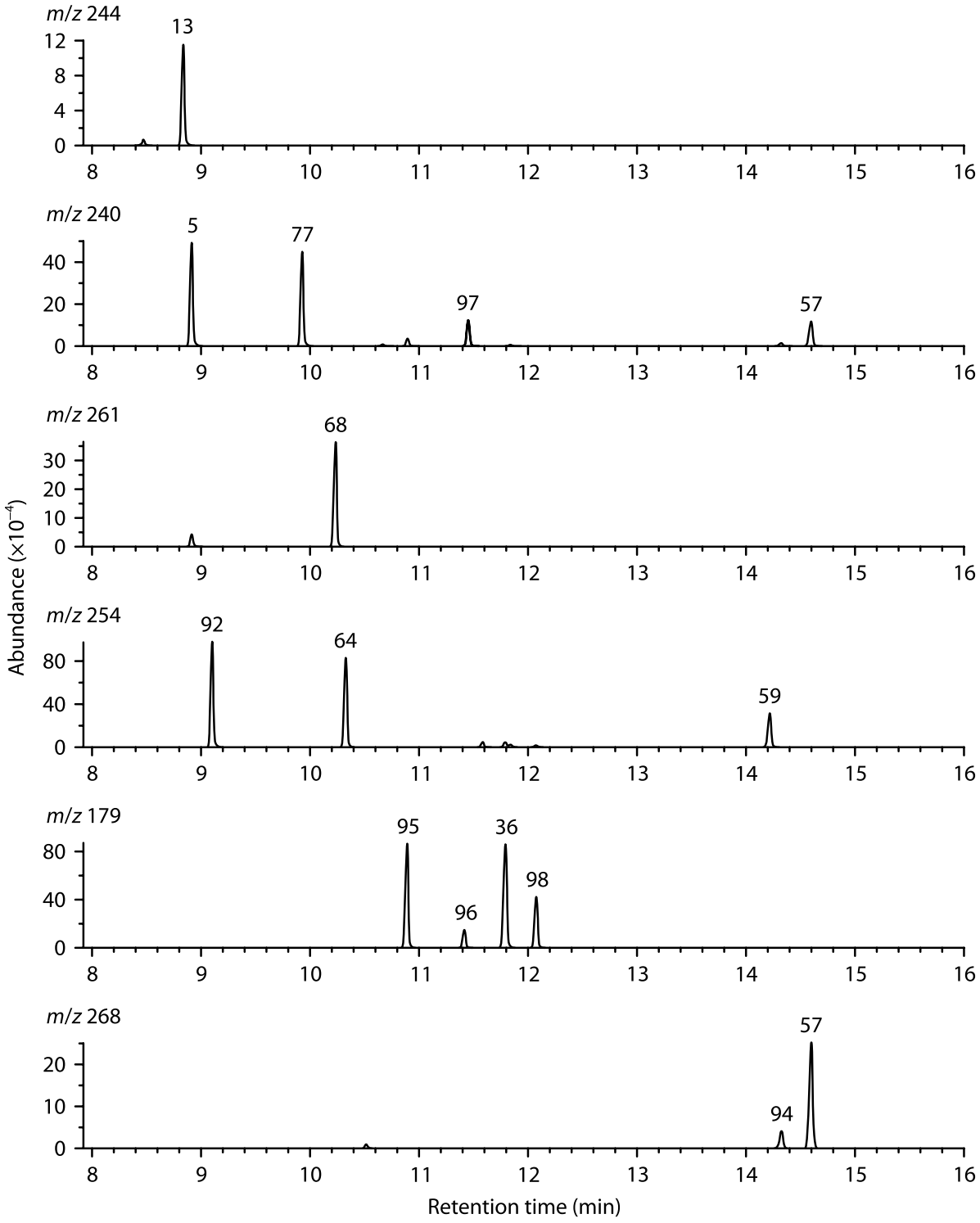

Figure 2. Typical extracted ion chromatograms (EIC) of mixed heptafluorobutyryl and trimethylsilyl derivatives by GC-MS in scan mode (time in minutes)

GC Peak Identification: See Table 10 for identification of numbered GC peaks. (But note that retention times in Table 10 do not correspond to those in Figure 1 because a different U.S. Pharmacopeia (USP) G27 column and instrument was used.)

APPENDIX:

A. REAGENTS and SOLUTIONS:

1. 4,4'-Dibromooctafluorobiphenyl is optional. It is useful for monitoring instrument tuning and autosampler performance.
2. Primary amines form Schiff bases and enamines with ketones and aldehydes. These may in turn form derivatives with the acylating reagents. The use of acetone must strictly be avoided prior to the analytes being derivatized. Glassware and equipment rinsed with acetone must be thoroughly dried. Toluene should be avoided for making up standard solutions because it usually contains benzaldehyde, an oxidation product of toluene. Condensation products have been observed between primary amines and benzaldehyde. The only solvents recommended for the preparation of stock solutions and dilutions thereof are methanol (preferably) and isopropanol.

B. EQUIPMENT:

1. Wipe media: Besides cotton gauze, 4"X4" (10 cm x 10 cm) 4-ply MIRASORB® (Johnson and Johnson), and 4"X4" (10 cm x 10 cm) AlphaWipe® (TX1004, Texwipe Corp) were acceptable wipe media and can be used in the absence of cotton gauze. MIRASORB®, a non-woven cotton/polyester blend, is discontinued but counterparts exist that claim to be of identical construction and fiber composition. AlphaWipe® is a hydrophilic, highly adsorbent, tightly knitted continuous filament polyester wipe. Precision and accuracy data for MIRASORB® are given in the Backup Data Report [4].
2. Shipping containers: The 50-mL polypropylene centrifuge tubes with caps are preferred for one or two gauze wipes and are not as breakable as the 40-mL VOA vials. The 40-mL VOA vials are acceptable for single gauze wipes. Larger containers (glass with a PTFE lined cap) should be used for combining more than two gauze wipes into a single sample. The size of the container for two or more wipes should be approximately 25 mL per gauze wipe (e.g., a minimum size of 100-mL for up to four gauze wipe samples). There needs to be enough extra headspace in the shipping container to allow the desorption solution to cover the gauze wipes and to percolate freely through the wipe sample(s) during mixing.
3. Each regulatory agency having legal jurisdiction over the contaminated site may require different but specific off-site preparation and on-site sampling procedures. It is important to consult local regulatory agencies or departments of health having legal jurisdiction over contaminated sites to determine specific sampling, quality control, analyses, and reporting requirements.

C. SAMPLING:

1. Follow specific requirements of surface area to be wiped (usually 100 cm^2 or 1000 cm^2) and action threshold (or maximum allowable residual level) set by the state or specified by the client. Uptake rates depend upon the wipe sampling method used, so the specific wipe technique used must be specified, and any deviations from the required wipe sampling requirements noted.

   Note: To ensure that samples have not been tampered with, the use of custody seals and a chain-of-custody form is strongly recommended.
2. Prepare a rigid template from disposable cardstock or a sheet of PTFE having either a 10 cm × 10 cm or 32 cm × 32 cm square-cut hole. The template must be able to retain its shape during wiping to ensure that the areas wiped were either 100 cm^2 or 1000 cm^2. Secure the template(s) to the area(s) to be wiped (e.g., with tape along outside edge of template). If a single-use disposable template is not used, clean the template between samples to avoid cross-contamination, and provide the laboratory with a blank wipe of the cleaned template between samples to determine that no cross-contamination has occurred.
3. A template might not always be applicable, as in curved or odd-shaped areas such as around burners on stove tops or a fan blade. In such cases sample an area as close to either 100 cm^2 or 1000 cm^2 as feasible and provide the measurement to the regulatory agency and to the analytical laboratory for proper reporting. Tape can be used to delineate the sampling area.
4. It is recommended to provide extra wipe media from the same lot for required media blanks, field-equipment blanks, samples, and quality-control samples.

