Designation: E2857 – 11

StandardGuide for Validating Analytical Methods[1]

This standard is issued under the fixed designation E2857; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This guide describes procedures for the validation of chemical and spectrochemical analytical methods of analysis that are used by a metals, ores, and related materials analysis laboratory.

1.2 This guide may be applied to the validation of laboratory developed (in-house) methods, addition of analytes to an existing standard test method, variation or scope expansion of an existing standard method, or the use of new or different laboratory equipment.

1.3 This guide may also be used to validate the implementation of standard test methods used routinely by laboratories of the mining, ore processing, and metals industry.

2. Referenced Documents

2.1 *ASTM Standards:*[2]

E135 Terminology Relating to Analytical Chemistry for Metals, Ores, and Related Materials

E1601 Practice for Conducting an Interlaboratory Study to Evaluate the Performance of an Analytical Method

E1763 Guide for Interpretation and Use of Results from Interlaboratory Testing of Chemical Analysis Methods

2.2 *ISO Standard:*[3]

ISO/IEC 17025 General requirements for the competence of testing and calibration laboratories

3. Terminology

3.1 *Definitions*—For definitions of terms used in this guide, refer to Terminology E135.

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *validation (of an analytical method), n*—confirmation, by the provision of objective evidence and examination, that a method meets performance requirements and is suitable for its intended use.

4. Significance and Use

4.1 Method validation is a process of demonstrating that the method meets the required performance capabilities. International standards such as ISO/IEC 17025, certifying bodies, and regulatory agencies require evidence that analytical methods are capable of producing valid results. This applies to laboratories using published standard test methods, modified standard test methods, and in-house test methods.

4.2 Although a collaborative study is part of this guide, this guide may be used by a single laboratory for method validation when a formal collaboration study is not practical. This guide may also be applied before a full collaboration study to predict the reliability of the method.

4.3 The use of multiple validation techniques described in this guide increases confidence in the validity or application of the method.

4.4 It is beyond the scope of this guide to describe fully the fundamental considerations in Section 5. For a more descriptive definition of these concepts, refer to the International Union of Pure and Applied Chemistry (IUPAC) technical report, "Harmonized Guidelines for Single Laboratory Validation of Methods of Analysis,"[4] the *IUPAC Compendium of Analytical Nomenclature* (Orange Book),[5] and the Eurachem publication, *The Fitness for Purpose of Analytical Methods, A Laboratory Guide to Method Validation and Related Topics*.[6]

5. Fundamental Considerations

5.1 During the process of method validation, the user of an analytical method should apply a number of fundamental tenets

[1] This guide is under the jurisdiction of ASTM Committee E01 on Analytical Chemistry for Metals, Ores, and Related Materials and is the direct responsibility of Subcommittee E01.22 on Laboratory Quality.

Current edition approved Nov. 1, 2011. Published January 2012. DOI: 10.1520/E2857–11.

[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

[3] Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036, http://www.ansi.org.

[4] M. Thompson, S. Ellison, and R. Wood, "Harmonized Guidelines for Single-Laboratory Validation of Methods of Analysis," *Pure Appl. Chem.*, Vol 71, No. 2, 2002, pp. 835-855. http://iupac.org/publications/pac

[5] *International Union of Pure and Applied Chemistry Compendium of Analytical Nomenclature: Definitive Rules 1997,* http://old.iupac.org/publications/analytical_compendium/

[6] EURACHEM Guide, *The Fitness for Purpose of Analytical Methods, A Laboratory Guide to Method Validation and Related Topics*, LGC, Teddington, Middlesex, United Kingdom, 1998. www.eurachem.org

of analytical chemistry as they relate to the development and implementation of test methods. It is important to make the distinction between the validation of a test method by a standards-developing organization and the implementation of that test method by a laboratory. Whether the test method was developed by a committee of experts or by one chemist in a company laboratory, the laboratory shall implement the method in the laboratory and shall demonstrate that the method is being performed sufficiently well and that the results meet the goals for data quality. That is, they should ascertain that the measurement process provides sufficient levels of performance fit for the purpose of testing the materials at hand. It is advisable to determine and document performance characteristics of the method including repeatability precision, limit of detection, limit of quantification, and perhaps other parameters. The laboratory is advised to evaluate the method for bias and for susceptibility to introduction of bias (namely, ruggedness). A number of important considerations are discussed in 5.1.1-5.1.7, but specific procedures for determination and calculation are beyond the scope of this guide.

