Standard Practice for
Uncertainty Assessment in the Context of Seized-Drug Analysis[1]

This standard is issued under the fixed designation E2764; 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 practice provides guidance on the concept of uncertainty and its application to the qualitative and quantitative analysis of seized drugs. In this context, uncertainty encompasses limitations of qualitative methods as well as numerical ranges as applied to quantitative analyses.

1.2 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

1.3 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]
E2329 Practice for Identification of Seized Drugs
E2327 Practice for Quality Assurance of Laboratories Performing Seized-Drug Analysis
E2549 Practice for Validation of Seized-Drug Analytical Methods
2.2 *ISO Standards:*[3]
ISO 3534-1:1993 Statistics—Part 1: Probability and General Statistical Terms

3. Significance and Use

3.1 *Application of Uncertainty*—Qualitative and quantitative analyses require different approaches, refer to the references for additional information. Analysts shall understand the limitations of qualitative and quantitative determinations and have tools to estimate a value for measurement uncertainty of relevant, but not necessarily all, numerical results. In this regard, efforts should be made to use the vocabulary, symbols, and formatting expressed in documents published by international standardizing organizations such as ISO and ASTM International.

3.1.1 An understanding of uncertainty is fundamental to the interpretation and reporting of results.

3.1.2 The term "uncertainty" does not imply doubt; rather, its consideration provides assurance that results and conclusions from methods and analytical schemes are fit for purpose.

3.1.3 The concept of uncertainty shall be considered for both qualitative and quantitative results.

3.1.4 Laboratory management shall ensure that uncertainty be addressed through the provision of training, procedures and documentation.

3.1.5 Laboratory management should consider customer requirements, such as a request for qualitative versus quantitative determinations, which influence the assessment of uncertainty.

3.2 The benefits of understanding and determining uncertainty in this context include:

3.2.1 Enhancing confidence through increased understanding of results,

3.2.2 Providing a mechanism to express the reliability of results,

3.2.3 Enabling the laboratory management and customer to evaluate the fitness for purpose of results,

3.2.4 Facilitating the identification of procedural limitations and providing a basis for improvement, and

3.2.5 Complying with accreditation requirements.

4. Qualitative Analysis

4.1 The identification of seized drugs requires the combination of methods to form an analytical scheme (see Practice E2329).

4.2 Individual methods have limitations and, consequently, uncertainty. Uncertainty of qualitative methods is not typically amenable to being expressed in numerical terms.

4.3 Understanding these limitations enables laboratory personnel to build an appropriate analytical scheme to correctly identify a drug or other chemical.

4.3.1 It is expected that in the absence of unforeseen error, an appropriate analytical scheme effectively results in no uncertainty in reported identifications.

4.3.2 Relevant limitations of an analytical scheme (for example, inability to differentiate isomers, unavailability of reference standard, limits of detection and resolution) should be documented and might need to be included in the report (see reporting examples in 7.2).

5. Quantitative Measurements

5.1 Quantitative measurements have an associated uncertainty, which is defined as "an estimate attached to a test result which characterizes the range of values within which the true value is asserted to lie" (ISO 3534-1:1993).

5.2 A precise calculation of measurement uncertainty may not always be required.

5.2.1 Laboratory personnel shall understand the contributing factors of measurement uncertainty for each analytical procedure and evaluate them with respect to customer, accreditation, and jurisdictional requirements.

5.2.2 Where a value is critical, such as a weight or purity level close to a statutory threshold, an appropriate measurement uncertainty determination shall be applied.

5.3 Primary numerical values reported in the analysis of seized drugs are weight and purity. Where other values are measured (for example, size, volume, estimated tablet numbers), the same principles stated herein apply.

