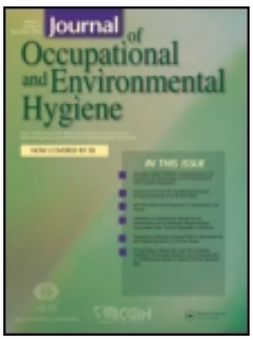

Journal of Occupational and Environmental Hygiene

ISSN: 1545-9624 (Print) 1545-9632 (Online) Journal homepage: http://www.tandfonline.com/loi/uoeh20

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To cite this article: Amy Ekechukwu , Warren Hendricks , Kenneth T. White , Albert Liabastre , Melecita Archuleta & Mark D. Hoover (2009) Validation of Analytical Methods and Instrumentation for Beryllium Measurement: Review and Summary of Available Guides, Procedures, and Protocols, Journal of Occupational and Environmental Hygiene, 6:12, 766-774, DOI: 10.1080/15459620903260536

To link to this article: http://dx.doi.org/10.1080/15459620903260536

Published online: 05 Nov 2009.

Journal of Occupational and Environmental Hygiene, 6: 766–774
ISSN: 1545-9624 print / 1545-9632 online
DOI: 10.1080/15459620903260536

Validation of Analytical Methods and Instrumentation for Beryllium Measurement: Review and Summary of Available Guides, Procedures, and Protocols

Amy Ekechukwu,[1] Warren Hendricks,[2] Kenneth T. White,[3] Albert Liabastre,[4] Melecita Archuleta,[5] and Mark D. Hoover[6]

[1]Savannah River National Laboratory, Aiken, South Carolina
[2]Occupational Safety and Health Administration, Sandy, Utah
[3]Consultive Services, Virginia Beach, Virginia
[4]U.S. Army Center for Health Promotion and Preventive Medicine, Ft. McPherson, Georgia
[5]Sandia National Laboratories, Albuquerque, New Mexico
[6]Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Morgantown, West Virginia

This document provides a listing of available sources that can be used to validate analytical methods and/or instrumentation for beryllium determination. A literature review was conducted of available standard methods and publications used for method validation and/or quality control. An annotated listing of the articles, papers, and books reviewed is given in the Appendix. Available validation documents and guides are listed therein; each has a brief description of application and use. In the referenced sources, there are varying approaches to validation and varying descriptions of the validation process at different stages in method development. This discussion focuses on validation and verification of fully developed methods and instrumentation that have been offered for use or approval by other laboratories or official consensus bodies such as ASTM International, the International Standards Organization, the International Electrotechnical Commission, and the Association of Official Analytical Chemists. This review was conducted as part of a collaborative effort to investigate and improve the state of validation for measuring beryllium in the workplace and the environment. Documents and publications from the United States and Europe are included.

Keywords analytical method development, beryllium, validation, protocol

Address correspondence to Amy Ekechukwu, Savannah River National Laboratory, Analytical Development Building 773-41A, Aiken, SC 29808; e-mail: amy.ekechukwu@srnl.doe.gov.

INTRODUCTION

Numerous guides, procedures, and protocols at the international, regional, national, and local levels pertain to the validation and quality control of analytical methods and/or instrumentation for determination of metals and metalloids such as beryllium. Recognizing the origins, content, and applicability of these resources and requirements can be daunting.

The following sections provide a review and summary of key issues and terms and a snapshot of available sources which can be used to validate methods and/or instrumentation. This review was conducted as part of a collaborative effort to investigate and improve the state of validation and quality control for measuring beryllium in the workplace and the environment. A literature review was conducted of available standard methods and publications used for method validation and/or quality control. A comprehensive annotated listing of the articles, papers, and books reviewed is given in the Appendix. Available validation documents and guides are listed therein; each has a brief description of application and use.

In the referenced sources, there are varying approaches to validation and varying descriptions of the validation process at different stages in method development. This review focuses on validation and verification of methods and instrumentation that have been made available for use or approval by other laboratories or official consensus standards bodies, such as ASTM International, the International Standards Organization (ISO), the International Electrotechnical Commission (IEC), and the Association of Official Analytical Chemists (AOAC). Documents and publications from the United States and Europe are included.

Unless otherwise specified, all referenced documents were published in English. Critical parameters in a typical validation protocol are delineated, and some basic issues for practitioners

are provided. The challenge to practitioners is to conduct appropriate method validation tests and use caution to ensure that their reliance on the available standards and guidelines is appropriate for each application.