NOTE 1—In the following discussion, the term measurement process is taken to mean the entire process by which a laboratory performs a test including sample preparation, measurements, and calculation of results.

5.1.1 *Precision*—The first step in development and implementation of an analytical method is demonstration that measurements can be made with sufficient repeatability for the purpose of quantitative analysis. Precision is defined as the degree of agreement among a set of values. Precision under repeatability conditions is measured by having a single analyst in a single laboratory use a single set of equipment to prepare and analyze portions of a homogeneous material. Precision under reproducibility conditions is measured by having a number of different analysts at different laboratories prepare and analyze portions of a homogeneous material. Any number of conditions intermediate between repeatability conditions and reproducibility conditions may be used if the data serves a useful purpose. A good example is having multiple analysts in a single laboratory perform the analyses, perhaps on multiple days. In the terminology of Committee E01, repeatability is synonymous with within-laboratory standard deviation, S_r, which is defined as the standard deviation of results collected on the same material in the same laboratory on different days. In contrast, reproducibility is synonymous with between-laboratory standard deviation, S_R, which is defined as the standard deviation of results obtained on the same material in different laboratories.

5.1.1.1 The most common estimators of precision are standard deviation, relative standard deviation, and variance. Equations and examples are available in many texts on statistics.

5.1.1.2 The concept of maintenance of the repeatability over a period of time is known as statistical control. The laboratory can implement tools such as control charts to demonstrate statistical control.

5.1.2 *Limit of Detection (L_D)*—The detection limit is defined as the lowest amount of analyte that can be distinguished from background by an analytical method. It is important to demonstrate that the measurement process has the capability to detect a significantly lower amount (concentration or mass fraction) of the analyte than the laboratory must quantify. For additional information, consult the IUPAC Orange Book and the Currie paper.[7]

5.1.3 *Limit of Quantification (L_Q)*—The limit of quantification is defined as the amount of analyte above which the estimated relative standard deviation (RSD) is ≤10 %. It is important to demonstrate and document that the measurement process has the capability to quantify amounts less than or equal to those found in materials to which the test method is applied. For additional information, consult the IUPAC Orange Book and the Currie paper.[7]

5.1.4 *Bias*—Bias is the difference between the obtained result for a measurand and the true value of the measurand. An analytical method may be subject to a known amount of bias that was estimated when the standard test method was developed and validated by a committee. In an analogous manner, a laboratory developing a new test method or implementing a published standard test method shall perform tests to estimate bias and demonstrate the method's resistance to introduction of additional bias, that is, ruggedness. Documentation of this performance enables the laboratory to elucidate the scope of the method and defend the results obtained using the method.

NOTE 2—Accuracy is a concept related to both bias and precision. It is the combination of knowledge of both the precision obtainable under various conditions and the amount of bias inherent in a given result. The concept of accuracy is often used in discussions of the fitness for purpose and the reliability of results from a test method. In a published standard test method, the statements of precision and bias taken together provide the basis for judgments of the accuracy of the test method.

5.1.5 *Selectivity*—The selectivity of a method is its ability to produce a result that is not subject to change in the presence of interfering constituents. The selectivity of a method can be investigated by introducing or varying amounts of substances and evaluating the results for changes. By understanding the principal of measurement, the analyst may be able to define a short list of suspected interferences and, thereby, limit the amount of effort needed to establish the significant interference effects.

5.1.6 *Calibration Model*—Relative methods require calibration using measurements of suitable reference materials and mathematical fitting of the measured responses to an algorithm, that is, an equation thought to describe adequately the relationship between the amount of analyte and the measured response. Algorithms are almost always an approximation of the real world, and as such, their ability to fit the data has limits that can be tested by a variety of means including, but not limited to, analyses of certified or other reference materials and statistical evaluation of confidence intervals bracketing the calibration curve and extrapolating performance predictions beyond the range of the calibrants.

5.1.6.1 *Working Range*—The term working range is a name given to the concept of a portion of a calibration curve that provides valid results as opposed to portions that are not fit for purpose. The range in which the method is considered to be valid can be characterized using a number of approaches. The

[7] L. A. Currie, "Nomenclature in Evaluation of Analytical Methods Including Detection and Quantification Capabilities," *Pure Appl. Chem.*, Vol 67, No. 10, 1995, pp. 1699-1723. http://iupac.org/publications/pac