5. Gauze in sterile packaging is recommended to minimize the chance for cross-contamination, which can more easily occur with open bulk packaged cotton gauze.
6. To prevent contamination in the field, another alternative is to pre-wet and insert the gauze wipes into the sample containers off-site. This avoids any possibility of the bottle of methanol or isopropanol becoming contaminated on-site with methamphetamine (or other analytes). If the wipes were prepared off-site, then remove pre-wetted gauze wipe from sample container, opening only one sample container at a time. In either case, squeeze out and discard any excess solvent from the gauze wipe. Use fresh latex or nitrile gloves for each separate sample and blank. Do not use vinyl gloves due to the potential for leaching of phthalate plasticizers and contamination of the samples.
7. Wipe techniques
   a. Concentric Squares Wiping Technique (particularly suitable for smooth and non-porous surfaces and described by OSHA [25]): Fold the pre-wetted gauze in half and then fold in half again. Using firm pressure wipe the area within the template. Start at one of the inside corners of the template and wipe in concentric squares, progressing toward the center. End with a scooping motion. Without allowing the gauze to touch any other surface, reverse the last fold so that the exposed side of the gauze is facing inward and using a fresh surface of the gauze, wipe the same area in the same manner as before. Roll or fold the gauze again and insert into the shipping container.
   b. Side-to-side Wiping (or Blotting) Technique (particularly suitable for rough, porous, and/or soiled surfaces): Fold the pre-wetted gauze in half and then fold in half again. Using firm pressure wipe or blot the area within the template with at least five overlapping side-to-side horizontal passes (see NOTE) beginning at the top and progressing to the bottom in a "Z" pattern. End with a scooping motion. If blotting, blot at least five times on each horizontal pass (see NOTE). Without allowing the gauze to touch any other surface, reverse the last fold so that the exposed side of the gauze is facing inward. Using a fresh surface of the gauze, wipe or blot the area again with at least five overlapping top-to-bottom vertical passes beginning at the left side and progressing to the right in an "N" pattern. If blotting, blot at least five times on each vertical pass. Roll or fold the gauze again and insert into the shipping container. Blotting is suggested in areas so soiled or rough that the threads of the gauze media are continually snagged.
      NOTE: On areas larger than 100 cm^2, more than five passes and blots will be needed.
   c. Repeat or Serial Wiping: If isopropanol is used for wiping, a serial or repeat wipe sample of the same area with a fresh gauze wipe will improve sampling efficiency. (See recoveries for second wipe in Tables 9a and 9b.) For serial wiping, repeat the wiping procedure described above (APPENDIX 6a or 6b) with a fresh gauze wipe. Place the second gauze wipe into the same shipping container as the first gauze. The 50-mL polypropylene centrifuge tubes are large enough to contain up to two gauze wipes.
      NOTE: If the area to be wiped remains substantially wet from the first gauze, the second gauze wipe might be used in the dry state to soak up the residual solvent from the first gauze wipe.
8. Composite sampling: Composite samples are allowed by some regulatory agencies. Their use for quantitative purposes may be subject to the permission and guidance of regulatory agencies. Refer to guidelines of regulatory agency for directions on composite sampling. A basic default guideline for composite sampling is as follows: Do not mix inconsistent samples, that is, areas wiped must be equal in area, sampled areas must have the same high or low probability of contamination, and sampled areas must relate to a specific target appliance or site and not to several appliances or incongruous sites combined.
   NOTE: Composite samples cannot meet specific action-threshold requirements for discrete sampling locations. Nor do composite samples consisting of four wipes, for example, improve the sensitivity by decreasing the LOD four fold; instead it raises the LOD by a factor related to the extra volume of desorption solution that is required to desorb a larger number of wipes. The following example illustrates these two points. Assume that the action level was 0.1 µg/100 cm^2. If the analysis gave an LOD of 0.06 µg/sample for a single wipe or discrete sample covering an area of 100 cm^2, then the LOD for the analysis could be expressed as 0.06 µg/100

cm^2, which is low enough to be able to determine whether any discrete sample is at or exceeds the action level. Now if a composite of four wipes was taken, each with an area of 100 cm^2 for a total area wiped of 400 cm^2, the LOD for that composite sample is not 0.06 µg/400 cm^2 nor is it 0.015 µg/100 cm^2; it is actually several times larger than 0.06 µg/400 cm^2. First of all it increases relative to the ratio of the volume of desorption solution used to desorb the sample compared to that used for the calibration standards. Secondly it has nothing to do with the AREA that was wiped, because the LOD for the calibration curve is determined in terms of µg per sample, independent of the area. To explain the first point, assume approximately 90 mL was used (for ease in calculation) to desorb the four wipes and 30 mL (the normal amount for a single wipe) was used to desorb each calibration standard. The calculation of the LOD for the four composited samples would be µg/sample x (desorption volume for 4 wipes)/(desorption volume for the calibration standards), or 0.06 µg/sample x (90 mL/30 mL), or 0.18 µg/sample for the composited sample. Since the area wiped for the composite sample was 400 cm^2, the LOD for that sample could be expressed as 0.18 µg/400 cm^2. Regarding the second point, this value, 0.18 µg/400 cm^2, cannot be construed or mathematically reduced to 0.045 µg/100 cm^2 because it cannot be known whether three of the four wipes were blank and the fourth wipe just under the value of 0.18 µg. Hence, the effective LOD per individual wipe has to be regarded not only as 0.18 µg/400 cm^2 but also as 0.18 µg/100 cm^2 because any value determined for entire 400 cm^2 might have come from just one of those 100 cm^2 areas. Thus, for composite samples, the LOD must be expressed in terms of the entire area wiped and not extrapolated to some portion thereof. In this example, an LOD of 0.18 µg/100 cm^2 is above the action threshold of 0.1 µg/100 cm^2, meaning that this composite sample cannot satisfy the requirement that residual levels be below 0.1 µg/100 cm^2. It remains for the regulatory agency and not the laboratory to determine how to apply results for composite samples to the established action levels. The same consideration that is given above for the LOD applies to results that are greater than the LOD. To avoid confusion in reporting concentrations for composite samples, it is recommended that the sample concentration (in µg/sample, whatever the sample size) and the total area wiped (in cm^2) be reported separately. For example, a result of 0.4 µg/sample for a sample consisting of four separate wipes of 100 cm^2 each (for a total area wiped of 400 cm^2), is to be reported as 0.4 µg/400 cm^2 and not averaged to 0.1 µg/100 cm^2. This manner of reporting may be required by some regulatory agencies.

9. For quality assurance purposes, regulatory agencies may require duplicate samples to be taken in the field. If such is the case, an area contiguous with and adjacent to the first area, if possible, should be wiped as described under SAMPLING. Do not re-wipe the previously wiped area. This sample is a blind sample and should not be identifiable by the analytical laboratory as a duplicate of any other sample. These are distinct from the laboratory duplicates of a single sample described in step 14 of the method. Field duplicates are useful for evaluating the consistency of sampling technique, assuming uniformity of contamination on adjacent sampling sites. Laboratory duplicates are useful for evaluating consistency of sample preparation and instrumental analysis.

D. DESORPTION FROM MEDIA:

1. An internal standard spiking solution volume of 60 µL was selected for ease in scaling from 60 µL per 30 mL to 80 µL per 40 mL of desorption solution. In either case the rate of 2 µL internal standard spiking solution per mL desorption solution was used. However, any convenient volume of internal standard spiking solution (e.g., 50 µL) that can be delivered reproducibly is acceptable. Whatever volume is chosen, there must be no variation in the volume of the internal standard spiking solution used in preparing each of the calibration standards. If spiking strategy A is used (see step D3 of APPENDIX), it is critical to know the exact volume of internal standard spiking solution that is applied to each sample (V_1), the media blanks (V_5), and the calibration standards (V_2), since these volumes are used for internal standard spiking solution volume corrections in step 19.
2. It is not necessary to know the exact volume of desorption solution added to each sample or the volume of residual wetting alcohol because differences in the volumes are normalized through the use of internal standards added prior to desorption.

3. Alternate strategy for spiking internal standards (spiking strategy B below): By using the exact same volume of internal standard spiking solution in all samples, blanks, QC samples, and calibration standards, regardless of the volume of desorption solution added or residual wetting alcohol, the volume corrections in step 19 (V_1/V_2 and V_5/V_2) drop out of the equation. However, the internal standard GC peak areas must still be measurable in samples where larger volumes of desorption solution are used (such as for composite samples). Because of the increased dilution of the internal standard in larger samples, this approach should be limited to desorption solution volumes of about 120 mL or less.

NOTE: There are two separate strategies for handling larger samples requiring larger volumes of desorption solvent. These are outlined below as strategies A and B.

Number of Wipes	Size of Shipping Container (mL)	Volume of Internal Standard Spiking Solution (µL)		Volume of Desorption Solution (mL) (Strategies A and B)
		Strategy A	Strategy B	
1	40 to 50	60	60	30
2	50	80	60	40
4 (e.g., composite)	100 to 120	160	60	80
		Apply volume correction factors at step 19.	Do not apply volume correction factors at step 19.	

With either strategy, if two gauze wipes were included in the samples, then use 40 mL of desorption solution. If four gauze wipes were included in the samples, then use 80 mL of desorption solution.

a. In strategy A, the volume of internal standard spiking solution is kept at a constant ratio of 2 µL per mL of desorption solution added. This enables larger samples to be desorbed without diminishing the area of the GC peak for the internal standard. However, a volume correction factor (V_1/V_2) is needed in the final calculations in step 19. Therefore, the exact volume of internal standard added to each of the samples relative to that added to the calibration standards must be known.

b. In strategy B, the volume of internal standard spiking solution is kept constant for all samples and calibration standards, but need not be exactly 60 µL. This enables the final calculations to be made in step 19 without a volume correction factor. However, the area of the GC peak for the internal standard will vary with sample desorption volume and the internal standard must be concentrated enough to be measurable where larger volumes of desorption solution are used.

E. SOLID PHASE EXTRACTION PROCEDURE:

The following SPE columns were investigated and found to work adequately for this method: BOND ELUT-CERTIFY® (200 mg/3mL); Clean Screen® (300 mg/3 mL) ; Oasis® MCX (60 mg/3 cc); or Speedisk® H2O-Philic SC-DVB. Two columns (Clean Screen® and BOND ELUT-CERTIFY®) are based upon a silica support. The other two (Oasis® and Speedisk®) are based upon an organic polymer support. The precision and accuracy data in Tables 7a and 7b were generated using the Waters Oasis® MCX 3cc/60 mg column.

F. DERIVATIZATION:

There are unique advantages and disadvantages in using the mixed MSTFA + MBHFBA reagent. The disadvantages with some possible remedies are listed as follows.

