Chemistry Unit
Procedures for Estimating Measurement Uncertainty

1 Purpose

No measurement is exactly known. Measurement uncertainty is the variability associated with a quantitative measurement result based on the information known about the measurement method. This document describes the Chemistry Unit's (CU) approach to estimating measurement uncertainty. The approach is based on a simplified version of the "Guide to the Expression of Uncertainty in Measurement" or the "GUM"; a widely-accepted method for evaluating, estimating, and expressing measurement uncertainty, as well as the National Institute of Standards and Technology (NIST) 8-Step Process.

2 Scope

This document applies to CU personnel recording and/or reporting measurement results that require an estimation of measurement uncertainty. Measurement uncertainty will be estimated for all reported quantitative results.

Additionally, measurement uncertainty will be estimated and reported for the following conditions:

- The measurement uncertainty is relevant to the validity or interpretation of the examination results.
- The measurement uncertainty is required by the contributor.
- The measurement uncertainty affects compliance to a specification limit.

3 Records

The following supporting records related to the estimation of measurement uncertainty will be maintained. This information may be recorded in multiple locations to include: standard operating procedures, validation binders, measurement uncertainty records (to include electronic files, e.g., Excel® spreadsheets), and case files.

- Statement defining the measurand (i.e., the quantity intended to be measured)
- Statement of how traceability is established for the measurement
- The equipment [e.g., measuring device(s) or instrument(s)] used
- All uncertainty components considered

- All uncertainty components of *significance* (see section 4.2) and how they were evaluated
- Data used to estimate repeatability, intermediate precision, and/or reproducibility
- All calculations performed
- The combined standard uncertainty, the coverage factor (k), the confidence level (also known as the coverage probability) and the resulting expanded uncertainty
- The schedule to review and/or recalculate the measurement uncertainty

4 Estimating Measurement Uncertainty

The eight steps listed below are used to estimate measurement uncertainty in the CU:

- Step 1: Specify the measurement process
- Step 2: Identify uncertainty components
- Step 3: Quantify uncertainty components
- Step 4: Convert quantities to standard uncertainties
- Step 5: Calculate combined standard uncertainty
- Step 6: Expand the combined standard uncertainty by coverage factor (k)
- Step 7: Evaluate the expanded uncertainty
- Step 8: Report the uncertainty

The CU utilizes uncertainty budgets for performing estimation of measurement uncertainty calculations. An example spreadsheet is shown in Figure 1.

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4.1 Step 1: Specify the Measurement Process

In the first step, the measurand is defined. The measurand is the quantity intended to be measured. It is important to be as specific as possible when defining the measurand. The measurand will likely be determined by a combination of measurement processes. If necessary, include a reference to a specific standard operating procedure, instrument, etc., in the statement defining the measurand to distinguish one measurement process from another.

4.2 Step 2: Identify Uncertainty Components

Possible uncertainty components associated with the measurement process should be assembled into a reasonably comprehensive list. This list must include all uncertainty components considered, and which uncertainty components were deemed to be *significant*. An uncertainty component is considered *significant* if a change in the uncertainty component corresponds to a change in the significant figures of the stated value or uncertainty of the measurement result. Several uncertainty components that may be considered in this process are provided below.

The specific measuring device or instrument used for a reported test result must be evaluated in the estimation of measurement uncertainty for the associated test method.

- Sampling (homogeneity, physical state, environment, etc.)
- Sample preparation (homogenizing, dissolving, extracting, diluting, concentrating, derivatizing, etc.)
- Reference materials (purity, ability to matrix match, etc.)
- Uncertainty of a calibration (pipettes, balances, etc.)
- Calibration curves (uncertainty of calibrators, matrix matching of calibrators, etc.)
- Analysis (systematic errors, random errors, environment, matrix interferences, run-to-run precision, etc.)

4.2.1 Reconciliation of Uncertainty Components

Reconciliation simplifies the uncertainty budget. In this step, a review is conducted to determine whether a listed uncertainty component is adequately accounted for by existing data (usually repeatability data) or small experiments are planned to account for the uncertainty component. The basis for this step lies in the fundamental assumption that if an uncertainty component is representatively varied during the course of a series of observations, then the uncertainty associated with that component is adequately accounted for in the repeatability of those observations. Of course, it is important that those uncertainty components that are reconciled in this step are truly represented through the existing data or planned experiments.