6. Estimation of Measurement Uncertainty for Quantitative Determinations

6.1 *Sources of Uncertainty for Weight Determinations*—The uncertainty of a reported value is dependant on the weighing process. Factors for consideration include:

6.1.1 Single versus multiple items (number of weighing operations),

6.1.2 Tare function as a separate weighing operation,

6.1.3 Extrapolation of population weight from limited sampling of multiple items,

6.1.4 Aggregate weighings,

6.1.5 Incomplete recovery of material from the packaging,

6.1.6 Balance selection (for example, readability, capacity), and

6.1.7 Balance operation (for example, sample placement on pan, environmental conditions).

6.2 *Sources of Uncertainty for Purity Determination*—The uncertainty of a reported purity value is dependant upon the entire quantitation process. Factors for consideration include:

6.2.1 *Sampling Plan* (for example, handling of multiple exhibits):

6.2.1.1 Sample homogeneity.

6.2.2 *Analytical Method:*

6.2.2.1 Sample preparation (for example, sample size, matrix effects, solubility),

6.2.2.2 Analytical technique,

6.2.2.3 Reference material (for example, purity of standard),

6.2.2.4 Equipment and instrument properties (for example, glassware, pipetters, balances, chromatographs),

6.2.2.5 Concentration of analyte, and

6.2.2.6 Environmental conditions.

6.3 *Factors Relevant to Estimation of Measurement Uncertainty:*

6.3.1 When estimating measurement uncertainty, consider the following sources of error:

6.3.1.1 *Analytical Error*—Systematic and random error both contribute to measurement uncertainty and shall be addressed through method validation and quality assurance practices (see Practices E2327 and E2549). Systematic error should be characterized and minimized for all validated procedures.

6.3.1.2 *Sampling Error*—The sample and sampling procedure are often the greatest contributors to measurement uncertainty.

6.3.2 Where appropriate, confidence levels (for example, 95 % or 99.7 %) shall be determined based on considerations relevant to the analytical context.

6.3.3 Record uncertainty information in validation documents, case records, or both.

6.4 *Approaches for Estimating Measurement Uncertainty:*

6.4.1 *Uncertainty Budget Approach:*

6.4.1.1 In this approach all sources of error are separately identified and tabulated.

6.4.1.2 A value is assigned to each source of error (collectively or individually) using either: empirical data (for example, from validation process, historical performance data, control chart data, proficiency tests); published data (for example, volumetric glassware tolerances); or combination of empirical and published data.

6.4.1.3 Where a source has an uncertainty which is insignificant compared to other sources, it can be excluded. Document the reasons for any exclusions.

6.4.1.4 The remaining significant values are used to calculate the combined standard uncertainty and expanded uncertainty.

6.4.2 *Non-Budget Approaches:*

6.4.2.1 The sources of uncertainty that are separately assessed in the budget method are collectively assessed by experimental measurement. In this approach data obtained from a statistically significant number of replicate analyses utilizing a validated method with an appropriate sampling plan may be utilized to calculate the standard or expanded uncertainty.

6.4.2.2 An alternate approach involves the use of two standard deviations (2σ) of the test method results from reproducibility data from the validation studies. This provides an approximation of the measurement uncertainty for non-critical values.

7. Reporting of Uncertainty

7.1 *Reporting*—Uncertainty should be reported when appropriate. Factors which influence the decision to report uncertainty include:

7.1.1 *Jurisdictional:*

7.1.1.1 Prevailing statutory requirement,

7.1.1.2 Relevant governing body (agency) requirements,

7.1.1.3 Customer requests, and

7.1.1.4 Potential exculpatory value.

7.1.2 *Types of Analysis:*

7.1.2.1 *Qualitative*—Qualitative results where limitations of analytical scheme are known and relevant (for example, inability to differentiate isomers, unavailability of a reference standard), and

7.1.2.2 *Quantitative*—Quantitative measurements where a value is critical (for example, weight or purity level close to a statutory threshold).

7.1.3 *Laboratory Accreditation Requirements.*

7.2 *Reporting Examples of Uncertainty*—Reporting requirements and styles differ among agencies and jurisdictions. The examples listed below are drawn from laboratories with varied requirements. The expression of uncertainty is in italics and bold.