1. A few percent of trifluoroacetyl derivatives of secondary amines are formed (presumably from MSTFA) in competition to the intended heptafluorobutyryl derivatives.

a. Remedy #1: This artifact is eliminated by replacing MSTFA with MSHFBA (N-methyl-N-trimethylsilyl heptafluorobutyramide, Alltech Associates, Deerfield, IL). However, precision and accuracy were not evaluated for NIOSH 9109 using MSHFBA instead of MSTFA.
b. Remedy #2: If ephedrine compounds or compounds containing free hydroxyl groups are not to be analyzed, MSTFA might be omitted and MBHFBA used alone.

2. Use of the mixed reagent often results in over-silylation, the production of unintended silylation artifacts [14], particularly of amides. The primary over-silylation artifact with primary amines is the N-trimethylsilyl derivative of the N-acyl derivative. The GC peak area for this artifact can be significant; under certain circumstances it is nearly equal to that of the intended N-acyl derivative.
   a. Remedy #1: The presence of ammonium chloride from the SPE eluates seems to prevent or greatly reduce over-silylation of amides. These artifacts can be ignored when using the SPE columns with the 80:20:2 methylene chloride:isopropanol:ammonium hydroxide eluent.
   b. Remedy #2: If ephedrine compounds or compounds containing free hydroxyl groups are not to be analyzed, silylating reagents (MSTFA or its alternate, MSHFBA) might be omitted and MBHFBA used alone.
3. The mass spectrometer may need more frequent cleaning to maintain sensitivity. This is offset by the shorter sample preparation time, especially for large numbers of samples.
4. When the fused silica capillary columns become exposed to the mixed silanization-acylation reagents, the column may become unsuitable for other types of samples.
5. The chromatograms are cluttered with silylation by-products making it difficult to detect low levels of unknown (non-target) compounds if a drug screen for unknown compounds is an objective. For this objective, the liquid-liquid extraction procedure of NIOSH 9106 [6] provides cleaner chromatograms with less interference from reagent by-products.
6. The advantages of the mixed MSTFA+ MBHFBA reagent, when used with SPE, are as follows:
   a. Faster preparation time (no heating in an oven, no cool-down time, no evaporation or neutralization of the reagents, and no reconstitution with solvent thereafter).
   b. No heat or acid induced isomerization or dehydroxylation of the ephedrine or other hydroxyl containing compounds (e.g., ephedrine, norephedrine, pseudoephedrine, phenylephrine, etc.).
   c. The method can be extended to easily hydrolyzed phenolic and polyhydroxy compounds of aryl-alkyl-amines (e.g., Albuterol, epinephrine and metabolites [15], metabolites of MDMA, and phenylephrine) because of the thermal stability of the trimethylsilyl ether groups on phenols and trimethylsilyl ester groups.
   d. Hindered amines such as MDEA are derivatized more completely but still require an internal standard with structural similarity.

G. MEASUREMENT:

Recoveries for the laboratory control matrix spike samples (QC and QD) must meet the guidelines of the specific regulatory agency involved (80-120% is a reasonable target in the absence of specific guidance).

NOTE 1: The QC samples (QC and QD) in this method may be referred to in some guidance documents as matrix spike and matrix spike duplicate samples (MS/MSD) but serve the same purpose. Analyze and report field-equipment blanks as samples. Do not subtract their values from any other sample.

Recoveries of CCV standards must meet guidelines of regulatory agency (80-120% is a reasonable target in the absence of specific guidance). The CCV standards may be referred to in some guidance documents as 'QC samples' but such QCs are equivalent to liquid standards (not matrix spiked samples) and serve the same purpose of the CCVs in this method.

NOTE 2: With the GC/MS it is possible to achieve the lower limit of 0.05 µg or less per sample for methamphetamine in either the scan mode or SIM mode. The scan mode is essential where the identification of unknowns is an analytical objective. If lower limits of detection are desired or difficult to obtain in the scan mode, or for routine target compound only analyses, the instrument may be operated in the SIM mode.

H. MAKING DILUTIONS:
If the samples exceed the upper calibration range for the analysis, one of the following procedures may be used to estimate the high level concentrations.

1. Dilution procedure A (dilution of the derivatization mixture within a GC vial): Transfer an aliquot of the derivatization sample mixture from the GC vial to a clean low-volume GC vial and add acetonitrile, MSTFA, and MBHFBA. For example, for a 10:1 dilution transfer 20 µL of sample to a clean vial and add 120 µL of acetonitrile and 30 µL each of MSTFA and MBHFBA, for a total volume of 200 µL. For a 4:1 dilution, transfer 50 µL of sample to a clean vial and add 100 µL of acetonitrile and 25 µL each of MSTFA and MBHFBA, for a total volume of 200 µL. Cap the GC vial, mix by inversion a few times, and analyze diluted sample. Do not include the dilution factor in step 19 since the internal standard will be diluted along with the target analyte.
   NOTE: For dilutions greater than 10, the internal standard may become too diluted to quantify. In such a case, use the following procedure B.
2. Dilution procedure B (dilution of the original sample desorbate): In this procedure, an aliquot of the original sample desorbate is diluted with a simulated blank solution and then transferred to a SPE column in step 8d. For example, for a 10:1 dilution, dilute 0.5 mL of sample desorbate solution from step 7f in a clean test tube containing 4.5 mL of a simulated blank solution, mix, and then transfer the entire contents to a pre-conditioned SPE column. For a 50:1 dilution, dilute 0.1 mL of sample desorbate solution from step 7f in a clean test tube containing 4.9 mL of a simulated blank solution, mix, and then transfer the entire contents to a pre-conditioned SPE column. Proceed thereafter to step 8d as normal. The simulated sample blank should be prepared identically to the sample needing dilution, using the same volumes of internal standard spiking solution and desorption solution that were used with the sample in the original desorption. For example, if the original sample was desorbed with 40 mL desorption solution with 80 µL of added internal standard spiking solution, then prepare the simulated blank in the same way. The volume of wetting alcohol is estimated (e.g., about 3 mL per 3"x3" 12-ply cotton gauze wipe). Include a dilution factor (V_3/V_4) in the calculations in step 19 (e.g., V_3/V_4 = 5 mL divided by the volume in mL of original desorbate diluted to 5 mL with solution from the simulated blank). The dilution factor in the above examples are 5 mL/0.5 mL or 10 for a 10:1 dilution and 5 mL/0.1 mL or 50 for a 50:1 dilution. Correct for differences in internal standard spiking solution volumes in step 19 (if applicable) using for V_1 the volume of internal standard spiking solution which was added to the original undiluted sample.

   Caution: This dilution procedure gives quantitative results only if the residual volume of methanol (or isopropanol) used for wetting the sample wipes was exactly the same as the volume used in preparing the calibration standards (normally about 3 mL, see Table 6). Deviations of a few milliliters in residual wetting alcohol will not affect the results for undiluted samples but will amount to an error of a few percent in the final results of samples that are diluted.
   The potential error due to differences in residual wetting solvent can be estimated for specific volumes of desorption solution and wetting alcohol. Assume the sample wipes and calibration standards are both desorbed in 30 mL of desorption solution and 3 mL of alcohol is added to the calibration standards. The potential error in volume (and final results) in the samples is approximately ±3.03% (inversely proportional) per mL difference in the residual alcohol in the samples (i.e. ±1 mL difference in 33 mL). For 40 mL of desorption solution and 4 mL of alcohol added to the calibration standards, the error is ±2.27% for every mL difference (i.e. ±1 mL difference in 44 mL). However, since the volume of residual wetting alcohol is not known and cannot be determined once the sample wipe has been desorbed, the actual error cannot be determined.

   However, the maximum possible error can be calculated. Since the maximum amount of alcohol that a 3"x3" 12-ply (or 4"x4" 8-ply) cotton gauze can hold is about 6 mL when saturated (dripping wet), there can only be a deviation of plus or minus 3 mL from the 3 mL alcohol added to the calibration standards. Therefore, the maximum error in a result due to differences in the volume of residual alcohol in a cotton gauze sample compared to

the standards can only be three times the error for a 1 mL difference in volume. Since the error for ±1 mL is ±3.03%, the maximum error for ±3 mL is three times larger, or ±9.1%. In practice, the error will be less than this because it is unlikely that the gauze samples will be completely dry or completely saturated after squeezing out the excess alcohol and wiping a surface. The practical amount of alcohol that remains in the 3"x3" 12-ply (or 4"x4" 8-ply) cotton gauze wipes when the excess is squeezed out is between 1 and 2 mL. This translates into an error that is between +3% and +6% in the final results for diluted samples. Undiluted samples will not be affected. This error is within the overall accuracy for the method for methamphetamine.

3. Dilution procedure C (dilution of desorbates from dried samples): Dilution errors for over-range samples may be corrected by knowing the exact amount of residual alcohol in the samples. The volume (or weight) of residual solvent in each gauze wipe might be determined by the difference between a wet weight and dry weight. Better yet, the error might be eliminated for diluted samples by adding, after the samples are dried (without taking any weight), the same known volume of wetting alcohol that is added to the calibration standards (i.e. 3 mL). Thereafter, if any samples need dilution, there will be no dilution errors due to differences in residual alcohol, because all samples and standards will have the same volume of alcohol and total volume of desorption solution. However, air drying of the samples is not recommended because of the possible loss of methamphetamine due to its volatility when it is not in the salt form, which form cannot be assured in field samples. Also, manipulating the samples for weighing and drying might introduce contamination. Drying is not recommended as a procedure for analytes having a vapor pressure high enough to be lost in the process, or that tend to form azeotropes with alcohols, especially when the critical action levels for remedial cleanup are at the lower end of the method calibration range. Drying is not an option if the samples have already been desorbed.