KEY ISSUES AND TERMS

Validation

As defined in the ISO/IEC 17025 *General Requirements for the Competence of Testing and Calibration Laboratories*, validation is the confirmation by examination and the provision of objective evidence that the particular requirements for a specific intended use are fulfilled.

Method Validation

Method validation is the process of evaluating whether an analytical method is acceptable for its intended purpose. For pharmaceutical methods, guidelines from the United States Pharmacopeia (USP), International Conference on Harmonization (ICH), and the United States Food and Drug Administration (FDA) provide a framework for performing such validations. In general, methods for regulatory compliance must include studies on specificity, linearity, accuracy, precision, range, detection limit, quantitation limit, and robustness. Elements of these guidelines are readily adapted to the issue of validation for beryllium sampling and analysis.

Benefits of Validation

Validation is used to establish the validity of use of a new or revised method or instrument to provide accurate data for a specific analyte or group of analytes in a given sample matrix (for example, the determination of total beryllium in soils). Although a thorough validation cannot rule out all potential problems, the process of method development and validation should address the most common issues such as sampling errors, proper and appropriate sample preparation procedures, analytical recovery, matrix interferences with the analyte determination, stability of materials, and general robustness. In addition, the specified parameters of detection limits, precision, accuracy, bias, and quantitation limits can also be verified. Validation also provides the appropriate quality assurance documentation for the method.

Mechanics of Validation

Normally, an entity such as a laboratory or an organization will internally develop an analytical method and perform validation tests for the candidate method by following a defined validation protocol with specified acceptance criteria for the validation tests. A round-robin test is often conducted as part of the validation in which several participating laboratories not associated with development of the method agree to analyze samples prepared by the entity that produced the method. The participating laboratories are instructed to use the candidate method for guidance to analyze the samples. The round-robin test is a measure of the robustness of the method, and results from the test are usually included as part of the completed method. Accrediting organizations may require that laboratories use only validated methods, possibly in accordance with applicable consensus standards.

An instrument supplier or manufacturer may develop an instrument that is intended to fill some specific need, such as the measurement of beryllium in air. The manufacturer might either internally perceive the need, or may be requested to develop the instrument by an external organization. The instrument, and perhaps interim methods that employ the instrument, are usually developed and tested by the manufacturer. End users of the instrument may wish to either submit samples for analysis by the instrument manufacturer, or use the instrument on site to analyze samples that are representative of their location. In this way the instrument manufacturer and end users can work together to establish the capabilities and limitations of the instrument and its associated methodology. End users may then wish to develop and validate analytical methods using the instrument for their particular application. Users should thoroughly document any "modifications" of the method if modifications are required for a particular application (e.g., substitution of reagents or alteration of solvent compositions or concentrations to address unique matrix conditions). Undocumented modifications of an existing method may prevent proper interpretation or replication of results.

Sometimes a test-bed platform is used for the development and implementation of large development projects. A test bed allows for rigorous, transparent, and replicate testing of scientific theories, computational tools, and other new technologies. Test beds commonly involve multiple laboratories or organizations, and tests are performed by each entity. Typical parameters for a validation protocol involving multiple laboratories or organizations are described below.

ELEMENTS OF VALIDATION

The following list of validation elements is not comprehensive, but the subject matter is typical of many validation protocols.

Specificity

Specificity is the ability to distinctively and accurately measure the analyte(s) of interest in the presence of other components that may be expected to be present in the sample matrix and may potentially interfere with the measurement. Specificity is a measure of the freedom from interference by such potential contributors as other active ingredients, other analytes, impurities, and degradation products, thereby ensuring that a measured response is due to a single component analyte only (or analytes if multi-species analysis is of interest).

Accuracy

The accuracy of a method, the closeness of the measured value to the true value for the sample, can be assessed in a

number of ways. Most commonly, accuracy is assessed by analyzing a sample of known concentration and comparing the measured value to the true value. National Institute of Standards and Technology (NIST) Standard Reference Materials (SRMs), NIST-traceable standards, and other certified reference materials (CRMs) are often used for this purpose. Another approach is to compare test results from the new method with results from an existing reference method that is known to be accurate. Spike recovery, involving measuring the analytical recovery of known amounts of analyte spiked into sample matrix, is also used for method confirmation purposes.

The fourth approach is the technique of standard addition, which can also be used to determine recovery of spiked analyte. This approach is used if it is not possible to prepare a sample matrix that is chemically and physically representative of the samples that the method is designed to process, but without the presence of the analyte (e.g., beryllium). This can occur, for example, when there is interaction among constituents in a sample so that the resultant signal is significantly different when the analyte is absent or when there is a high background signal in the range where the analyte is being measured.