4.3 Step 3: Quantify Uncertainty Components

Once the uncertainty components have been identified and reconciled, the standard deviation of each will be determined. The approach to calculating the standard deviation is dependent on whether the uncertainty component is classified as a *Type A* or *Type B*.

4.3.1 *Type A* Uncertainty

Type A uncertainty is evaluated by the statistical analysis of data from a series of measurements, assuming a normal distribution. The CU relies on the use of "historical" data (e.g., method validation data, positive control data) to establish a historical standard deviation for the measurement process. The historical standard deviation is the value assigned to the *Type A* uncertainty associated with the measurement process and the equation for calculating the historical standard deviation (s_{hist}) is shown below. This standard deviation may be referred to interchangeably in the CU by a variety of terms including: historical standard deviation, sample standard deviation, method standard deviation, process standard deviation, and standard deviation. Additionally, the use of the symbol, σ (traditionally used to indicate the population standard deviation) in place of the symbol, s, when referring to a sample standard deviation in the CU is acceptable as long as the associated calculations are clearly defined.

$$s_{hist} = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{n-1}} \ ,$$

where $\bar{x} = \frac{1}{n}\sum_{i=1}^{n} x_i$ (i.e., $\bar{x}$ is the average measurement result),

and $n =$ the number of measurements

There may be instances where the standard deviation for a measurement process is calculated to be extremely small or even zero due to the standard deviation being less than the resolution of the measuring device. In these instances, the estimated standard deviation (s_p) will be calculated from the below equation, where d = the measuring device resolution. The estimated standard deviation will be compared to the observed standard deviation and the larger value will be used.

$$s_p = \frac{d}{\sqrt{3}}$$

4.3.1.1 Measurement Assurance and Updating the Historical Standard Deviation

At least one positive control sample is analyzed with each measurement process. A range of acceptable values for positive control samples is defined in the associated CU standard operating procedures. If a value that does not fall within the acceptable range is observed, then the result will be investigated. If the value cannot be explained (e.g., human error, instrument malfunction) then an appropriate statistical analysis will be performed to determine if the value is an outlier. An outlier value will be rejected and not used to calculate the updated standard deviation. Otherwise the value will be included in the updated standard deviation calculation.

The schedule to update the repeatability component (i.e., standard deviation) used in uncertainty calculations will be defined within standard operating procedures.

4.3.1.2 Adjustments to the Historical Standard Deviation when Reporting the Average of Multiple Measurements of a Case Specimen (Standard Deviation of the Mean)

It is common for multiple measurements of a case specimen to be made and the average of the multiple measurements to be reported. These repeat measurements provide more information and more confidence in the reported result. In these instances, the standard deviation of the mean (s_{mean}) will be calculated as follows, where s_{hist}= the historical standard deviation, and n

= the number of measurements used to calculate the average value of the case specimen:

$$s_{mean} = \frac{s_{hist}}{\sqrt{n}}$$

The standard deviation of the mean is then used as the *Type A* uncertainty value.

As an example, if a historical standard deviation for a procedure was equal to 4.3_8% and a case specimen measurement result was based on an average of 5 measurements, then the standard deviation of the mean would be calculated as $[(4.3_8\%) / \sqrt{5}\,] = 1.9_6\%$. This value of 1.9_6% would then be used as the *Type A* uncertainty value in the estimation of measurement uncertainty calculations (note- in this example three significant figures are carried forward as indicated by the subscript in the hundredths place, with the intention of rounding up to two significant figures at the conclusion of the uncertainty calculations).

4.3.2 *Type B* Uncertainty

Type B uncertainty is evaluated by means other than the statistical analysis of data from a series of observations. No single approach is applicable for evaluating and quantifying these uncertainty components. Examples of *Type B* uncertainty components include uncertainty of a calibration (i.e., external calibration services), uncertainty of a reference material, and uncertainty of volumetric glassware.

