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Medical laboratories — Practical guidance for the estimation of measurement uncertainty

Laboratoires médicaux — Lignes directrices pratiques pour l'estimation de l'incertitude de mesure

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 212, *Clinical laboratory testing and in vitro diagnostic test systems*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

Improved standardization and harmonization of medical laboratory practices worldwide benefits society as patients and healthcare professionals increasingly move within and between healthcare services in the global economy. To help achieve the objective of improved standardization among medical laboratories, ISO 15189 focuses on the application of the quality systems approach in the medical laboratory. Since the first version of ISO 15189 was published in 2003, this international standard has been increasingly adopted worldwide as a desirable (and in some cases mandatory) quality system standard for medical laboratories.

To ensure that measurement results are useful and safe in medical practice and to permit meaningful comparison with medical decision limits and previous results of the same kind in the same individual, medical laboratories require estimates for the overall variability in values reported by their measurement procedures. To achieve this, ISO 15189:2012, 5.5.1.4, requires that "…(medical laboratories)… shall determine measurement uncertainty for each measurement procedure in the examination phase used to report measured quantity values on patients' samples." Additionally, "Upon request, the laboratory shall make its estimates of measurement uncertainty available to laboratory users."

For medical laboratories and healthcare providers, measurement uncertainty (MU) estimates:

— indicate that multiple values are possible for a given measurement;

— provide evidence that the term 'true value' of a quantity is a theoretical concept;

— quantify the quality of a result relative to its suitability for use in making medical decisions;

— assume that known medically significant bias is eliminated;

— assist in identifying technical steps to reduce MU;

— allow combination with other sources of uncertainty;

— can be used to determine if medically allowable analytical performance specifications can be achieved;

— support interpretation of patient results close to medical decision limits.

To enable fulfilment of the requirement of ISO 15189 for estimation of MU, it is essential that medical laboratories be provided with a coherent, standardized, and best practice approach to the terminology, principles and statistical methods required for estimation of MU. *Evaluation of measurement data — Guide to the expression of uncertainty in measurement* (GUM) JCGM 100:2008, a definitive reference on the topic of MU, provides in-depth information regarding the mathematical and metrological considerations appropriate for a detailed estimation of elements to be considered in the estimation of MU for a broad range of measuring systems, across many disciplines in science and engineering. In the Scope, GUM subclause 1.2, states that "This document is primarily concerned with the expression of uncertainty in the measurement of a well-defined physical quantity that can be defined by an essentially unique value." GUM, Scope subclause 1.4, goes on to say that "…(GUM) provides general rules for evaluating and expressing uncertainty in measurement rather than detailed, technology-specific instructions. (GUM) … does not discuss how the uncertainty of a particular measurement result, once evaluated, may be used for different purposes, for example, to draw conclusions about the compatibility of that result with other similar results, to establish tolerance limits in a manufacturing process, or to decide if a certain course of action may be safely undertaken. Therefore, it may be necessary to develop particular standards based on (GUM) that deal with the problems peculiar to specific fields of measurement or with the various uses of quantitative expressions of uncertainty. These standards may be simplified versions of (GUM) but should include the detail that is appropriate to the level of accuracy and complexity of the measurements and uses addressed."

This document is therefore concerned with practical approaches to estimation of MU, to be applied in medical laboratory settings for the purpose of estimating MU of values produced by measurement procedures intended to measure a broad range of biological measurands. The measurands of interest

are subject to measurement for the purpose of providing medical diagnostic information to health care practitioners and are typically present in complex biological fluid and tissue matrices. In contemporary medical laboratory settings, the vast majority of these measurements are performed with commercial devices, including automated instrumentation and packaged reagent kits. Characterization of the performance of these measurement procedures in an end-user laboratory environment is typically limited to the gathering of empirical performance data using surrogate quality control samples designed to emulate the intended patient samples. Such data, commonly known as internal quality control (IQC) data, may be appropriate for characterization of repeatability and long-term imprecision of a given measurement procedure. Additional uncertainty information regarding higher order elements of the calibration hierarchy for a given measurement procedure should be available from the manufacturer, and should be accounted for in the medical laboratory's process for estimation of MU. As such, a GUM top down approach is appropriate, and a particular application for use in medical laboratories is outlined in Clause 6.

Medical laboratories — Practical guidance for the estimation of measurement uncertainty

1 Scope

This document provides practical guidance for the estimation and expression of the measurement uncertainty (MU) of quantitative measurand values produced by medical laboratories. Quantitative measurand values produced near the medical decision threshold by point-of-care testing systems are also included in this scope. This document also applies to the estimation of MU for results produced by qualitative (nominal) methods which include a measurement step. It is not recommended that estimates of MU be routinely reported with patient test results, but should be available on request.

NOTE See Annex B for an example of application of the MU.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at http://www.electropedia.org/

3.1
analyte
component represented in the name of a measurand

Note 1 to entry: Constituent of a sample with a measurable property.

EXAMPLE In the measurand (measured quantity) "mass of total protein in 24-hour urine", "total protein" is the analyte (and “mass” is the property.) In "amount of substance concentration of glucose in plasma", "glucose" is the analyte (and “amount of substance concentration” is the property.)

[SOURCE: ISO 18113-1:2009, modified]

Note 2 to entry: JCGM 200:2012, 5.4, states that a primary measurement standard may be “…prepared by dissolving a known amount of substance of a chemical component to a known volume of solution”.

3.2
calibration
operation that, under specified conditions, in a first step, establishes a relation between the quantity values with associated measurement uncertainties provided by measurement standards (calibrators) and their corresponding indications and, in a second step, uses this relationship to establish a measurement result from an indication (for an unknown sample).

Note 1 to entry: A calibration may be expressed by a statement, calibration function, calibration diagram, calibration curve, or calibration table. In some cases, it may consist of an additive or multiplicative correction of the indication with associated MU.

Note 2 to entry: Calibration should not be confused with adjustment of a measuring system, often mistakenly called “self-calibration”, nor with verification of calibration.