Sensitivity

For an analytical method, sensitivity refers to the ability of the method to detect small amounts of, or small changes in the amount of, the analyte of interest. Sensitivity is both a function of the method detection limit (such as 1 microgram versus 1 milligram in a sample) and of how well the method detects small changes.

Analytical Range, Precision, and Detection Limit

The range of an analytical method is the concentration interval over which acceptable accuracy, linearity, and precision are obtained. In practice, the range is determined using data from linearity and accuracy studies. Assuming that acceptable linearity and accuracy (analytical recovery) results will have been obtained as described earlier, the only remaining factor to be evaluated is precision. The precision of the method can be estimated from the replicate analyses (triplicate at a minimum) of spiked samples, CRMs, or other suitable replicate samples in the accuracy study. The detection limit of a method is the lowest analyte concentration that produces a response that is discernibly above the noise level of the system. A variety of methods can be used to establish the detection limit. One approach is to use a multiple of (e.g., three times) the background noise level of replicate blank measurements. Precision data can be established through round-robin testing, for example, in accordance with ASTM standard E691.

TYPICAL PARAMETERS FOR A VALIDATION PROTOCOL INVOLVING MULTIPLE LABORATORIES OR ORGANIZATIONS

Initially, minimum requirements or acceptance specifications for the method or instrument should be established and agreed upon by the developer and the entities conducting the validations. The attached annotated appendix describes a number of documents on requirements and guidelines for validation. Typical parameters for a validation protocol involving multiple laboratories or organizations involve:

- Inclusion of an appropriate number of laboratories in the validation or test-bed process (e.g., minimum of four according to requirements of the National Institute for Occupational Safety and Health (NIOSH); a minimum of six for ASTM) (see descriptions of inter-laboratory testing contained in ASTM standards E177 and E691);
- Agreement among participants on the scope and division of work (including possible separation of method validation into discrete steps such as digestion and analysis);
- Establishment of appropriate test phases, such as a first phase in which a designated provider sends standards or instructions on how to prepare standards to test-bed labs and the laboratories perform the analyses, followed by a second phase in which the test-bed laboratories prepare blind standards using a specified protocol to be analyzed by the supplier at its facility;
- Description and consensus on the testing protocol, including all details of the method and associated instrument operating parameters;
- Description of the anticipated limitations and attributes of the method or instrument;
- Consensus (prior to test initiation) on the criteria for success in accordance with applicable performance criteria;
- Specification of sample matrices, including what matrices are compatible or incompatible with the instrument and/or method;
- Estimation and sharing of information on detection limits and practical quantitation or reporting limits;
- Specification of minimum sample requirements, including details of the minimum required sample size (volume or mass);
- Description of the initial samples to be analyzed, including who will provide the samples, or detailed instructions on their preparation;
- Assurance that samples submitted for analysis will be representative of media and analyte concentration that would be encountered in the field of study;
- Description of what constitutes a "difficult sample," including information as to the limitations and interferences that may affect data;
- Examination of typical samples, worst case, and best case (standards), to ensure that samples to be analyzed are at or within appropriate criteria, such as twice the detection limit and 10 times the minimum detection limit in both clean matrices (calibration standards) and challenging matrices;
- Assurance that standards are representative and reproducible;
- Application of the test method or instrument according to the stated parameters of the protocol;

- Performance of tests on laboratory challenge parameters (e.g., high and low detection limits, matrix spikes and interferences, particulate samples);
- Statistical evaluation of data to determine true precision, accuracy, and bias/overall uncertainty (e.g., as per ISO GUM);
- Engagement of participants in compilation and critical review of the resulting test data into a single document to support establishment of a validated method, series of validated methods, or consensus standards (see, for example, A. Agrawal et al.: Validation of a standardized portable fluorescence method for determining trace beryllium in workplace air and wipe samples. *J. Environ. Monit. 8*:619–624 (2006); K. Ashley et al: Ultra-trace determiniation of beryllium in occupational hygiene samples by ammonium bifluoride extraction and flourescence detection using hydroxybenzoquinoline sulfonate. *Anal. Chim. Acta 584*:281–286 (2007)); and,
- Sharing of the results with all interested parties.