Some *Type B* uncertainty values can be derived from sources of information that are readily available in the CU. These sources include:

- Calibration certificates of reference materials, instrumentation, and equipment
- Manufacturer's specifications for volumetric glassware, instrumentation, and equipment
- Reference data from handbooks

When information sources such as those listed above are not available for deriving *Type B* uncertainty values, but the upper and lower limits of the instrument or device are known, then the uncertainty value will be estimated using the Rectangular Distribution or Triangular Distribution approaches described below. When in doubt, use the Rectangular Distribution approach as it is the more conservative approach.

4.3.2.1 *Type B* Uncertainty- Rectangular Distribution

A Rectangular Distribution approach can be used to estimate a *Type B* uncertainty component if the following criteria are met: the upper and lower limits of the instrument or device are known, the probability that a value lies outside of these limits is zero, and one value is just as likely as another value between the limits (equal probability). For a Rectangular Distribution, the upper limit = +*a*, the lower limit = -*a*, and the possible range of values = (+*a*) – (-*a*) = 2*a*. The calculation to estimate the equivalent of one standard deviation is defined as:

$$s = \frac{a}{\sqrt{3}}$$

For example, if a 100 mL volumetric flask has a tolerance of ±0.2 mL, then the upper limit = +0.2 mL, the lower limit = -0.2 mL, and the range of the outer limits = 0.4 mL. The estimated standard deviation is calculated as:

$$s = \frac{0.2\ mL}{\sqrt{3}} = 0.1_2\ mL$$

4.3.2.2 Type B Uncertainty- Triangular Distribution

A Triangular Distribution approach can be used to estimate a *Type B* uncertainty component if the following criteria are met: the upper and lower limits of the instrument or device are known and a value near the center is more likely than one at the upper or lower limit. For a Triangular Distribution, the upper limit is still equal to +*a*, and the lower limit is still equal to -*a*. The calculation to estimate the equivalent of one standard deviation is defined as:

$$s = \frac{a}{\sqrt{6}}$$

4.4 Step 4: Convert Quantities to Standard Uncertainties

Standard uncertainty is simply the measurement uncertainty expressed as a standard deviation. All statistically calculated uncertainty components (*Type A*, *Type B*- Rectangular Distribution, and *Type B*- Triangular Distribution) should already be expressed as one standard deviation.

For an uncertainty component that is being evaluated and quantified as *Type B* from a calibration certificate (or other information source), the certificate (or information source) must be carefully reviewed in order to arrive at the standard uncertainty. For example, calibration certificates generated by NIST are typically calculated assuming a normal distribution and reported at a 95% confidence level ($k = 2$). In this case, the reported uncertainty on the certificate will be divided by the coverage factor, 2, to arrive at the standard uncertainty.

In preparation for the next step, all standard uncertainties must be expressed in the same measurement unit. If the same measurement unit is not associated with each standard uncertainty, then convert each standard uncertainty into a percentage (i.e., relative standard uncertainty).

4.5 Step 5: Calculate Combined Standard Uncertainty

In this step, all of the individual standard uncertainties are combined to calculate a standard uncertainty of the measurement process, which is an estimated standard deviation. This combined standard uncertainty [$u_c\ (y)$] is calculated as the positive square root of the variance of all the combined uncertainty components:

$$u_c(y) = \sqrt{s_p^2 + u_0^2 + u_1^2 + u_2^2 + \ldots\ldots + u_i^2}\ ,$$

where s_p is the *Type A* calculated standard uncertainty for the measurement process and u_i are the *Type B* calculated standard uncertainties.