7.2.1 *Qualitative Results:*

7.2.1.1 Contains ephedrine **or** pseudoephedrine. Item tested: 5.2 g net.

7.2.1.2 Contains cocaine (**salt form not determined**).

7.2.2 *Quantitative Results*—Factors to be considered when reporting measurement uncertainty include use of significant figures, confidence intervals and rounding/truncating of results.

7.2.2.1 Active drug ingredient (established or common name) methamphetamine hydrochloride:

Gross weight:	25.6 g
Net weight:	5.2 g
Concentration or purity:	54.7 % (±2.8 %)[A]
Amount of actual drug:	2.8 g
Reserve weight:	5.1 g

[A] This value represents the quantitative uncertainty measurement estimate for the laboratory system.

7.2.2.2 Positive for cocaine in the sample tested:

Net weight of total sample:	5.23 g ± 0.03 g
Quantitation:	54.7 % ± 2.8 %

7.2.2.3 Sample tested positive for cocaine:

Net weight:	5.23 g
Purity:	54.7 %
Confidence range:	±2.8 %[A]
Calculated net weight of drug:	2.8 g of cocaine

[A] Confidence range refers to a 95 % confidence level.

7.2.2.4 Cocaine was identified in the Item 1 powder at a purity of 65 ± 9 % (99.7 % confidence level). The Item 1 powder weighed 800 mg ± 4 mg (99.7 % confidence level).

7.2.2.5 *White Powder: 5.6 g*—The range of heroin concentration identified in the sample was not less than 53.2 % and not more than 56.2 %.

8. Training

8.1 Individuals responsible for determining, evaluating and documenting uncertainty in the context of seized-drug analysis shall be capable of competently demonstrating familiarity with foundational concepts and principles of estimating uncertainty. Useful topics to review include:

8.1.1 General metrology to include: terminology, symbols, formulae, publications, international organizations, and global application as related to seized-drug analysis;

8.1.2 The concepts of random and systematic error, accuracy, precision (repeatability, reproducibility, and their conditions), statistical control, standard and expanded uncertainty, and propagation of error;

8.1.3 Reporting conventions including use of significant figures, truncation, and rounding; and

8.1.4 Basic statistics (descriptive and inferential) to include: measures of central tendency (for example, median), measures of variation, statistical modeling, sampling, probability, confidence interval, and significance level.

8.2 All analysts shall be capable of explaining their laboratory's procedures for evaluating uncertainty of qualitative and quantitative analyses.

REFERENCES

(1) E29 – 04: Standard Practice of Using Significant Digits in Test Data to Determine Conformance with Specifications, West Conshohosken, PA.

(2) The International Vocabulary of Basic and General Terms in Metrology, International Organization for Standardization, Switzerland, 2008.

(3) ISO 3534-1: Statistics — Vocabulary and Symbols, Part 1: Probability and General Statistical Terms; ISO 3534-2: Statistics — Vocabulary and Symbols, Part 2: Statistical Quality Control; International Organization for Standardization, Switzerland, 2006.

(4) ISO 5725-1: Accuracy (Trueness and Precision) of Measurement Methods and Results Part 1: General Principles and Definitions, International Organization for Standardization, Switzerland, 1994.

(5) ISO/IEC 17025: General Requirements for the Competence of Testing and Calibration Laboratories, International Organization for Standardization, 2005.

(6) Guide to the Expression of Uncertainty in Measurement, ISBN 92-67-10188-9, International Organization for Standardization, Switzerland, 2008.

(7) Guidelines for Evaluation and Expressing the Uncertainty of NIST Measurement Results, National Institute of Standards and Technology, NIST Technical Note 1297, 1994 Edition.

(8) Kimothi, S.K., The Uncertainty of Measurements Physical and Chemical Metrology Impact and Analysis, Milwaukee American Society for Quality, 2002.

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(13) Taylor, B.N., *Guide for the Use of the International System of Units (SI)*, National Institute of Standards and Technology, April 1995 .