BASIC ISSUES FOR PRACTIONERS

In selecting, validating, and controlling a protocol for beryllium analysis, it is prudent for the practitioner to thoroughly consider and address each of the parameters listed above with the following basic issues in mind:

- Be aware that a variety of recommendations and guidelines exist, and that details appropriate for one analytical situation may not apply to a different one;
- Anticipate and address the range of operational conditions that are likely to exist for each parameter in the validation and control protocol, especially issues related to sample matrices and interferences;
- Recognize when operating conditions change in the field or laboratory;
- Evaluate changes that may be needed in the analytical protocol;
- Control the analytical protocol to account for changing conditions, including appropriate documentation of any changes in procedures; and,
- Document all aspects of the protocol, including its scope, types, and matrices of samples, quantities, and limitations.

CONCLUSION

This document provides a listing of available sources that can be used to validate and control analytical methods and/or instrumentation for beryllium determination. The depth and breadth of available resources is substantial. The challenge to practitioners is to conduct appropriate due diligence and use caution to ensure that all reliance on the available standards and guidelines is appropriate for each application.

ACKNOWLEDGMENTS

The authors would like to thank Kevin Ashley, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, for the contributions he made to this document and the assistance he provided. Preparation of this document was a voluntary collaborative effort that was conducted in conjunction with activities of the Beryllium Health and Safety Committee (www.sandia.gov/BHSC). The findings and conclusions in this report are those of the authors and do not necessarily represent the views of their respective employers or organizations.

APPENDIX—LITERATURE REVIEW: METHOD VALIDATION

Guidance Documents

- OSHA Guidelines for Spectroscopy, available at http://osha.gov/dts/sltc/methods/spectroguide/spectroguide.html

These evaluation guidelines were developed to provide OSHA with a uniform and practical means for evaluating sampling methods that utilize spectroscopic analytical techniques. The guidelines define sampling and analytical parameters; specify required laboratory tests, statistical calculations, and criteria for acceptance; and provide a detailed outline for preparation of written reports. Descriptions are provided for tests to evaluate sampler capacity, digestion efficiency, sampling interferences, cassette wiping, analytical detection limit, instrument calibration, analytical interference, detection limit of the overall procedure, reliable quantitation limit, precision of the overall procedure, and reproducibility of the method. Results of the evaluation tests are intended to be included in the written sampling and analytical methods.

The overall goal of these guidelines is to provide OSHA with sampling and analytical methods that can clearly be defended with evaluation data. Other tests deemed necessary for any evaluation are permissible, and a description of these tests and the resultant experimental data shall be included in the back-up data section following the format prescribed in this document. Summary results of these tests shall be presented in the main body of the method. These guidelines are continually open to examination by OSHA and refinements are formally made on a periodic basis. The resulting evolution in the guidelines is apparent when comparing early methods with more recent ones.

- NIOSH Guidelines for Air Sampling and Analytical Method Development and Evaluation, available at http://www.cdc.gov/niosh/docs/95-117/pdfs/95-117.pdf

The objective of this protocol is to determine if a candidate method will provide results that are within ±25% of the true concentration at least 95% of the time. The experiments described in the protocol include determination of analytical recovery from the sampler, sampler capacity, storage stability of samples, and effect of environmental factors. Also included

are evaluation criteria for the experiments, and an appendix to assist users in estimating method bias, precision, and accuracy.

Other appendices are included that detail statistical equations, limits of detection and of quantitation, reports and methods, and other subjects of interest. The work described in the protocol can be summarized in five steps: 1) selection of analytes for testing; 2) development of the sampling and analytical method; 3) evaluation of the method; 4) preparation of a written method; and 5) preparation of a technical report on the development and evaluation.

■ Standard Practice for Applying Statistical Quality Assurance Techniques to Evaluate Analytical Measurement System Performance—ASTM D6299, available at http://www.astm.org/Standards/D6299.htm

This ASTM practice is used to continuously demonstrate the proficiency of analytical measurement systems that are used for establishing and ensuring the quality of petroleum and petroleum products. Data accrued using the techniques included in this practice provide the ability to monitor analytical measurement system precision and bias. These data are useful for updating test methods as well as for indicating areas of potential measurement system improvement. This practice provides information for the design and operation of a program to monitor and control ongoing stability and precision and bias performance of selected analytical measurement systems using a collection of generally accepted statistical quality control (SQC) procedures and tools.

