Introduction to measurement uncertainty

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Overview

- What is measurement uncertainty?
- Why do we need to know the uncertainty?
- ISO 15189 requirements
- Sources of information
- Documenting uncertainty

Measurement uncertainty

ISO 'GUM' definition

"A parameter, associated with the result of a measurement, that characterises the dispersion of the values that could reasonably be attributed to the measurand"

The part of the result after the ±

ISO/IEC Guide 98-3:2008 Uncertainty of measurement-Part 3: Guide to the expression of uncertainty in measurement (GUM:1995) is the primary document applicable to uncertainty estimation. [Available as free download 'JCGM 100:2008' from www.bipm.org]

ISO use a lengthy definition; the short form is rather easier to remember!

In the definition, 'measurand' refers to the quantity intended to be measured, for example, the concentration of creatinine in serum.

It is important to note that measurement uncertainty applies to the result of a measurement. There will be a number of factors associated with the method of measurement that will contribute to the uncertainty in the result.

Measurement uncertainty describes a range of values. If the uncertainty has been evaluated correctly, the range should include the true value for the measurand.

What information does it give?

The concentration of alcohol in a blood sample is:

70 ± 5 mg per 100 mL

The concentration is between 65 and 75 mg per 100 mL

A RANGE containing the TRUE VALUE

Another way of reading the ISO definition is ‘What range of answers could reasonably be given, after taking into account everything that is known about the measurement?’

In general, $x \pm y$ is interpreted by the analyst as ‘the true value is somewhere in this range’. Uncertainty estimation, done well, permits that interpretation.

When evaluating uncertainty the most important things we need to know about the measurement result are first, how it was calculated (the ‘model’); second, the numbers used to calculate it; and third, any other effects that could change the answer.

Why do we need to know the uncertainty?

- Indication of quality of results
  - are results ‘fit for purpose’ ?
- Interpretation of results
  - are these results really different ?
  - what confidence can be placed in decisions based on results?
    - what does it mean for the patient?
    - does it effect results at clinical decision values?
- Knowledge of the uncertainty should
  - improve understanding of test methods
  - give confidence to users of results
  - increase acceptability of results

Uncertainty – the story so far…

- MU evaluation well established for physical measurements (length, mass…..)
  - fundamental to the work of National Measurement Institutes (e.g. NPL) and calibration labs
- 1970s: International intercomparisons showed wide variation in the way MU was calculated
  - estimates not comparable
- 1980: BIPM working party convened to make recommendations
- 1993: ISO Guide to the Expression of Uncertainty in Measurement (GUM) published
- 1990s: Approaches for evaluating MU in chemical measurements developed
- 1999: Accreditation requirement for testing labs (ISO/IEC17025)
- 2003: mentioned in ISO 15189
- 2007: CPA standard aligned with ISO 15189:2007
- 2012: Requirement in ISO 15189

Measurement uncertainty has always been important in physical metrology, where the estimation of uncertainty on the basis of a known physical model has a number of important functions.

In physical measurement, National Measurement Institutes (NMIs) compare their results regularly under the auspices of BIPM,* and increasing global trade gave that activity more emphasis in the 1970s. It quickly became apparent that the methods of uncertainty estimation used by the NMIs differed, with some including only the precision of replicate results, and others employing extensive error propagation calculations. Concepts differed too, with very different treatments of random and systematic effects.

BIPM set up a working group to recommend a way forward, which duly reported back in 1980, and the recommendations, concepts, definitions and a method of implementation were eventually collated and published in the form of the ISO Guide to the expression of uncertainty in measurement (‘the GUM’). This document is now very widely accepted as the fundamental document for measurement uncertainty in all fields of measurement.

*International Bureau of Weights and Measures

Accreditation requirements

ISO 15189:2012 'Medical laboratories – Requirements for quality and competence'

- § 5.5.1.4 Measurement uncertainty of measured quantity values
  - laboratory shall determine measurement uncertainty for each measurement procedure in the examination phase…
  - laboratory shall define the performance requirements for the measurement uncertainty … and regularly review estimates…
  - Notes
    - measurement uncertainties may be calculated using…measurement of quality control materials under intermediate precision conditions…

Of the accreditation standards available to laboratories, measurement uncertainty is covered in most detail in ISO/IEC 17025 General requirements for the competence of testing and calibration laboratories.

However, since 2012 evaluation of measurement uncertainty has also been a requirement in ISO 15189 – the accreditation standard for medical laboratories. (ISO/IEC 17025:2005 is a normative reference in this standard but note that a revised version was published in November 2017.)