BERYLLIUM in Surface Wipes by Fluorometry

9110

Be MW: 9.0121 CAS: 7440-41-7 RTECS: DS1750000

METHOD: 9110, Issue 2 **EVALUATION:** FULL **Issue 1:** 6 April 2007 **Issue 2:** 12 December 2015

OSHA: none for surfaces
MSHA: none for surfaces
DOE: 3 µg per 100 cm^2 (housekeeping), 0.2 µg per 100 cm^2 (equipment release) [1]
OTHER OELs: [2]

PROPERTIES: solid, d 1.85 g/mL, MP 1,278 °C, VP 0 kPa (0 mm Hg) @ 25 °C

SYNONYMS: beryllium metal, beryllia (BeO)

SAMPLING

SAMPLER: WIPE (cellulosic or polyvinyl alcohol)

WIPE AREA: 100 cm^2 minimum

SHIPMENT: routine

SAMPLE STABILITY: stable

BLANKS: 3 field blanks min.

ACCURACY

RANGE STUDIED: 0.0001 to 6 µg per wipe [3,4]

BIAS: negligible [3,4]

OVERALL PRECISION ($\hat{S}_{rT}$): 0.094

ACCURACY: 18.9%

MEASUREMENT

TECHNIQUE: UV/VIS FLUOROMETRY

ANALYTE: complex of hydroxybenzoquinoline sulfonate (HBQS) with beryllium

DISSOLUTION: ammonium bifluoride (aqueous), 10 g/L

DETECTION SOLUTION: contains 63.4 µmol/L HBQS, 2.5 mmol/L EDTA, and 50.8 mmol/L lysine monohydrochloride (optional); pH adjusted to 12.85 with 10 mol/L NaOH, as necessary

DETECTOR: excitation, 360 nm to 390 nm; emission, integrated between 470 and 480 nm ($\lambda_{max} \approx 475$ nm)

CALIBRATION: beryllium standard solutions

RANGE: (0.005 to 6) µg per wipe [3,4]

ESTIMATED LOD: 0.0001 µg per wipe

PRECISION ($\bar{S}_r$): 0.021 at ≈0.2 µg per wipe, 0.076 at ≈1.5 µg per wipe, 0.052 at ≈3 µg per wipe

APPLICABILITY: The working range of the method is 0.0005 µg to 6 µg for surface wipe samples. The analysis is for total beryllium and is not compound specific.

INTERFERENCES: Minor interference from iron can result if iron concentrations are high. Samples high in iron demonstrate a yellow or gold coloration. This interference can be minimized by allowing the solution to sit for at least two hours, during which time the solution clears, and then filtering the sample extract before use. An alternative method is to filter the solution (after 30 minutes of standing) through a hydrophilic filter of pore size of 0.2 µm or smaller.

OTHER METHODS: Method 7300 (hot plate digestion and inductively coupled plasma atomic emission spectrometry) is an alternative procedure for the determination of elemental beryllium [5], but with higher detection limits. ASTM method D7202 is a similar procedure to detect elemental beryllium by fluorescence [6].

REAGENTS:

1. Ammonium bifluoride.*
2. Ethylenediaminetetraacetic acid (EDTA), disodium salt, dihydrate.
3. 10-Hydroxybenzo[*h*]quinoline-7-sulfonate (HBQS) [5].
4. L-Lysine monohydrochloride
5. Sodium hydroxide.*
6. Water, deionized.
7. Dissolution solution:* aqueous ammonium bifluoride, 10 g/L (prepared by dissolving ammonium bifluoride in deionized water)
8. Detection solution:* 63.4 µmol/L HBQS, 2.5 mmol/L EDTA, and 50.8 mmol/L lysine monohydrochloride; pH adjusted to 12.85 with 10 mol/L NaOH). An alternative preparation of dye solution without lysine (lysine-free) may be made by adding 1.104 g of EDTA and 64 µmoles of the 10-HBQS dye in 900 ml of water. After a clear solution is obtained, 114.5 ml of 2.5 N NaOH is added and mixed to obtain the final dye solution. The pH of the dye solution is 13.2. The lysine-free dye solution (commercially available) may be used for all analytical purposes and also provides superior detection limits.
9. Beryllium standard solution,* 1,000 mg/L (commercially available).
10. Beryllium-spiked media* (commercially available).

*See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: wipe, cellulosic, 47 mm diameter minimum.
   NOTE: Polyvinylalcohol (PVA) media are also suitable for this method [7]
2. Template, disposable/reusable, 100 cm^2 minimum area.
3. Tape, masking
4. Ultraviolet/visible (UV/Vis) fluorometer, with excitation lamp (λ = 380 nm) and time-integrating visible detector (400 nm to 700 nm, $\lambda_{max} \approx$ 475 nm) or optical filters for appropriate wavelengths (excitation of 360 nm to 390 nm; emission of ≈475 nm, with full width at half maximum of ±5 nm).
5. Mechanical agitator, shaker, or rotator.
6. Hot block (for beryllium oxide extraction).
7. Fluorescence cuvettes, disposable, 10 mm diameter, transparent to UV/Vis radiation.
8. Centrifuge tubes, plastic, 15 mL
9. Syringe filters, hydrophilic polypropylene, 0.2 µm pore size, 25-mm diameter, in plastic housings.
   NOTE: Polytetrafluoroethylene (PTFE) filters are unsuitable for this method
10. Pipettors, mechanical, of assorted sizes. Pipet tips, plastic, disposable, of assorted sizes.
11. Labware, plastic (e.g., beakers, flasks, graduated cylinders), of assorted sizes.
12. Tweezers, plastic or plastic-coated.
13. Laboratory wipes.
14. Personal protective wear (e.g., respirators, gloves, lab coats, safety eyewear), as needed

SPECIAL PRECAUTIONS: Wear appropriate personal protection during sampling activities and analysis. It is essential that suitable gloves, eye protection, laboratory coat, etc., be used when working with the chemicals. Perform sample preparation and analysis in a clean, well-ventilated area that is well removed from any possible beryllium contamination. Any area of skin affected by the dissolution or detection solutions must be immediately washed with plenty of water. Ammonium bifluoride will etch glass, so it is essential that all ammonium bifluoride solutions be contained in plastic labware. Avoid exposure by contact with skin or eyes, or by inhalation of vapor.

SAMPLING [8,9]:

1. Don a clean pair of gloves.
2. Demarcate the sampling area (100 cm^2 minimum) using a clean template or tape. If a template is used, tape the outside edges of the template to the surface to prevent its moving during sampling.
3. Wet a clean wipe with 0.2 mL of deionized water and wipe the surface to be sampled with firm pressure, using 3 to 4 vertical S-strokes. Fold the exposed side of the wipe in and wipe the area with 3 to 4 horizontal S-strokes. Fold the wipe once more and wipe the perimeter of the area.
4. Fold the wipe sample, exposed side in, and place into a labeled 15 mL plastic centrifuge tube.

SAMPLE PREPARATION:

5. Add 5 mL of the dissolution solution (ammonium bifluoride, 10 g/L) to each 15 mL centrifuge tube containing a wipe sample, and cap each tube.
6. Place each tube into a mechanical rotator, and rotate for at least 30 min.
   NOTE: Rotator may also be substituted by a shaker or an agitator as long as the dissolution solution wets the wipe well. Sonication has also been shown to be effective. For dissolution of refractory materials such as high-fired beryllium oxide, agitation of the dissolution solution with the media must be replaced by heating to 85 °C for 60 minutes or more. Any standard dissolution process is particle-size dependent [10]. The two sources of BeO used to validate the method are described in the backup data report [11].
7. Filter each solution with a hydrophilic polypropylene syringe filter into a clean tube.
   NOTE: This tube should be able to accept a cap so that the solution may be saved and used later for reanalysis if required.
8. Pipet 0.1 mL of each sample filtrate into cuvettes containing 1.9 mL of the detection solution. Cap and mix briefly.
   NOTE: The above procedure is typically used to analyze a range of 0.05 µg to 6 µg of beryllium on the sampling media. Alternative ratios of dissolution solution and detection solution may be used for analyzing alternative ranges of beryllium concentration. To test a range of 0.005 µg to 0.4 µg of beryllium on the sampling media, 0.4 mL of the sample filtrate is added to 1.6 mL of the detection solution in the cuvettes. The lysine-free dye solution may also be used for obtaining even lower detection limits at a dilution ratio of 3x, where 1.33 mL of the dye solution is mixed with 0.67 mL of the filtered solution extracts (Table 3), and beryllium in the range of 0.0005 µg to 0.4 µg may be determined.
   NOTE: If high iron or titanium concentration is suspected or is evident (owing to the appearance of suspended precipitate), allow the solution to settle and filter the solution using a hygroscopic syringe filter (e.g., polyethersulfone, or hydrophilic polypropylene).
   NOTE: The stability of the detection and the dissolution solution is more than six months and of the mixed measurement solution comprising both is greater than 30 days. The solutions must be kept in sealed containers, and the detection and mixed solutions must be stored away from light.
   NOTE: If the samples are suspected of having a contaminant that fluoresces and has excitation and emission spectra that overlap with that of the signal produced by the fluorescent dye bound to beryllium, then this contaminant needs to be removed. The presence of such a contaminant can be verified by subjecting the filtered sample to fluorescence excitation after the extraction step (without adding the fluorescent dye). If a fluorescence signal is detected, then that signal is ascribed to the presence of a fluorescent contaminant. To remove the contaminant, high-purity activated charcoal is added to the beryllium extraction solution (~10mg/mL) and the extraction procedure is carried out at elevated temperature (80 to 90 °C for at least 45 minutes). If the beryllium extraction procedure has already been performed, then after the addition of activated charcoal, the extraction process is repeated at the elevated temperature. The solution is filtered to remove the activated charcoal before adding this to the detection solution to make the measurement solution. Details of this process have been published [12,13].