A complete list of criteria for selecting measurement systems to which this practice should be applied, and for determining the frequency at which it should be applied, is beyond the scope of this practice. However, some factors to be considered include 1) frequency of use of the analytical measurement system, 2) importance of the parameter being measured, 3) system stability and precision performance based on historical data, and 4) regulatory, contractual, or test method requirements. This practice is applicable to stable analytical measurement systems that produce results on a continuous numerical scale, as well as laboratory test methods. This practice does not address statistical techniques for comparing two or more analytical measurement systems applying different analytical techniques, or equipment components that purport to measure the same property, so it could not be used to validate a new analytical method by comparison with an existing standard method.

■ Huber, L.: *Validation and Qualification in Analytical Laboratories*: London: Informa Health Care, Interfarm/CRC, 1998.

This validation reference book provides a guide for all validation and qualification processes to comply with Good Laboratory Practices (GLP), Good Clinical Practice (GCP), Current Good Manufacturing Process (cGMP), and ISO 17025. It covers qualification of equipment, reference materials, people, and validation of analytical procedures and systems. The book contains the following:

- Overview on regulations, quality standards, and related guidelines on validation and qualification (FDA, Environmental Protection Agency (EPA), cGMP, GLP, GCP, ISO9000, United States Pharmacopeia [USP], and ISO 17025)
- How to deal with multiple regulations and Quality Standards
- Developing an overall validation strategy (terminology, validation needs, strategy for implementation)
- Risk based validation and qualification, calibration, verification, and validation of equipment
- Analytical instrument qualification
- Validation of software and computer systems
- Validation of analytical routine, nonroutine, and standard methods.

■ Bansal S.K., T. Layloff, E.D. Bush, M. Hamilton, E.A. Hankinson, J.S. Landy, S. Lowes, M.M. Nasr, P.A. St. Jean, V.P. Shah: Qualification of analytical instruments for use in the pharmaceutical industry: a scientific approach. *AAPS PharmSciTech, 5(1)*:1–8 (2004).

The pharmaceutical industry relies on the precision and accuracy of analytical instruments to obtain valid data for research, development, manufacturing, and quality control. Through published regulations, regulatory agencies require pharmaceutical companies to establish procedures ensuring that the users of analytical instruments are trained to perform their assigned tasks. The regulations also require the companies to establish procedures ensuring that the instruments that generate data supporting regulated product testing are fit for use. The regulations, however, do not provide clear and authoritative guidance for validation/qualification of analytical instruments. Consequently, competing opinions abound regarding instrument validation procedures and the roles and responsibilities of the people who perform them. The American Association of Pharmaceutical Scientists sponsored a workshop entitled, "A Scientific Approach to Analytical Instrument Validation," which the International Pharmaceutical Federation (FIP) and International Society for Pharmaceutical Engineering (ISPE) cosponsored and from which this article was generated. The conference's objectives were to:

- Review and propose an effective and efficient instrument validation process that focuses on outcomes, and not only on generating documentation.
- Define the roles and responsibilities of those associated with an instrument's validation.
- Determine whether differences exist between validations performed in laboratories that adopt GLP regulations and those that adopt GMP regulations. Establish the essential parameters for performing instrument validation.
- Establish common terminology.

- Publish a white paper on analytical instrument validation that may aid in the development of formal future guidelines, and submit it to regulatory agencies.

■ Chan, C.C., H. Lam, Y.C. Lee, and X.-M. Zhang: *Analytical Method Validation and Instrument Performance Verification.* John Wiley & Sons, 2004.

Validation describes the procedures used to analyze pharmaceutical products so that the data generated will comply with the requirements of regulatory bodies of the United States, Canada, Europe, and Japan. This book provides a thorough explanation of both the fundamental and practical aspects of biopharmaceutical and bioanalytical methods validation. It teaches the proper procedures for using the tools and analysis methods in a regulated lab setting, including appropriate procedures for calibration of laboratory instrumentation and validation of analytical methods of analysis.

■ Fitness for Purpose of Analytical Methods—A Laboratory Guide to Method Validation and Related Topics, available at www.eurachem.org

Method validation is an important requirement in the practice of chemical analysis. However, information concerning its importance, why and when it should be done, and the tasks involved, is lacking. The purpose of this guide is to discuss the issues related to method validation and increase readers' understanding of how it can be achieved. The guide is expected to be of most use to 1) laboratory managers who are responsible for ensuring the methods within their responsibility are adequately validated, and 2) the analysts responsible for carrying out studies on methods for validation purposes. Other staff may find the guidance of use as a source of background information—senior staff from a management point of view and junior staff from a technical point of view. The guide is aimed at laboratories needing to validate methods but working in isolation, with no immediate possibility of participation in collaborative trials. Those personnel with a working knowledge of simple statistics will find the method validation process easier to understand and implement. Where appropriate, formulae are included.