4.6 Step 6: Expand the Combined Standard Uncertainty by Coverage Factor (*k*)

The combined standard uncertainty calculated in the previous step is an estimated standard deviation with a confidence level of 68.27% ($k = 1$). In the CU, the combined standard uncertainty will be expanded by an appropriate coverage factor (k) to yield a confidence level of ≥99.7%. The specific value for the coverage factor is based on the amount of data that is available for the measurement process (i.e., *Type A* data). Table 1 provides the coverage factor (k) to apply based on the degrees of freedom (n-1), where n is equal to the number of *Type A* data points. Coverage factors other than those shown in Table 1 can be calculated using the TINV function in Excel®. The combined standard uncertainty [$u_c\ (y)$] is simply multiplied by the coverage factor to yield the expanded uncertainty (U) as shown below:

$$U = k * u_c(y)$$

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	A	B	C
1	**Degrees of Freedom (*n*-1)**	**Probability**	***k*-value (99.73% CL)**
2	1	0.0027	235.7837
3	2		19.2060
4	3		9.2187
5	4		6.6201
6	5		5.5070
7	6		4.9040
8	7		4.5299
9	8		4.2766
10	9		4.0942
11	10		3.9569
12	11		3.8499
13	12		3.7642
14	13		3.6941
15	14		3.6358
16	15		3.5864
17	16		3.5441
18	17		3.5075
19	18		3.4754
20	19		3.4472
21	20		3.4221
22	25		3.3296
23	30		3.2703
24	35		3.2291
25	40		3.1987
26	45		3.1755
27	50		3.1571
28	100		3.0767
29	∞		3

4.7 Step 7: Evaluate the Expanded Uncertainty

In this step the expanded uncertainty (*U*) is evaluated to determine if it "makes sense" and is "reasonable". This evaluation may identify calculation errors that can be corrected. Additionally, if pre-determined "acceptable limits" were defined for measurement uncertainty, then the expanded uncertainty should be evaluated against the "acceptable limits". If the measurement uncertainty is deemed to be unacceptable, areas of method improvement can be identified and evaluated for their impact on the estimation of measurement uncertainty using the information available from Steps 3 and 4.

4.8 Step 8: Report the Uncertainty

Expanded uncertainty will be rounded up and reported with two or less significant figures. This rounding up should only be done at the end of the measurement uncertainty calculation, to prevent cumulative effects from rounding up each standard uncertainty value. The reported measurement result will be truncated to the same level of significance that the rounded expanded uncertainty is reported. For example, if the measurement uncertainty of methamphetamine concentration in blood is 29 ng/mL (99.7% confidence level), and the measurement result for the case specimen is 498.23 ng/mL, then the measurement result will be truncated and reported as 498 ng/mL.

When reporting quantitative values in a *Laboratory Report*, the CU will include the measurement result with the associated expanded uncertainty and the confidence level. For example, a report may state that "Ethanol was identified in the Item 1 blood specimen at a concentration of 0.19 ± 0.03 gram % (99.7% confidence level)."

5 References

Joint Committee for Guides in Metrology (JCGM), *Evaluation of measurement data- Guide to the expression of uncertainty in measurement* (GUM) (GUM 1995 with minor corrections). (Sevres, France: International Bureau of Weights and Measures [BIPM]-JCGM 100, September 2008). Available at http://www.bipm.org/en/publications/guides/gum.html.

National Institute of Standards and Technology, *SOP 29 – Standard Operating Procedure for the Assignment of Uncertainty*, (Gaithersburg, Maryland, February 2012). Available at http://www.nist.gov/pml/wmd/labmetrology/upload/SOP_29_20120229.pdf.

Rev. #	Issue Date	History
5	02/09/18	Defined "NIST" in section 1, used acronym in remainder of document. Edited section 2 to include applicable personnel and to align language with ASCLD/LAB policy and QAM. Changed "document" and related to "record" and related in section 3. Edited last paragraph in section 4 to remove specific Excel reference. Removed "personal bias" from last bullet in section 4.2. Replaced "subunit" with "CU" in section 4.3.1.1. Changed confidence level in section 4.6 from 99.73% to ≥ 99.7%. Changed to "*Laboratory Report*" in section 4.8 and changed "Q1" to "Item 1".
6	09/13/19	Removed reference to ASCLD/LAB guidance documents in section 1 and references section. Expanded the scope in section 2 to all reported quantitative results. Added "intermediate precision" and reference to "coverage probability" in section 3. Removed "subunit" in sections 3 and 4.3.1.1, replaced with "standard operating procedures" in section 4.3.1.1.

Approval

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