CALIBRATION AND QUALITY CONTROL:

9. Calibrate the fluorometer with beryllium stock standard solutions. Prepare a calibration graph of fluorescence intensity vs. beryllium concentration (ng/mL) in the stock standard.
   NOTE: To test a range of 0.05 µg to 6 µg of beryllium on the sampling media, beryllium stock standard solutions are made up using beryllium spectrometric standards diluted with the ammonium bifluoride dissolution solution. A recommended series of stock standard solutions is (800, 200, 40, 10, and 0) ng/mL. As with the samples, the stock standards are prepared for analysis by

adding 0.1 mL of beryllium stock standard into 1.9 mL of detection solution (20-fold dilution). Please see Table 1. Either of the two detection solutions may be used.

NOTE: To test a range of 0.005 µg to 0.4 µg of beryllium on the sampling media, a recommended series of stock standard solutions is (80, 20, 4, 1, and 0) ng/mL. These standards with lower beryllium concentration can be prepared by 10-fold dilution of the stock standards mentioned in the note above. As with the samples, these stock standards are prepared for analysis by adding 0.4 mL of beryllium stock standard into 1.6 mL of detection solution (5-fold dilution). Please see Table 2. Either of the two detection solutions may be used.

NOTE: When using the lysine-free dye solution ONLY, a range can be tested of 0.0005 to 0.4 µg of beryllium on the media using a recommended series of stock solutions is (0, 0.15, 0.3, 0.6 and 2.4) ng/mL. These standards with lower beryllium concentration can be prepared by dilution of the stock standards mentioned in the note above. The standards are prepared for analysis by adding 0.67 mL of beryllium stock standard into 1.33 mL of detection solution (3-fold dilution). This dilution will result in 0, 0.05, 0.1, 0.2 and 0.8 ppb of beryllium in these standards; see Table 3. Cellulosic filters (47 mm in diameter) were spiked with a solution of beryllium acetate and analyzed in triplicate after extracting beryllium in 5 ml of 1% ABF solution at 85°C for 60 minutes and then mixed with lysine-free dye solution in a 3-fold dilution; these results are shown in Table 4. The difference in the average fluorescent signals from blanks and the 0 ppb standard were subtracted from the fluorescent readings of the spiked filters.

NOTE: If alternative ratios of dissolution solution and detection solution are used for sample preparation, then a similar ratio for calibration solutions is required.

10. Analyze a stock standard, a reagent blank, and a media blank at least once every 20 samples. Ensure that the concentration range of the stock standards spans the beryllium levels found in the samples.
11. Analyze one media spike and one quality control blind spike per 20 samples (minimum of three each per sample set) to insure that percent recovery is in control (e.g., 100 ± 15). Correct sample results for the average recovery if it differs significantly from 100%.

NOTE: If it is suspected that beryllium oxide may be present, then it is recommended to use beryllium oxide for media and blind spikes.

MEASUREMENT:

12. For each sample, obtain the fluorescence intensity at λ_{max} or with optical filter for appropriate wavelength.
13. If the fluorescence response for any of the samples is above the range of responses for the stock standards, dilute the sample filtrate with dissolution solution, reanalyze, and apply the appropriate dilution factor (*D*) in subsequent calculations.

CALCULATIONS:

14. Obtain the solution concentration for each sample filtrate, C_s (ng/mL), and the average media blank, C_b (ng/mL) from the calibration graph.
15. Using the dissolution volumes (normally 5 mL) of sample, V_s (mL), and media blank, V_b (mL), calculate the concentration, *C* (µg/m^2), of Be in the surface area sampled, *A* (cm^2), while accounting for the dilution factor (*D*).

$$C = D \times (C_s V_s - C_b V_b)/(10 \times A) \ \mu g/100\ cm^2$$

NOTE: Tables 1, 2 and 3 can be used for correlating the amount of beryllium in the sampling media with the concentrations of beryllium in solution. Table 1 is for testing media with 0.05 µg to 6 µg of beryllium at 20-fold dilution; Table 2 is for testing media with 0.005 µg to 0.4 µg of beryllium at 5-fold dilution; and Table 3 is for testing media with 0.0005 µg to 0.012 µg of beryllium at 3-fold dilution. Lysine-free dye solution may be used for any of these dilutions, but for 3x dilution, lysine-free dye solution must be used.

Table 1. Correlation of amount of Be in sampling media with Be concentration in stock standard and Be concentration as analyzed, assuming 0.1 mL of sample or stock standard is added to 1.9 mL of detection solution (20-fold dilution).

Be concentration in stock standard (ng/mL)	Be concentration as analyzed (ng/mL)	Amount of Be in the media* (ng)
0	0	0
10	0.5	50
40	2	200
200	10	1000
800	40	4000

*Equals stock standard Be concentration (ng/mL) × volume (5 mL) of dissolution solution used to extract media.

Table 2. Correlation of amount of Be in sampling media with Be concentration in stock standard and Be concentration as analyzed, assuming 0.4 mL of sample or stock standard is added to 1.6 mL of detection solution (5-fold dilution).

Be concentration in stock standard (ng/mL)	Be concentration as analyzed (ng/mL)	Amount of Be in the media* (ng)
0	0	0
1	0.2	5
4	1	25
20	4	100
80	16	400

*Equals stock standard Be concentration (ng/mL) × volume (5 mL) of dissolution solution used to extract media.

Table 3. Correlation of amount of Be in sampling media with Be concentration in stock standard and Be concentration as analyzed, assuming 0.67 mL of sample or stock standard is added to 1.33 mL of lysine-free dye solution (3-fold dilution).

Be concentration in stock standard (ng/mL)	Be concentration as analyzed (ng/mL)	Amount of Be in the media* (ng)
0	0	0
0.15	0.05	0. 75
0.3	0.1	1.5
0.6	0.2	3
2.4	0.8	12

*Equals stock standard Be concentration (ng/mL) × volume (5 mL) of dissolution solution used to extract media.

Table 4: Analysis of beryllium spiked cellulosic filters (47mm in diameter) using 3-fold dilution of the extraction solution with lysine-free dye solution. Beryllium concentration of calibration solutions after mixing with the dye solutions were 0, 0.05, 0.1, 0.2 and 0.8 ng/ml. Samples analyzed in triplicate, Averages and standard deviations are shown both in ppb in the solution and as µg on the filter.

Nominal Be concentration on the spiked filter, µg	Be concentration measured in the mixture of dye and sample solution, ppb ± Std Dev	Be concentration measured on the wipes, µg ± Std Dev
0	0.0003±0.0057	0.0000±8.5E-5
0.0005	0.0375±0.0073	0.00056±11.0E-5
0.001	0.0735±0.0058	0.0011±8.7E-4
0.002	0.1262±0.0047	0.0019±7.11E-4
0.005	0.3396±0.0093	0.0051±1.39E-4
0.05	3.275 ±0.051	0.049±7.58E-4
0.48	32.29±0.293	0.484±4.40E-3

EVALUATION OF METHOD:

The method was evaluated [3,4,11,14] in accordance with published guidelines [15]. Experiments were conducted [11] using an Ocean Optics® portable fluorescence device with the following components:

> USB 200 spectrometer with spectral grating #2 (UV/Vis 600), LS-1 lamp (380 nm) in LS-450 housing, UV-2 casting, OFLV linear filter 200-850, L2 collection lens and slit-200.

Tests were carried out in relative irradiance mode using 2- or 5-second integration times.

The method was evaluated using beryllium oxide spiked onto mixed cellulose ester (MCE) filters at levels of (0, 0.02, 0.1, 0.2, 0.3, 0.4, 1.5, 3.0, and 6.0) µg (five samples at each level) [12]. The procedure was also evaluated on polyvinyl alcohol (PVA) wipes in an interlaboratory trial with media spiked with BeO at 0.030, 0.16, 0.32, 1.8, 2.8 and 5.6 µg [7].

Long-term stability of samples was verified from spikes (number [*n*] = 30) of 0.1 µg Be on MCE filters [9]. Samples were analyzed at day one ($n = 12$) and then one week ($n = 6$), ten days ($n = 3$), two weeks ($n = 3$), three weeks ($n = 3$), and one month ($n = 3$) after spiking. No diminution of fluorescence signal was observed from samples prepared and analyzed after having been stored for up to thirty days.