■ Guidelines for Collaborative Study Procedures to Validate Characteristics of a Method of Analysis—Appendix D, AOAC International, 2002 available at http://www.aoac.org

These guidelines incorporate symbols, terminology, and recommendations accepted by consensus by the participants at the IUPAC Workshop on Harmonization of Collaborative Analytical Studies, Geneva, Switzerland, May 4–5, 1987 [*Pure Appl. Chem. 60*:855–864 (1988); published as "Guidelines for Collaborative Study of Procedure to Validate Characteristics of a Method of Analysis," *J. Assoc. Off. Anal. Chem. 72*:694–704 (1989)]. The original guidelines were revised at Lisbon, Portugal, August 4, 1993, and at Delft, The Netherlands, May 9, 1994, *Pure Appl. Chem. 67*:331–343 (1995). These revised, harmonized guidelines have been adopted by AOAC International as the guidelines for the AOAC Official Methods Program, *J. AOAC Int. 78(5)*:143A–160A (1995). Although the directions were developed for chemical studies, some parts may be applicable to all types of collaborative studies, including those involving beryllium determination.

■ Validation Of Analytical Procedures: Methodology (CPMP/ICH/281/95)—ICH Harmonized Tripartite Guideline, The European Agency for the Evaluation of Medicinal Products, Step 4, Consensus Guideline, November 6, 1996

This guideline is complementary to the parent guideline, which presents a discussion of the characteristics that should be considered during the validation of analytical procedures. Its purpose is to provide some guidance and recommendations on how to consider the various validation characteristics for each analytical procedure. The document considers the various validation characteristics in distinct sections. The arrangement of these sections reflects the process by which an analytical procedure may be developed and evaluated.

■ Guideline for Industry—Text on Validation of Analytical Procedures—FDA Guidance Document, ICH-Q2A, March 1995, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformationGuidances/UCM073381.pdf

This document presents a discussion of the characteristics for consideration during the validation of the analytical procedures included as part of registration applications submitted within the European Union, Japan, and the United States. The document provides a collection of terms and their definitions that serve to bridge the differences that often exist among various compendia, and regulators of the European Union, Japan, and the United States. A tabular summation of the characteristics applicable to identification, control of impurities, and assay procedures is included. The discussion of the validation of analytical procedures is directed to the three most common types of analytical procedures:

- Qualitative identification tests,
- Quantitative tests for impurities' content, and
- Limit tests for the control of impurities if applicable.

■ Guide to Quality in Analytical Chemistry—CITAC/Eurochem Guide, 2002

The Cooperation on International Traceability in Analytical Chemistry (CITAC) has prepared this guide to provide laboratories with guidance on best practice for the analytical operations they carry out. The guidance covers both qualitative and quantitative analysis carried out on a routine or non-routine basis. A separate guide covers research and development work (CITAC/EURACHEM Guide reference A1 on page 43). The guidance is intended to help those implementing quality assurance in laboratories. For those working toward accreditation, certification, or other compliance with particular quality requirements, it will help explain what these requirements

mean. The guidance will also be useful to those involved in the quality assessment of analytical laboratories against those quality requirements. Cross-references to ISO/IEC 17025, ISO 9000, and OECD GLP requirements are provided.

Journal Articles

- Taverniers, I., M. De Loose, and E. Van Bockstaele: Trends in quality in the analytical laboratory II. Analytical method validation and quality assurance. *Trends Anal. Chem.,* 23(8): 535–552 (2004).

This article places validation of analytical methodologies in the broader context of quality assurance (QA). It deals with the concepts of single-laboratory or in-house validation, inter-laboratory or collaborative study, standardization, internal quality control (IQC), proficiency testing (PT), accreditation, and, finally, analytical QA (AQA).

- Feinberg, M., B. Boulanger, W. Dewé, and P. Hubert: New advances in method validation and measurement uncertainty aimed at improving the quality of chemical data. *Anal. Bioanal. Chem*. *380(3)*:502–514 (2004).

This paper discusses the effects of quality systems on the development of an analytical procedure. It emphasizes the importance of method validation and how validation must be fully integrated into the basic design of the method.

- Van Zoonen, P., R. Hoogerbrugge, S.M. Gort, H.J. Van de Wiel, and H.A. Van't Klooster: Some practical examples of method validation in the analytical laboratory. *Trends Anal. Chem. 18(9)*:584–593 (1999).

