TOX 09: Uncertainty of Measurement

1. Purpose

1.1. The toxicology section shall maintain traceability and an estimation of uncertainty of measurement for all analytical procedures that report a quantitative measurement.

2. Scope

2.1. Calculations related to the reported estimation of measurement uncertainty will be maintained by the Toxicology Technical Leader.

2.2. The uncertainty related to each quantitation will be from data evaluated at all laboratories and the greatest value reported (excludes ethanol).

2.3. All uncertainty components, Type A and B, are considered.

2.4. Measurement Traceability is established by the use of certified reference material (CRM) and calibrated equipment (e.g. pipettes, volumetric flasks).

3. Uncertainty Budget

3.1. Estimation of the uncertainty of measurement shall be conducted and documented using an uncertainty budget.

3.2. The uncertainty budget for a given procedure shall include both random (Type A) and systematic (Type B) uncertainties.

3.3. In order to combine the uncertainty, the uncertainty values should be measured in the same units.

3.3.1. The necessity to convert measurements to the same units can be eliminated if all uncertainty values are expressed as a percentage (%).

4. Type A (Random) Standard Uncertainty

4.1. Random (Type A) uncertainty results from measurement values being scattered in a random fashion due to laws of chance and has a normal or Gaussian shaped distribution.

4.2. Random (Type A) uncertainty is best determined by historical data of a large number of repeated measurements.

4.3. A control chart is a graphical representation of statistically analyzed data that is designed to monitor an analytical process. Control charts are used to establish the historical standard deviation for quantitative procedures.

4.3.1. Examples of historical control data can include, but is not limited to:

4.3.1.1. Externally purchased controls.

4.3.1.2. Internally prepared controls.

4.3.1.3. Check Standards.

4.4. The control chart shall plot single or multiple lot control samples, however delineated as to where and when the change of lot numbers occurred.

4.5. Data plotted on the control chart can be used to periodically update the uncertainty calculations.

5. Type B (Systematic) Standard Uncertainty

5.1. Systematic uncertainty results from the natural biases that are present in measuring systems and quantitative methods. Systematic uncertainties can be minimized through method optimization, but never eliminated.
5.2. Systematic (Type B) uncertainties resulting from measurement bias typically have an equal chance of falling within a range and therefore follow a rectangular or random distribution.
5.3. Examples of systematic uncertainties:
5.3.1. Preparation of a calibrator or control using a volumetric flask.
5.3.2. Using an analytical pipet to spike/prepare calibrator or controls.
5.3.3. Using a Hamilton diluter to prepare samples for Blood Alcohol Analysis.
5.3.4. Using a pipette (volumetric or serological) to aliquot.
5.4. Note: if the stated uncertainty on a reference standard certificate of analysis is 95.45%, this is equivalent to 2σ and should be divided by 2 for use in uncertainty calculations.
5.5. The scope of the control data used in the estimation of Type A uncertainty (control data gathered by all CBI laboratories) already encompasses some associated Type B uncertainties including instruments, maintenance, and analysts.
5.6. Some of these uncertainties are due to the bias of various equipment involved in the measuring process. The uncertainty of each component used shall be that provided on the calibration certificate for each piece of equipment. Standard uncertainty shall be determined based on the parameters given on such calibration certificate.
5.7. The use of an internal standard for quantitative analysis minimizes other sources of uncertainty including instrumental factors such as the injector, GC column, and detector which have no significant impact on the overall estimation of uncertainty and are not included in the calculation.

6. Calibration Model

6.1. The calibration model for each method shall be determined during validation.
6.2. If the calibration model is linear, uncertainty may only be determined at one concentration.
6.3. If the calibration is not linear, uncertainty may need to be determined at multiple concentrations.

7. Calculation and Expansion of the Combined Uncertainty

7.1. The Measurement Uncertainty Estimation Form provided by ANAB (formerly ASCLD-LAB) was used to calculate the expanded uncertainties.
7.2. A 95.45% confidence level when K=2.
7.3. A 99.73% confidence level when K=3.

8. Reporting the Estimated Uncertainty of Measurement

8.1. Laboratory system-wide uncertainties will be formally reported for any quantitated results that include:
8.1.1. Ethanol and delta-9-Tetrahydrocannabinol.
8.1.2. For other drugs that are quantitated, Uncertainty of Measurement shall be known and provided upon request, however shall not be formally reported on a routine basis.

8.1.3. The determined uncertainty is a relative percent that is applied to a result and the calculation is expressed as an absolute value.

8.1.3.1. Example: Ethanol uncertainty is 5% and the result is 0.078 g/100mLs
Reported as 0.078 g/100mLs +/- 0.004 g/100mLs

8.1.4. The reported uncertainty will be rounded and reported.

8.1.4.1. To (3) decimal places for ethanol determinations or to the thousands place.

8.1.4.2. For drug quantitation, values greater than 10 shall be reported as a whole number and for values less than 10, to the tenths place.

8.2. Uncertainty of Measurement shall also include a confidence level on the reports.

8.3. Uncertainty of Measurement can be administratively set after evaluation of the calculated control chart data (Ethanol 5%).

9. Reporting the Estimated Uncertainty of Measurement for many drugs within a class

9.1. When a test method measures and reports multiple measured values, the components giving the largest standard uncertainties within a method shall be used.

9.1.1. For example, the Pain Management method measures and reports analyte concentrations for codeine, morphine, hydrocodone, etc. If the morphine reproducibility is higher than the others', the morphine reproducibility estimate of uncertainty shall be used to estimate uncertainty for the entire Pain Management method.

10. Data

10.1. The data collected and calculations are documented in the most recent version of the Toxicology Uncertainty of Measurement excel chart for each method.

10.2. The Uncertainty of Measurement for each method changes with the addition of new control data being populated within the control chart excel files. These control charts, along with the Uncertainty of Measurement, are reviewed and documented approximately every six months.

10.2.1. Cannabinoid and Ethanol Uncertainty of Measurement are recalculated and updated on an annual basis for routine reporting.

11. References

11.1.1.1. ASCLD/LAB Policy on Measurement Uncertainty. (AL-PD-3060 Ver. 1.0)

11.1.1.2. ASCLD/LAB Guidance on the Estimation of Measurement Uncertainty – ANNEX D, Toxicology Testing Discipline. (AL-PD-3065 Ver. 1.0)

11.1.1.3. Gullberg, R. G. "Estimating the Measurement Uncertainty in Forensic Blood Alcohol Analysis." Journal of Analytical Toxicology 36.3 (2012): 153-61. Print.