Interference tests were carried out using solutions of 0 nmol/L, 100 nmol/L, and 1.0 µmol/L Be in the presence of 0.4 mmol/L Al, Ca, Co, Cu, Fe, Ti, Li, Ni, Pb, Sn, U, V, W, or Zn (separate experiments were carried out for each potential interferant) [13]. Interlaboratory evaluations of the method were also performed [4,7,14].

The method using the lysine-free detection solution was compared and tested (with the detection solution with lysine for comparison) (Table 4) and this was carried out on a Glomax™ spectrometer (Turner Biosystems, Sunnyvale, CA) with an emission filter of 475 ± 5 nm and the excitation was at 360 nm

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METHAMPHETAMINE on Wipes by Liquid Chromatography/Mass Spectrometry

9111

$C_6H_5 \cdot CH_2 \cdot CH(CH_3) \cdot NH \cdot CH_3$ MW: 149.2 CAS: 537-46-2 RTECS: SH4910000

METHOD: 9111, Issue 1 **EVALUATION: Partial** **Issue 1: 17 October 2011**

OSHA: None for surfaces
NIOSH: None for surfaces
Other OELs and guidelines: [1, 2, 3]

PROPERTIES: White solid, MP 171 - 175 °C; VP 0.163 mm Hg @ 25 °C; pK_a = 9.87 @ 25 °C; Water Sol. (1.33 g/100 mL @ 25 °C). Log P = 2.07 (octanol-water partition coefficient).

SYNONYMS: (*S*)-*N*,*α*-Dimethylbenzeneethanamine; (*S*)-(+)-*N*,*α*-Dimethylphenethylamine: *d*-1-Phenyl-2-methylaminopropane. Methedrine; Desoxyn; chalk; crank; crystal; glass; ice; meth, speed; upper.

SAMPLING

SAMPLER: Wipe

SAMPLE AREA: 100 cm^2 or 1000 cm^2

SHIPMENT: Ship refrigerated preferably

SAMPLE STABILITY: At least 7 days at 22 °C
At least 30 days at <6 °C

FIELD BLANKS: 2 to 10 blanks per set

MEASUREMENT ACCURACY

RANGE STUDIED: Not Determined

BIAS: Not Determined

OVERALL PRECISION ($\hat{S}_{rT}$): Not Determined

ACCURACY: Not Determined

MEASUREMENT

TECHNIQUE: LIQUID CHROMATOGRAPHY/MASS SPECTROMETRY-SIM mode. See Table 1.

ANALYTE: Methamphetamine

DESORPTION: 0.1 M sulfuric acid

INJECTION VOLUME: 50 µL

MOBILE PHASE: A: 5/95 acetonitrile/water, 0.1% acetic acid
B: 95/5 acetonitrile/water, 0.1% acetic acid

COLUMN: 150 mm x 4.6 mm, 5 µm film of dimethyl-n-octadecylsilane (C18) stationary phase to silica gel. Column temperature 40 °C.

GRADIENT: 100% A for one min, gradient to 100% B (9 min), hold 5 min, gradient to 100% A (2 min), hold 8 min. Flow rate is 0.50 mL/min

CALIBRATION: Media spiked standards to cover the range (See Table 1)

RANGE: 0.1 – 100 µg/sample

ESTIMATED LOD: 0.1 µg/sample

PRECISION ($\bar{S}_r$): 0.067 [4]

APPLICABILITY: For methamphetamine the range is approximately 0.1 to 100 µg/sample (sample = 100 cm^2).

INTERFERENCES: No chromatographic interferences detected.

OTHER WIPE METHODS: NIOSH 9106 uses liquid-liquid extraction and gas chromatography/mass spectrometry (GC/MS) to measure multiple drugs [5]. NIOSH 9109 uses solid-phase extraction and GC/MS to measure multiple drugs [6].

REAGENTS:

1. Methamphetamine.* 1 mg/mL in methanol.
2. Methamphetamine-D_{14} 1 mg/mL in methanol.
3. Solvents, residue free analytical grades:
   a. Isopropanol (IPA) *
   b. Acetic Acid *
   c. Acetonitrile *
   d. Methanol *
4. Concentrated sulfuric acid (AR or trace metals analysis grade).*
5. Purified gas: nitrogen for drying.
6. Deionized water (ASTM type II).

SOLUTIONS:

1. Prepare spiking solutions of target analyte and internal standard. Keep solutions refrigerated. Protect solutions from light.
   a. Target analyte spiking solutions are prepared by diluting the 1000 µg/mL methamphetamine stock solution to 200 µg/mL and 20 µg/mL each in methanol.
   b. Dilute 1 mL of 1000 µg/mL methamphetamine-D_{14} stock solution to 10 mL for a 100 µg/mL (0.1 µg/µL) solution.
2. Desorption solution: 0.1 M sulfuric acid. Add 22 mL conc. sulfuric acid to 4 L deionized water.
3. Prepare Mobile Phase A: 0.1% acetic acid, 5% acetonitrile in water.
4. Prepare Mobile Phase B: 0.1% acetic acid, 95% acetonitrile in water.

* See SPECIAL PRECAUTIONS

EQUIPMENT:

1. Wipe, cotton gauze, 3" x 3" (7.6 cm x 7.6 cm) 12-ply or 4" x 4" (10.2 cm x 10.2 cm) 8-ply or equivalent.
2. Sample storage and shipping container: 50-mL polypropylene centrifuge tubes with caps or equivalent.
3. Liquid chromatograph/mass spectrometer, with integrator or computerized data collection system, and column.
4. LC autosampler vials, 2-mL, and caps.
5. Volumetric flasks: various sized flasks for making standards and spiking solutions. A 4-L bottle for making the desorption solution.
6. Liquid Transfer:
   a. Various microliter syringes for making and spiking standard solutions.
   b. Adjustable 10 to 50-mL desorption solution dispenser to fit 4-L bottle.
7. Forceps.
8. Latex or nitrile gloves. Avoid vinyl gloves. (See 9111-3, Sampling, Step 1, NOTE 2.)
9. Rotating mixer capable of 10 to 30 rpm.
10. Pasteur pipettes.
11. Template: 10 cm x 10 cm hole. Template made of relatively rigid disposable cardstock or sheet of PTFE.
12. Filters: Ion Chromatography filter media, 25 mm syringe filter with 0.45 µm film hydrophilic polyethersulfone (PES) membrane.
13. Ice or other cold media for shipping.

SPECIAL PRECAUTIONS: The solvents are flammable and have associated adverse health effects. Avoid breathing vapors. Avoid skin contact. Work should be performed in an adequate hood. Analysts must wear proper eye and hand protection (e.g. latex gloves) to prevent absorption of even small amounts of amines through the skin as well as for protection from the solvents and other reagents. Dissolving concentrated sulfuric acid in water is highly exothermic. Goggles must be worn.

Caution must also be exercised in the handling and analysis of samples. Clandestine drug labs may produce unknown and seriously toxic by-products.

SAMPLING:

See APPENDIX for special instructions on sampling.

1. Using a new pair of gloves, remove a gauze wipe from its protective package. Moisten the wipe with approximately 3 to 4 mL of methanol (or isopropanol).
   NOTE 1: Apply no more solvent than that needed to moisten approximately the central 80% of the area of the gauze wipe. Excess solvent may cause sample loss due to dripping from the wipe.

NOTE 2: Do not use vinyl gloves due to the potential for leaching of phthalate plasticizers and contamination of the samples.

2. Place the template over the area to be sampled (may tape in place along outside edge of template). Wipe the surface to be sampled with firm pressure, using vertical S-strokes. Fold the exposed side of the pad in and wipe the area with horizontal S-strokes. Fold the pad once more and wipe the area again with vertical S-strokes.
3. Fold the pad, exposed side in, and place in shipping container and seal with cap.
   NOTE: Keep samples refrigerated (<6 ºC). While methamphetamine and several related amines are stable on the recommended wipe media for at least 7 days at room temperature, refrigeration is recommended as soon as possible.
4. Clean the template before use for the next sample or use a new disposable template.
5. Label each sample clearly with a unique sample identifier.
6. Prepare a minimum of two field blanks with one field blank for every ten samples.
   NOTE: In addition, include at least 3 media blanks for the analytical laboratory to use for their purposes. The wipes used for the media blanks should be from the same lot as the field samples.

SAMPLE PREPARATION:

7. Desorption from media:
   a. Remove cap from shipping container. Sample media should fit loosely in the container. If not, rearrange media carefully with rinsed forceps or transfer to a larger container. If the sample media are transferred to a larger container, do not discard the original container. Samples may consist of more than one wipe. If this is the case, internal standard and desorption solution volumes may be adjusted accordingly.
   b. Spike exactly 50 µL of internal standard spiking solution onto each wipe sample.
   c. Add 30 mL desorption solution (0.1 M sulfuric acid). If the samples were transferred to a larger container, the original shipping container must be rinsed with the desorption solution first, shaken, and the rinsate decanted into the larger container.
   d. Cap securely and mix contents by inverting the tubes end over end on a rotary mixer at 10-30 rpm for at least one hour.
      NOTE 1: The desorption solution must percolate freely through the gauze wipes.
      NOTE 2: If there is reason to believe that the samples may be alkaline enough to overcome the acidity of the desorption solution (e.g. wipes of unpainted concrete or stucco surfaces), then the pH must be adjusted to about ≤ 4. See APPENDIX for instructions.
   e. Filter an aliquot of the sample through a 0.45 µm pore coated with hydrophilic polyether sulfone on the ion chromatography filter media (25-mm diameter) for analysis.
8. Transfer the filtered sample into a vial and cap.
9. Analyze samples, standards, blanks, and Quality Control samples (QCs) by LC-MS. (See MEASUREMENT, steps 13-15.)