In this article, validation is put in the context of the process of producing chemical information. Two practical examples are given.

- Boulanger, B., W. Dewé, A. Gilbert, B. Govaerts,and M. Maumy-Bertrand: Risk management for analytical methods based on the total error concept: Conciliating the objectives of the pre-study and in-study validation phases. *Chemometrics Intelligent Lab. Sys. 86(2)*:198–207 (2007).

This paper is a part of selected papers presented at the Chemometrics Congress "CHIMIOMETRIE 2005" in Lille, France, November 30 – December 1, 2005. It discusses two methods of checking the validity of a measurement method at the pre-study level. The first checks whether a tolerance interval for hypothetical future measurements lies within given acceptance limits; the second calculates the probability of a result lying within these limits and computes whether it is greater than a given acceptance level. The properties and respective advantages and limitations of these methods are investigated. A crucial point is to ensure that the decisions taken at the pre-study stage and in routine use are coherent. This paper shows how a laboratory can prevent its method from being rejected by choosing compatible validation parameters at both pre- and in-study levels.

- Moser, J., W. Wegscheider, and C. Sperka-Gottlieb: Quantifying the measurement uncertainty of results from environmental analytical methods. *Fresenius J. Anal. Chem. 370(6)*:679–689 (2001).

The Eurachem-CITAC Guide Quantifying Uncertainty in Analytical Measurement was put into practice in a public laboratory devoted to environmental analytical measurements. Consideration was given to the provisions of ISO 17025, and an attempt was made to base the entire estimation of measurement uncertainty on available data from the literature or from previously performed validation studies.

This paper describes ways and means of quantifying uncertainty for frequently practiced methods of environmental analysis. It was shown that operationally defined measures are no obstacle to the estimation process as described in the Eurachem/CITAC Guide if it is accepted that the dominating component of uncertainty comes from the actual practice of the method as a reproducible standard deviation.

- Reports by the Royal Society of Chemistry Analytical Methods Committee on Evaluation of Instrumentation.

This series of six reports provides guidance on how to evaluate different instrumentation and make comparisons between different instruments. Instrument criteria evaluation forms are provided that list features of interest and how those features are evaluated. The experimental sections provide tests to be performed and the appropriate treatment of data. The reports are as follows:

- Report by the Analytical Methods Committee: Evaluation of Analytical Instrumentation Parts III: Polychromators for Use in Emission Spectrometry with ICP Sources, Analytical Methods Committee, Royal Society of Chemistry. *Anal. Proc.,* April 1986, vol. 23.
- Report by the Analytical Methods Committee: Evaluation of Analytical Instrumentation Parts IV: Monochromators for Use in Emission Spectrometry with ICP Sources, Analytical Methods Committee, Royal Society of Chemistry. *Anal. Proc.,* January 1987, vol. 24.
- Report by the Analytical Methods Committee: Evaluation of Analytical Instrumentation Parts V: Inductively Coupled Plasma Sources for Use in Emission Spectrometry, Analytical Methods Committee, Royal Society of Chemistry. *Anal. Proc.,* September 1987, vol. 24.
- Report by the Analytical Methods Committee: Evaluation of Analytical Instrumentation Parts VI: Wavelength Dispersive X-Ray Spectrometers. Analytical Methods Committee, Royal Society of Chemistry. *Anal. Proc.,* December 1990, vol. 27.
- Report by the Analytical Methods Committee: Evaluation of Analytical Instrumentation Parts VII: Simultaneous

Wavelength Dispersive X-Ray Spectrometers, Analytical Methods Committee, Royal Society of Chemistry. *Anal. Proc.,* October 1991, vol. 28.

- Report by the Analytical Methods Committee: Evaluation of Analytical Instrumentation Parts VIII: Instrumentation for Gas Liquid Chromatography, Analytical Methods Committee, Royal Society of Chemistry. *Anal. Proc.*, July 1993, vol. 30.

■ Green, J.M.: A practical guide to analytical method validation. *Anal. Chem. 68*:305A–309A (1996).

This article gives a description of a set of minimum requirements for validation of an analytical method.

■ Binstock, D.A., P.M. Grohse, A. Gaskill, C. Sellers, H.M. Kingston, and L.N. Jassie: Development and validation of a method for determining elements in solid-waste using microwave digestion. *J. Assoc. Off. Anal. Chem. 74(2)*:360–366 (1991).

