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Laboratory medicine — Requirements for the competence of calibration laboratories using reference measurement procedures

Biologie médicale — Exigences relatives à la compétence des laboratoires d'étalonnage utilisant des procédures de mesure de référence

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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*.

This second edition cancels and replaces the first edition (ISO 15195:2003), which has been technically revised.

The main changes compared to the previous edition are as follows:

— inclusion of ISO/IEC 17025:2017 as a normative reference;

— removal of clauses that duplicate requirements in ISO/IEC 17025:2017;

— reorganization of this document so that it follows the structure of ISO/IEC 17025:2017.

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

The general requirements for the competence of calibration laboratories are specified in ISO/IEC 17025:2017 for testing and calibration laboratories. This document refers to the additional aspects for the competence of calibration laboratories in the field of laboratory medicine where such "calibration laboratories" are usually denoted as "reference measurement laboratories".

The results produced by medical laboratories should be traceable to reference materials and/or reference measurement procedures of higher order, whenever these are available. This is necessary to allow transferability of measurement results in patient samples irrespective of the place and time of measurement.

The metrological level of the results provided by calibration laboratories should be appropriate to support medical laboratories to fulfil medical requirements. The specific requirements of medical laboratories are addressed in ISO 15189.

Calibration laboratories should implement reference measurement procedures and produce results of measurement that are accurate and traceable to national or international primary reference materials when such are available. Whenever possible, traceability should be established to a reference material which forms an embodiment of the SI unit (ISO 17511).

The calibration laboratory should provide traceable values on reference materials supplied by customers to the highest available level of reference measurement procedures or reference materials.

In many instances, properties of biological materials cannot be expressed in SI units because the molecular structure of their analytes is not exactly known and can be different in a reference material from that in a native sample of human origin (e.g. state of glycosylation of a protein).

Even if the value for a property of a biological material is not traceable to an SI unit, each step of a reference measurement procedure (e.g. gravimetry, volumetry, thermometry, potentiometry) should have values that are traceable to the respective SI unit.

The traceability concept, including its applicability and limitations are described in detail in ISO 17511.

The requirements described in this document and in ISO/IEC 17025:2017 are prerequisites for calibration laboratories to perform their tasks adequately.

This document may form a basis for the accreditation of a calibration laboratory that applies for recognition of the performance of a reference measurement procedure.

Laboratory medicine — Requirements for the competence of calibration laboratories using reference measurement procedures

1 Scope

This document specifies the requirements for competence to carry out reference measurement procedures in laboratory medicine, using the requirements of ISO/IEC 17025:2017 as a normative reference and listing additional requirements for calibration laboratories to perform their tasks adequately.

The relationship between clauses in this document and ISO/IEC 17025:2017 are summarized in Annex A.

Examinations of properties with results reported on a nominal or ordinal scale are not included.

This document is not applicable to medical laboratories.

NOTE Requirements for medical laboratories are specified in ISO 15189[1].

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO/IEC Guide 98-3, *Uncertainty of measurement — Part 3: Guide to the expression of uncertainty in measurement (GUM:1995)*

ISO/IEC Guide 99, *International vocabulary of metrology — Basic and general concepts and associated terms (VIM)*

ISO 15193, *In vitro diagnostic medical devices — Measurement of quantities in samples of biological origin — Requirements for content and presentation of reference measurement procedures*

ISO 15194, *In vitro diagnostic medical devices — Measurement of quantities in samples of biological origin — Requirements for certified reference materials and the content of supporting documentation*

ISO/IEC 17025:2017, *General requirements for the competence of testing and calibration laboratories*

ISO 17511, *In vitro diagnostic medical devices — Measurement of quantities in biological samples — Metrological traceability of values assigned to calibrators and control materials*

ISO 18153, *In vitro diagnostic medical devices — Measurement of quantities in biological samples — Metrological traceability of values for catalytic concentration of enzymes assigned calibrators and control materials*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO/IEC Guide 99 and the following 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
measurement uncertainty
non-negative parameter characterizing the dispersion of the quantity values being attributed to a measurand, based on the information used

Note 1 to entry: Measurement uncertainty includes components arising from systematic effects, such as components associated with corrections and the assigned quantity values of measurement standards, as well as the definitional uncertainty. Sometimes estimated systematic effects are not corrected for but, instead, associated measurement uncertainty components are incorporated.

Note 2 to entry: The parameter may be, for example, a standard deviation called standard measurement uncertainty (or a specified multiple of it), or the half-width of an interval, having a stated coverage probability.