CALIBRATION AND QUALITY CONTROL:

10. Determine retention time using the column and chromatographic conditions specified on page 9111-1.
11. Calibrate daily with at least six media spiked calibration standards and a blank.
    a. Prepare the target analyte spiking solutions. (See SOLUTIONS, 9111-2)
    b. Prepare calibration standards and media blanks in clean shipping containers (e.g. 50-mL polypropylene centrifuge tubes.)
    c. Spike a known volume of target analyte spiking solution into each calibration standard by spiking directly onto the media. Use the spiking volumes suggested in Table 2 to cover the desired range.
    d. Analyze these along with the field samples. (See MEASUREMENT, steps 13-15.)

12. Prepare matrix-spiked and matrix-spiked duplicate quality control samples (QC and QD).
    a. Cotton gauze from the same lot used for taking samples in the field should be provided to the analytical laboratory to prepare these matrix-spiked QC samples.
    b. The quality control samples (QC and QD) must be prepared independently at concentrations within the analytical range. (See Table 2 for applicable concentration ranges.)
    c. One quality control media blank (QB) must be included with each QC and QD pair.
    d. The quality control samples must be prepared at the rate of one set (QB, QC, and QD) per 20 samples or less.
    e. Transfer clean gauze wipes to new shipping containers.
       NOTE: If two gauze wipes were used for the majority of samples in an analytical set, use two clean gauze wipes for each QB, QC, and QD.
    f. Spike QC and QD with a known amount of target analyte as suggested in Table 2.
    g. Process quality control samples along with the calibration standards, blanks, and field samples through steps 7 and 8.
    h. Analyze these along with the calibration standards, blanks, and field samples. (See MEASUREMENT, steps 13-15.)

MEASUREMENT:

13. Analyze the calibration standards, quality control samples, blanks, and samples by LC-MS.
    a. Use the following suggested analytical sequence.
       i. Calibration standards.
       ii. Matrix spiked quality control samples (QC and QD), one set for every 20 samples or less.
       iii. A media blank (QB), one for every 20 samples or less.
       iv. Samples (up to 10) including one sample duplicate.
       v. A continuing calibration verification (CCV) standard consisting of one of the initial calibration standards.
       vi. A media blank.
    b. Set liquid chromatograph according to manufacturer's recommendations and to conditions listed previously.
    c. Set mass spectrometer to scan for ions 119, 150, and 164 in SIM mode. Further suggestions for MS conditions are listed in Table 1 but will vary for particular instruments and conditions. See Note 2 in Table 1.
    d. Inject 50 µL of the sample aliquot into liquid chromatograph.
    e. After analysis, the vials should be promptly recapped and refrigerated if further analysis is anticipated. Samples are stable refrigerated for at least seven days.
14. Using extracted ion current profiles for the primary (quantification) ions specific to methamphetamine and the internal standard, measure the LC peak area of each respective peak and compute relative peak areas by dividing the peak area of the analyte by the area of the internal standard. Recommended primary (quantification) ions and internal standard ions are given in Table 1. Prepare a calibration graph (relative peak area vs. µg analyte per sample).
15. Samples from initial investigations of clandestine laboratories are likely to include highly contaminated samples. If sample results exceed the upper range of the calibration curve, the sample in the LC vial may be diluted with the sulfuric acid desorption solution and reanalyzed.

CALCULATIONS:

16. Determine the mass in µg/sample of methamphetamine found in the wipe samples and in the media blank from the calibration graph.

17. Calculate final concentration, C, of methamphetamine in µg/sample:

$$C = c\frac{V_1}{V_2} - b$$

Where:

c = concentration in sample (in µg/sample determined from the calibration curve)

$\frac{V_1}{V_2}$ = dilution factor, if applicable

V_1 = volume in µL of internal standard spiking solution used to spike samples.

V_2 = volume in µL of internal standard spiking solution used to spike the standards.

b = concentration in media blank (in µg/sample determined from the calibration curve).

18. Report concentration, *C'*, in µg per total area wiped (in cm^2) as follows:

$$C' = \frac{C}{A}$$

Where:

C = µg/sample (step 17).

A = Total area wiped in cm^2 per sample.

NOTE: For example, if the sample was a composite sample and the area was 400 cm^2, report results as µg/400 cm^2. In general, if the area wiped was greater than or less than 100 cm^2, do not convert value to µg/100 cm^2. To avoid confusion, report separately both µg/sample (C) and the total area wiped in cm^2 per sample (A) for both discrete and composite samples.

EVALUATION OF METHOD:

This method was evaluated for methamphetamine over a range of approximately 0.4 µg/sample to 17.8 µg/sample on cotton gauze. These concentration levels represent approximately 3 through 100 times the limit of quantitation (LOQ) level. Results are reported in the Backup Data Report for 9111s[4].

The limit of detection (LOD) and LOQ were determined by preparing a series of media spiked standards, desorbing in the sulfuric acid desorption solution and analyzing in the SIM mode. The LODs were estimated using the procedure of Burkart [7]. An LOD of less than 0.02 µg/sample for methamphetamine on wipes was achieved in the SIM mode. The LOD was set at 0.05 µg/sample and the LOQ at 0.15 µg/sample for method development purposes. Lower LODs can be achieved in practice by including calibration standards at lower concentration levels and with proper instrument maintenance. The cleanliness and performance of the mass spectrometer must be maintained such that at a minimum of 0.1 µg/sample a signal of at least 5 to 10 times the baseline noise is achievable.

Precision and accuracy were determined by analyzing 6 replicates at each of 4 concentration levels (nominally 0.44, 1.8, 4.4, and 18 µg/sample). Accuracy was calculated using equations and methodology found in the NIOSH Technical Report "Guidelines for Air Sampling and Analytical Method Development and Evaluation" [8]. Using all data, method precision (S_r) was 0.06663. Accuracy was 20.7% and mean bias was -0.09753.

Long term sample storage stability was determined for periods up to 30 days under refrigeration (4 °C ± 2 °C) and for up to 7 days at room temperature (22-24 °C). Since long term storage measures only the viability of

analytes on a particular media over time, this determination was not repeated for this particular method; the reader is directed to NIOSH 9106 [5] for more detail. All recoveries were found to be 93.5% or better.

Recovery of amphetamines from six different types of surfaces using cotton gauze was evaluated. The study and results are reported in NIOSH 9109 [6]. The practice of serial wiping (wiping the same surface area a second time with a second gauze wipe and combining both wipes as a single sample) was evaluated. Four solvents for wetting the gauze were tested (distilled water, 5% distilled white vinegar, isopropanol, and methanol). Six replicate samples were taken on a latex painted wall. Recovery and precision results are presented in the previously mentioned Backup Data Report. In summary, the effectiveness of the various solvents using a single wipe on a latex painted wall were as follows: water, 46% recovery; 5% distilled white vinegar, 55% recovery; isopropanol, 64% recovery and methanol, 87% recovery. Average recoveries with isopropanol from all the surfaces tested were greatly improved with a repeat (serial) wipe (11% improvement compared to only about 6% improvement with methanol). The serial wipe is added to the first wipe and constitutes a single sample.

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METHOD DEVELOPMENT BY:

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Table 1. Suggested Mass Spectrometer SIM Conditions

Ionization Mode:	API-ES (Atmospheric Pressure Ionization –Electrospray)
Polarity:	Positive
Fragmentator:	100
Gain:	3.0 EMV
Actual Dwell:	294
SIM ions:	119 Methamphetamine confirmation ion
	150 Quantitation ion for methamphetamine
	164 Ion for methamphetamine-D_{14}
Spray Chamber:	(Optimize for the particular instrument in use.)
Gas Temperature:	200 °C
Drying Gas:	12.0 L/min
Nebulizer Pressure	50 psig

Note 1: Methamphetamine and the internal standard essentially co-elute. Monitor *m/z* ions 119 and 150 for methamphetamine quantitation and 164 for methamphetamine-D_{14}.

Note 2: These instrumental conditions are suggestions and should be optimized by the analyst. Each mass spectrometer will be different and the acid concentration and composition will alter the conditions. Furthermore there is the possibility of using MS/MS for these analyses if the laboratory is equipped with that instrumentation. This tandem MS could add specificity and sensitivity to the method but was not part of this method development.