A microwave-assisted method for preparing samples for determination of elements in solid waste has been developed (draft EPA Method 3051). Validation of the sample preparation method was performed through a collaborative study to determine its precision and accuracy.

Standards and Guidelines

■ ISO/IEC 17025 General Requirements for the Competence of Testing and Calibration Laboratories, Second Edition, Date: May 5, 2005.

This document includes clause 5.4 on test and calibration methods and method validation; sub-clause 5.4.5 on validation of methods; and sub-clause 5.4.5.1 that states that validation is the confirmation by examination and the provision of objective evidence that the particular requirements for a specific intended use are fulfilled.

■ Validation of Analytical Chemistry Laboratories, Federal Construction Regulations (4510), COE EM 200-1-1, 1994.

■ Water Quality—Guide to Analytical Quality Control for Water Analysis: BSI DD ENV ISO 13530. Date: February 15, 1999.

■ ISO GUIDE 35 Reference Materials—General and Statistical Principles for Certification, Third Edition, 2006.

This guide gives statistical principles to assist in the understanding and development of valid methods to assign values to properties of a reference material, including the evaluation of their associated uncertainty, and establish their metrological traceability. Reference materials that undergo all steps described in this guide are usually accompanied by a certificate and called a CRM. This guide will be useful in establishing the full potential of CRMs as aids to ensure the comparability, accuracy, and compatibility of measurement results on a national or international scale.

■ Validation of Analytical Procedures: Definitions and Terminology, Directive75/318/EEC, November 1994.

■ Note for Guidance on Validation of Analytical Procedures Methodology, ICH Topic Q2B, Step 4 Consensus Guideline, November 6, 1996.

■ International Conference on Harmonization. Draft Guideline on Validation of Analytical Procedures: Definitions and Terminology, *Federal Register 60*:11260 (March 1, 1995).

This document was prepared by a working group to provide guidelines on the single-laboratory validation of methods of analysis. These guidelines provide minimum recommendations on procedures that should be employed to ensure adequate validation of analytical methods

Books

■ Swartz, M., and I.S. Krull (eds.): *Analytical Method Development and Validation.* CRC, 1997.

This book describes analytical methods development, optimization, and validation, and provides examples of successful methods development and validation in high-performance liquid chromatography (HPLC) areas. The text presents an overview of FDA/International Conference on Harmonization (ICH) regulatory guidelines, compliance with validation requirements for regulatory agencies, and methods validation criteria stipulated by the US Pharmacopeia, FDA, and ICH.

■ De Bièvre, P., and H. Günzler (eds.): *Measurement Uncertainty in Chemical Analysis*. New York: Springer, 2003.

This volume collects 20 papers on the topic of measurement uncertainty, mostly published from 1999–2002 in the journal *Accreditation and Quality Assurance*. They provide the rationale for why it is important to evaluate and report the uncertainty of a result in a consistent manner. They also describe the concept of uncertainty, the methodology for evaluating uncertainty, and the advantages of using suitable reference materials. The benefits to both the analytical laboratory and the user of the results are considered.

■ Parkany, M.: *Quality Assurance and Total Quality Management for Analytical Laboratories*. London, UK: Royal Society of Chemistry, 1993.

This book provides guidance, through the experience and expertise of professionals and academics, on how laboratories should proceed in implementing appropriate QA systems to enable accreditation in accordance with ISO 9000 series, the ISO/IEC Guide 25, EN 45000, and the ISO 14000 series. Examples from multiple laboratories (food, medicine, oil, clinical, forensic, environmental, industry, and university) are

given. It also contains the selected list of the relevant ISO International Standards and the ISO/IEC Guides.

■ De Bievre, P., and H. Günzler: *Validation in Chemical Measurement,* 1st ed. New York: Springer, 2005.

The validation of analytical methods is based on the characterization of a measurement procedure (selectivity, sensitivity, repeatability, reproducibility). This volume collects 31 outstanding papers on the topic, mostly published in the period 2000–2003 in the journal *Accreditation and Quality Assurance*. They provide the latest understanding, and possibly the rationale why it is to integrate the concept of validation into the standard procedures of every analytical laboratory. In addition, this anthology considers the benefits to both: the analytical laboratory and the user of the measurement results.

■ Swartz, M.E., and I.S. Krull: *Analytical Method Development and Validation.* New York: Marcel Dekker, Inc., 1997.

This book provides basic guidelines to develop a reliable and valid analytical method as well as guidelines for the evaluation of the method. Validation is treated as a part of the overall method development and implementation process.