A top down approach for measurement uncertainty by precision, accuracy and trueness (ISO 21748)

Introduction

Instead of evaluating the measurement uncertainty (MU) contributors in each step of an analytical method by the GUM method, the ISO 21748 standard document titled "*Guidance for the use of repeatability, reproducibility and trueness estimates in measurement uncertainty estimation*" describes a top down approach by studying the overall laboratory performance of the test method over a prolonged period of time through its quality control (QC) data.

Under the laboratory accreditation standards ISO 17025, all accredited laboratories are to have implemented their respective quality management system with valid QC data regularly collated. The basic criteria on holistic method performance are its precision (repeatability), reproducibility and biasness, if any. These data can also be referred from the method validation or verification report(s) prepared for accreditation.

Repeatability, Reproducibility and Trueness

The repeatability r is best determined by its intermediate precision, $s_{R'}$ which refers to analyze and obtain replicated data of a given QC check sample over time within the laboratory by different analysts, batches of reagents and/or analytical equipment used. Before adopting this uncertainty contributor, one has to confirm that the following criterion holds water:

$$D < 2 \times s_{R'}$$

where

D is the difference between the mean value found in a replicated analysis of another batch of reference material and its assigned value
$s_{R'}$ is the intermediate precision standard deviation

The reproducibility data can be obtained by taking part in established proficiency testing (PT) program(s) which will report the reproducibility R of that particular batch of exercise through statistically analyzing the acceptable data reported by the laboratory participants. It is important to note that such PT program must require the participants to follow exactly a stated standard test method for meaningful comparison. It is opined that a PT program allowing the laboratory participants to use different test methods for the same targeted analyte is a waste of time and effort.

If there is no such *R* data available, one can opt to use a series of in-house recovery experiments to demonstrate his technical competence in handling this particular analytical method over time. Recovery experiments are designed to check for the accuracy and determine if there is any systematic error or bias present. If there is any significant systematic error in the method, the error has to be eliminated or corrected if the source(s) of error cannot be found.

Even if there is no systematic error noted, the bias which is a measurement of accuracy is to be estimated as an uncertainty contributor.

The common approaches by this top down method are summarized below:

A. Evaluation of intermediate precision standard deviation, $s_{R'}$

1. For stable Quality Check CS Sample closed to actual sample matrix analyzed

The standard uncertainty of intermediate precision standard uncertainty $u_{R'}$ is equal to the standard deviation of intermediate precision after several repeated testing on a same CS over a period of time, after proving that the test results are random (i.e. normally distributed) and independent by the Anderson Darling test, Shapiro-Wilk or other common statistic tests for normality::

$$u_{R'} = s_{R'} \quad \text{.....(1)}$$

2. For using a spiked sample or prepared standard solution

When the conditions for equation (1) cannot be satisfied, a prepared standard solution can be used with different analtye levels and/or actual sample matrices and is analyzed as per normal sample. The equation (2) can then be used to estimate the $u_{R'}$:

$$u_{R'} = \sqrt{u^2_{R'(stand)} + u^2_{r(range)}} \quad \text{.....(2)}$$

where:

$u_{R'(stand)}$ —— standard uncertainty of prepared standard solution

$u_{r(range)}$ —— standard uncertainty of different analyte levels and/or matrices, where $\overline{R}$ is the range of duplicate mean values, and $u_r(range) = \frac{\overline{R}}{1.128}$ 。

B. Estimation of bias, u_b by using stable check sample

1. Using a single quality check sample

For a single Check Sample CS, its bias standard uncertainty u_b estimate uses the following equation (3)：

$$u_b = \sqrt{b^2 + \frac{s_b^{\,2}}{n} + u_{Cref}^{\,2}} \quad \text{……（3）}$$

where：

b——bias, i.e. the difference between mean result $\bar{x}$ 与 ARV (assigned reference value)。

s_b——standard deviation of the bias over n repeated analyses

u_{Cref} —— standard uncertainty of the ARV, estimated from the certificate or know given value

2. Using a number of check samples with different analyte levels

If the analytical method is handling a wide range of analyte levels, multiple quality check samples are to be used for u_b:

$$u_b = \sqrt{\frac{\sum b_i^{\,2}}{N} + \bar{u}_{Cref}^{\,2}} \quad \text{……..(4)}$$

where:

b_i - the bias for i^{th} sample, i.e. the difference between the i^{th} mean result $\bar{x}_i$ and ARV_i (assigned reference value of i^{th} sample)

N - the number of reference samples

$\bar{u}_{Cref}$ - the average value of all u_{Cref} under consideration

3. Using laboratory recovery study for estimation of bias

The above equations (3) and (4) can also be used for the laboratory recovery experiments on a single analyte level and multiple analyte levels, respectively.

For example, using different levels of analyte for recovery studies, the estimation of u_b refers to the equation (4A)：

$$u_b = \sqrt{\frac{\sum b_i^2}{m} + \bar{u}_{Cref}^2} \quad \text{……（4A）}$$

where：

b_i—— the difference between the i^{th} mean recovery and the average result

m—— the number of recovery experiments

C. Evaluation of final expanded uncertainty *U*

Under 95% confidence level， the expanded uncertainty can be estimated by equations (5) or (6)：

$$U = 2u_c = 2\sqrt{u_{R'}^2 + u_b^2} \quad \text{……（5）}$$

$$U_{rel} = 2u_{c,rel} = 2\sqrt{u_{R',rel}^2 + u_{b,rel}^2} \quad \text{……（6）}$$

where:

U or U_{rel} - expanded uncertainty or relative expanded uncertainty。

u_c or $u_{c,rel}$ - combined standard uncertainty or relative combined standard uncertainty

Conclusion

The above notes summarize the basic rules of this top down approach. It will be more appreciative when worked examples are being shown. These will be followed up in the next few blog articles.

However, it is obvious that this top down MU estimation method is much simpler and less tedious than the GUM method. The MU data produced are also dynamic in nature because the laboratory quality control management is an on-going process with continual method performance monitoring through check samples regularly for precision and PT programs or recovery studies for accuracy. Hence, its measurement uncertainty given to the client is current and practical.

Most laboratory operators adopting the GUM method tend to study the measurement uncertainty of a test method once and might not have established directive to regularly carry out updating it for a long time even when there is a major change of instrumentation and technical staff.