Table 2. Suggested spiking schedule for calibration standards

Standard	Volume (µL) of Methamphetamine Spiking Solution Spiked on Media		Internal Standard Spike (µL)	Desorption Solution (mL)	Final Concentration (µg/sample)
	200 µg/mL solution	20 µg/mL solution			
1	500		50	30	100
2	100		50	30	20
3	25		50	30	5
4	5		50	30	1
5		25	50	30	0.5
6		5	50	30	0.1
7		2.5	50	30	0.05
8		1.2	50	30	0.024

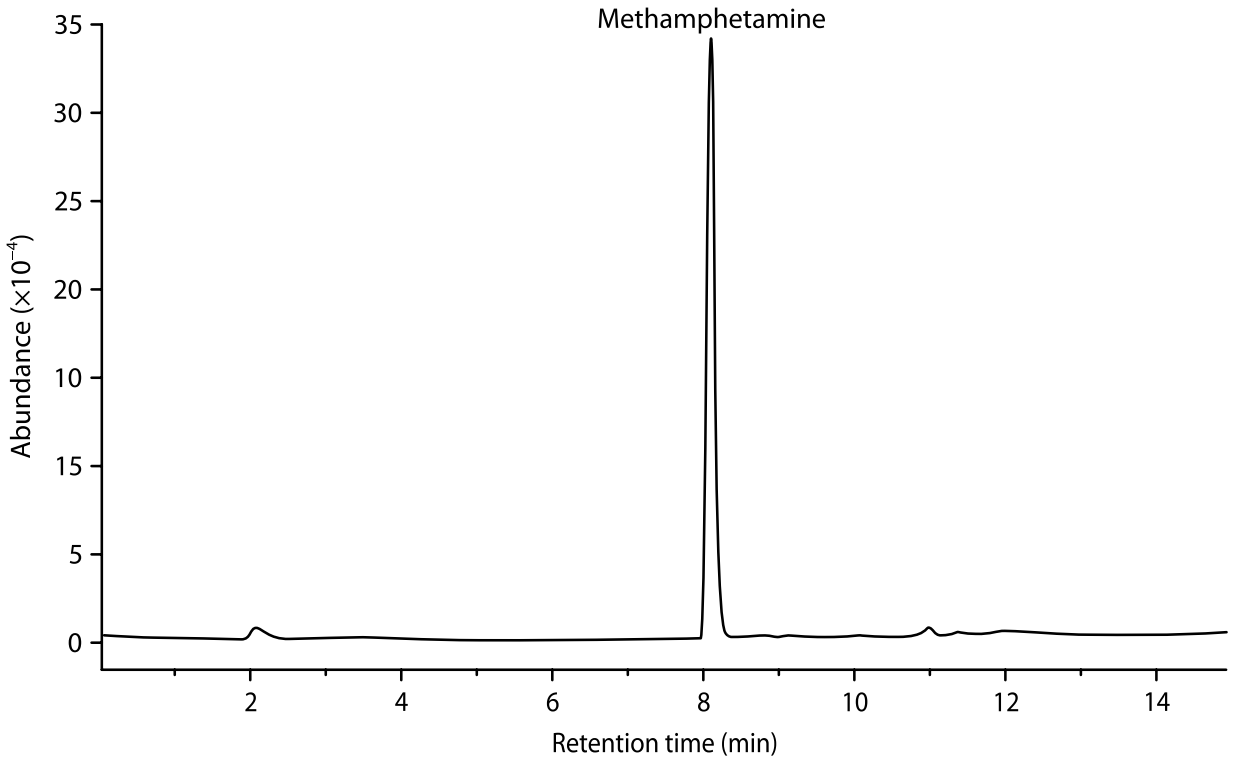

Figure 1. LC-MS total ion chromatogram of methamphetamine (*m/z* 119, 150, 164).

APPENDIX:

SAMPLING

NOTE: For further information and data on the effects of surface composition and porosity as well as the use of different solvents on the efficacy of wipe sampling, please see reports by Serrano et al [9] and Van Dyke et al [10].

1. Follow specific requirements of surface area to be wiped (usually 100 cm^2) and action threshold (or maximum allowable residual level) set by the agency having legal jurisdiction or specified by the client. Uptake rates depend upon the wipe sampling method used so the specific wipe technique used must be specified and any deviations from the required wipe sampling requirements noted.
2. The following steps only summarize the overall sampling procedure and are not intended to be used as a shortcut or wipe sampling procedures that may be specified by the legal jurisdiction or the client.
3. Prepare a rigid template from disposable cardstock or a sheet of PTFE having either a 10 cm x 10 cm or 1 ft x 1 ft (1000 cm^2) square hole cut according to the dimensions required by the regulatory agency. The template must be able to retain its shape during wiping to ensure that the areas wiped were 100 cm^2 or 1 ft^2. Single-use disposable cardstock is preferred because it eliminates the possibility for cross-contamination and the necessity to take a blank wipe between samples in step 3.
4. Provide enough wipe media from the same lot to cover all required laboratory media blanks, field-equipment blanks, samples and sample duplicates, and quality control samples. Use gauze in sterile packaging to minimize the chance for cross-contamination which might more easily occur with open bulk packaged cotton gauze. The gauze wipes needed for the laboratory media blanks and QC samples are to be sent to the laboratory in their unopened sterile packages.
5. Secure the template(s) to the area(s) to be wiped (e.g. with tape along outside edge of template). If a single-use disposable template is not used, clean the template between samples to avoid cross-contamination and provide laboratory with a blank wipe of the cleaned template between samples to ensure that no cross-contamination has occurred.
6. With freshly gloved hand, take one gauze and wet it with isopropanol or methanol (about 3-4 mL for either the 3" x 3" (7.5 cm x 7.5 cm) 12-ply or the 4" x 4" (10 cm x 10 cm) 8-ply cotton gauze wipes). Alternatively, pre-wet and insert the gauze wipes into the sample containers off-site. This avoids any possibility of the bottle of methanol or isopropanol becoming contaminated on-site with methamphetamine. If the wipes were prepared off-site, then remove pre-wetted gauze wipe from sample container, opening only one sample container at a time. In either case, squeeze out and discard any excess solvent from the gauze wipe. Use fresh latex or nitrile gloves for each separate sample and blank. Do not use vinyl gloves due to the potential for leaching of phthalate plasticizers and contamination of the samples.
7. Wipe Techniques
   a. Concentric Squares Wiping Technique (particularly suitable for smooth and non-porous surfaces): Fold the pre-wetted gauze in half and then fold in half again. Using firm pressure wipe the area within the template. Start at one of the inside corners of the template and wipe in concentric squares, progressing toward the center. End with a scooping motion. Without allowing the gauze to touch any other surface, reverse the last fold so that the exposed side of the gauze is facing inward and using a fresh surface of the gauze, wipe the same area in the same manner as before. Roll or fold the gauze again and insert into the shipping container.
   b. Side-to-side Wiping (or Blotting) Technique (particularly suitable for rough, porous, and/or soiled surfaces): Fold the pre-wetted gauze in half and then fold in half again. Using firm pressure wipe or blot the area within the template with at least five overlapping side-to-side horizontal passes (see NOTE) beginning at the top and progressing to the bottom in a "Z" pattern. End with a scooping motion. If blotting, blot at least five times on each horizontal pass (see NOTE). Without allowing the gauze to touch any other surface, reverse the last fold so that the exposed side of the gauze is facing inward. Using a fresh surface of the gauze, wipe or blot the area again with at least five overlapping top-to-bottom vertical passes beginning at the left side and progressing to the right in an "N" pattern.

If blotting, blot at least five times on each vertical pass. Roll or fold the gauze again and insert into the shipping container. Blotting is suggested in areas so soiled or rough that the threads of the gauze media are continually snagged.
NOTE: On areas larger than 100 cm^2, more than five passes and blots will be needed.

c. Repeat or Serial Wiping: If isopropanol is used for wiping, a serial or repeat wipe sample of the same area with a fresh gauze wipe will improve sampling efficiency. For serial wiping, repeat the wiping procedure described above (APPENDIX 7a or 7b) with a fresh gauze wipe. Place the second gauze wipe into the same shipping container as the first gauze. The 50-mL polypropylene centrifuge tubes are large enough to contain up to two gauze wipes of either the 3" x 3" 12-ply or 4" x 4" 8-ply sizes.
NOTE: If the area to be wiped remains substantially wet from the first gauze, the second gauze wipe might be used in the dry state to soak up the residual solvent from the first gauze wipe.

8. Cap shipping containers securely and keep refrigerated (<6 °C). Make sure caps are not cross-threaded. Containers must have no chips, fractures, or other irregularities on the sealing edge. Do not use polyethylene plastic bags. While methamphetamine and several related amines are stable on the recommended wipe media for at least 7 days at room temperature, refrigeration is recommended as soon as possible.
9. Label each sample clearly with a unique sample identification number or name, and the date, time, location, and initials or identification number of the individual taking the sample. The above information and a description of the sample and the area wiped should also be recorded in a logbook for later correlation with the analytical results.

SAMPLE PREPARATION

Samples requiring pH adjustment: If there is reason to believe that the samples may be alkaline enough to overcome the acidity of the desorption solution (e.g. wipes of unpainted concrete or stucco surfaces), then the pH must be adjusted to about ≤ 4. The pH may be checked with pH paper or monitored with the addition of about 2 drops of the mixed pH indicator solution of bromothymol blue and phenolphthalein. (The color should be yellow and not green or blue.) The preparation of this indicator solution can be found in NIOSH 9106 or NIOSH 9109 [5, 6]. If the pH needs to be adjusted, a solution of dilute (2.5 to 3 M) sulfuric acid is used and added dropwise. Mix the contents by shaking or inversion a few times by hand after each addition of acid before checking the pH.