Sources of uncertainty

- ISO 15189 ‘scope’ of uncertainty
  - uncertainties associated with the measurement process only
  - includes sample preparation within the laboratory
  - excludes pre- and post-examination steps
- Physical parameters
  - mass, volume, temperature…….
- Chemical
  - extraction, derivatisation…….
- Instrument
  - operating conditions, calibration…….
- Analyst

☒ Doesn’t include gross errors (mistakes!)

In medical analysis there are many potential factors, in addition to the end measurement, that can influence the measurement result (e.g. specimen collection and transport, patient state, biological variation, etc). However, ISO 15189 requires an estimate of the uncertainty for the measurement stage only. Although it is important to understand and control pre- or post-examination steps, their influence on the measurement result does not have to be accounted for in the uncertainty estimate.

For a given method there will be a number of sources of uncertainty. Some typical examples are shown on the slide.

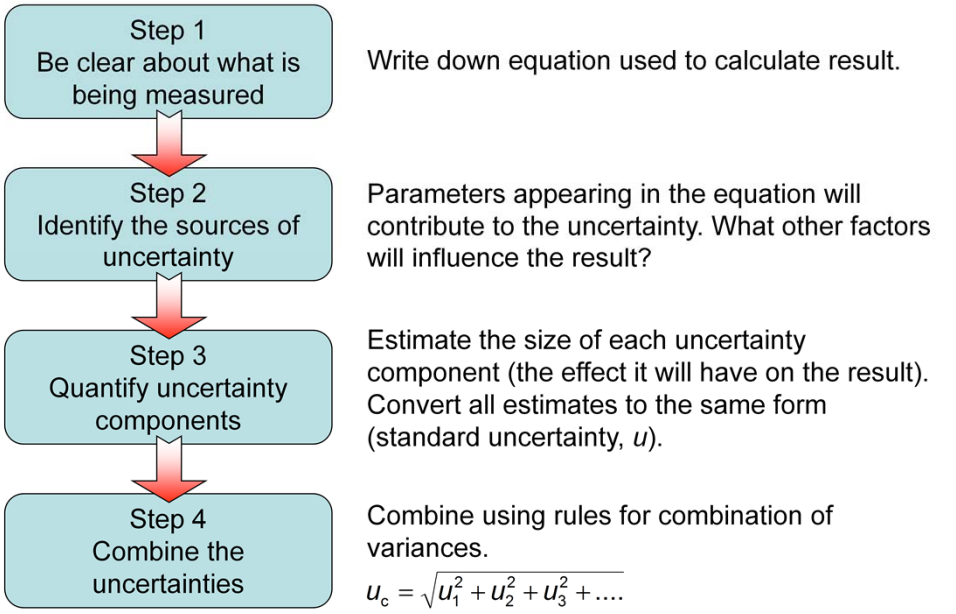
It is important to remember that an uncertainty estimate should apply to results that are obtained when the test method is under statistical control (i.e. the performance is consistent with that established during method validation). Therefore, an uncertainty estimate should not include the effect of gross errors (mistakes).

Sources of information

- Experimental studies
- Manufacturers' specifications
  - for equipment and reagents
- Calibration certificates
  - for equipment and reference materials
- Method validation data
  - in-house studies
  - results from inter-laboratory studies
- Quality control data (IQC and EQA)
- Literature data
- Experience
- Calculation

There are a number of sources of information that can contribute to an uncertainty estimate. A later presentation will explain how method validation and quality control data can be used.

Evaluating uncertainty – General approach



The slide shows the general approach to evaluating measurement uncertainty.

For each stage of the method, the analyst needs to identify factors which could cause the result to change; these will be sources of uncertainty.

The 'traditional' ISO approach involves quantifying each source of uncertainty separately. This is sometimes referred to as the 'bottom-up' approach. As we will see in a later session, this approach is often impractical for multi-stage methods such as those used in clinical chemistry. An alternative approach, which makes use of method performance data, is therefore frequently used when evaluating the uncertainty associated with the results from chemical tests. This is known as the 'top-down' approach.

Documenting uncertainty

- Documented procedure for evaluating uncertainty
- Laboratory's decision as to where uncertainty is recorded
  - ISO 15189: laboratory shall consider measurement uncertainty when interpreting measured quantity values
  - laboratory shall make its estimates of measurement uncertainty available on request

Summary

- What is measurement uncertainty?
  - $x \pm U_c$ gives a range containing the true value
  - has contributions from all significant factors that cause the result to vary
- Uncertainty estimation is now an accreditation requirement
- Method validation and QC data are an important source of information for uncertainty estimation