

Measurement Uncertainty, Scope of Application in Laboratory Medicine and Imaging and Functional Medicine

Reference Requirements: EN ISO/IEC 17025, 7.6
EN ISO 15189, 7.3.4
EA 4/16:2003, EA Guidelines on the Expression
of Uncertainty in Quantitative Testing

This document only concerns examinations that provide numerical (quantitative) results. According to SS-EN ISO/IEC 17025 and SS-EN ISO 15189 (1, 2), measurement uncertainty must be stated for accredited laboratory examinations.

Purpose

There are primarily two purposes for calculating measurement uncertainty. The primary purpose is to give the customer a reasonable understanding of the reliability of the measurement result, so they can, for example, assess whether a real change has occurred in the patient's condition. Such an assessment assumes that the reported measurement uncertainty applies to all instruments that the patient's sample material may have been analysed on.

The second purpose is to better align analysis methods on different platforms. In this aim, it is important to continuously monitor the systematic difference between various methods within an organisation and attempt to minimise these.

Basic Concepts

Measurement Uncertainty

The formal definition states that measurement uncertainty is a parameter associated with the measurement result that characterises the dispersion of values that could reasonably be attributed to the measurand. Measurement uncertainty includes a systematic and a random component, referred to as bias and imprecision, respectively.

Bias

A measure of the systematic deviation from a conventionally true result. This deviation includes both the difference between the organisation's average level and the true value, and the difference between different methods and instruments within an organisation. Since the true value is rarely known or even possible to define within laboratory medicine, systematic difference in this document exclusively refers to differences in measurement level between instruments within an organisation. It is assumed that bias, where possible, is minimised through traceable calibration and controlled with proficiency testing (e.g., inter-laboratory comparisons).

Imprecision

A measure of the random error.

Calculation and Reporting of Measurement

Uncertainty

An estimation of the measurement uncertainty should be available for every accredited method. When setting up a new method, the laboratory should report significant sources of uncertainty. Ideally, all parts of the measurement routine that can affect quality are included. In practice, this is not always possible. Pre-analytical factors, for example, are generally difficult to estimate and may be excluded from the calculation. Patient preparations, sampling, changes in samples during transport and storage, as well as biological variation, can, however, significantly affect results. The impact of the first three factors on total measurement uncertainty should therefore be minimised through appropriate procedures.

Measurement uncertainty calculations can be performed in fundamentally different ways. GUM (Guide to the Expression of Uncertainty in Measurement) (4) has been designated by EA (European co-operation for Accreditation) as the “master document” (5) for estimating measurement uncertainty. Guidelines have also been published by ILAC (International Laboratory Accreditation Cooperation) (6). SWEDAC has published an overarching policy document regarding measurement uncertainty (7).

Measurement uncertainty can be based on the observed variation in repeated measurements of internal control materials. The measurement period should be long enough for all significant sources of variation, such as reagent batch changes, staff changes, etc., to have had a reasonable probability of affecting the outcome.

Measurement uncertainty should meet the requirements that can reasonably be expected of the method from a medical point of view. If the measurement uncertainty for a method is deemed unsatisfactory, the laboratory should conduct a systematic survey of various potential sources of error. The laboratory can then, if necessary, establish a measurement uncertainty budget according to GUM or in another suitable manner.

The measurement uncertainty statement should apply to values within the clinically relevant measurement range and should be reported at least at two levels. Measurement uncertainty can be reported as CV%. Measurement uncertainty should be available to the customer, for example, in a sampling instruction or be provided in another way.

Measurement uncertainty should be regularly monitored by verifying established requirements for operational checks, patient sample comparisons, and/or proficiency testing (e.g., inter-laboratory comparisons). The frequency can be adjusted to the stability of the method.

When a laboratory organisation comprises several separate laboratory units (hospital laboratories), multiple instruments may be available for determining the same component. Instruments within the same laboratory unit can, from a customer perspective, be considered as one unit, and measurement uncertainty should therefore be calculated across all of them. This assumes that the methods have comparable analytical performance (small systematic difference, comparable precision). The systematic difference between laboratory units should be monitored and reported, for example, as the difference to a designated (“master”) instrument, to the organisation’s average measurement level, or to a reference method. Limits for the maximum acceptable systematic difference should be in place.

References

1. SS-EN ISO/IEC 17025, General requirements for the competence of testing and calibration laboratories, SIS, Stockholm, 2018
2. SS-EN ISO 15189, Medical laboratories - Particular requirements for quality and competence, SIS, Stockholm, 2022
3. SWEDAC DOC 01:55, Validation/verification of measurement methods, www.swedac.se
4. Guide to the Expression of Uncertainty in Measurement, International Organisation of Standardisation, ISO, Geneva, 1995, ISBN 92-67-10188-9
5. EA-4/16, EA Guidelines on the expression of uncertainty in quantitative testing, www.european-accreditation.org, EA, 2003
6. ILAC-G17:2002, Introducing the concept of uncertainty of measurement in testing in association with the application of the standard ISO/IEC 17025, www.ilac.org
7. SWEDAC DOC 04:5, SWEDAC's policy on measurement uncertainty in calibration and testing, www.swedac.se



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