Note 3 to entry: Measurement uncertainty comprises, in general, many components. Some of these may be evaluated by Type A evaluation of measurement uncertainty from the statistical distribution of the quantity values from series of measurements and can be characterized by standard deviations. The other components, which may be evaluated by Type B evaluation of measurement uncertainty, can also be characterized by standards deviations, evaluated from probability density functions based on experience or other information.

Note 4 to entry: In general, for a given set of information, it is understood that the measurement uncertainty is associated with the stated quantity value attributed to the measurand. A modification of this value results in a modification of the associated uncertainty.

[SOURCE: ISO/IEC Guide 99:2007, 2.26]

3.2
reference measurement procedure
measurement procedure accepted as providing measurement results fit for their intended use in assessing measurement trueness of measured quantity values obtained from other measurement procedure for quantities of the same kind, in calibration or in characterizing reference materials

[SOURCE: ISO/IEC Guide 99:2007, 2.7]

Note 1 to entry: When several reference measurement procedures exist for a given measurable quantity, it can be possible to arrange them in a hierarchy according to size of measurement uncertainty. A primary reference measurement procedure is sometimes termed as a “definitive method of measurement”, but not by ISO/IEC Guide 99:2007.

Note 2 to entry: The Consultative Committee for Amount of Substance (CCQM) of the International Bureau of Weights and Measures (BIPM) has defined a ‘primary method of measurement’ as a method having the highest metrological qualities, whose operation can be completely described and understood, for which a complete uncertainty statement can be written down in terms of SI units, and whose results are, therefore, accepted without reference to a standard of the quantity being measured. For amount of substance, the following principles of measurement were identified as suitable for primary measurement procedures: isotope dilution-mass spectrometry, coulometry, gravimetry, titrimetry and determination of colligative properties such as freezing point depression. (CCQM, 1995).

Note 3 to entry: The Analytical Chemistry Division of the International Union of Pure and Applied Chemistry (IUPAC) describes an allied concept, ‘absolute method’, wherein calculations are based on universal quantities and fundamental physical constants only.

Note 4 to entry: The phrase ‘higher order reference measurement procedure’ is often used to emphasize the position of these procedures within a calibration hierarchy as outlined in ISO 17511.

Note 5 to entry: The requirements for the content and presentation of reference measurement procedures relevant to *in vitro* medical devices are laid out in ISO 15193.

4 General requirements

The requirements of ISO/IEC 17025:2017, Clause 4 apply, including all the subclauses.

5 Structural requirements

The requirements of ISO/IEC 17025:2017, Clause 5 apply, including all the subclauses.

When the calibration laboratory is co-located with a medical laboratory, the organizational arrangements shall be such that they do not adversely influence the calibration laboratory's conformance with the requirements of this document.

6 Resource requirements

6.1 General

The requirements of ISO/IEC 17025:2017, 6.1 apply.

6.2 Personnel

The requirements of ISO/IEC 17025:2017, 6.2 apply, including all the subclauses.

6.3 Laboratory facilities and environmental conditions

The requirements of ISO/IEC 17025:2017, 6.3 apply, including all the subclauses.

6.4 Equipment

The requirements of ISO/IEC 17025:2017, 6.4 apply, including all the subclauses.

The laboratory shall be equipped with all items of equipment required for the correct performance of its listed reference measurement procedures. All equipment relevant to the measurements concerned shall be capable of achieving the measurement accuracy required. When processed signals (e.g. by built-in microprocessors) are used, calibration and transformation functions shall be validated and verified either by the manufacturer or independently. All equipment used in the reference measurement procedure shall be regularly inspected and maintained by authorized personnel. A program for calibration and verification of the functioning of the equipment shall be established. Relevant environmental conditions shall be maintained. Equipment operation manuals shall be kept up-to-date and readily available. Each item of equipment shall be uniquely identified. The use and maintenance of each major item of equipment shall be recorded in a log that contains:

— the type of measurement, control or maintenance procedure performed;

— the status of calibration and verification;

— the date of measurement or maintenance;

— the operator who performed measurement or maintenance;

— reasons for maintenance (prevention or malfunction repair);

— where relevant, specific operating conditions;

— unusual observations which shall require investigations where necessary.

For the fundamental quantities such as mass, volume and temperature, the laboratories shall have calibrated devices. The laboratory shall ensure that measurement results for fundamental quantities are traceable to SI units. Calibrations shall be performed within the required levels of measurement uncertainty and recorded. A calibration and verification schedule shall be established that ensures that the devices and equipment are operating within the measurement uncertainties ascribed to them.

When the measurement uncertainty of weighing of reference materials or other items necessary for calibration is a significant element in the combined standard measurement uncertainty, corrections for