SLOVENSKI STANDARD
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Nadomešča:
SIST EN ISO 15194:2009

Diagnostični medicinski pripomočki in vitro - Zahteve za certificirane referenčne materiale in vsebino podporne dokumentacije (ISO/DIS 15194:2023)

In vitro diagnostic medical devices - Requirements for certified reference materials and the content of supporting documentation (ISO/DIS 15194:2023)

In-vitro-Diagnostika - Messung von Größen in Proben biologischen Ursprungs - Anforderungen an zertifizierte Referenzmaterialien und an den Inhalt der Begleitdokumentation (ISO/DIS 15194:2023)

Dispositifs médicaux de diagnostic in vitro Mesurage des grandeurs dans les échantillons d'origine biologique Exigences relatives aux matériaux de référence certifiés et au contenu de la documentation associée (ISO/DIS 15194:2023)

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11.100.10	Diagnostični preskusni sistemi in vitro	In vitro diagnostic test systems

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In vitro diagnostic medical devices — Requirements for certified reference materials and the content of supporting documentation

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

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 third edition cancels and replaces the second edition (ISO 15194:2009), which has been technically revised.

The main changes are as follows:

— incorporated requirements, concepts and definitions for consistency with ISO 17511:2020;

— removed or reduced text regarded as redundant or of limited relevance. As a result Section 4 in the second edition - Systematic designation of CRM properties - has been deleted;

— expanded and clarified the Scope statement to specify requirements for higher-order CRMs whose intended for use is to underpin routine measurements in laboratory medicine;

— added requirements regarding description of the intended use and commutability of the CRM; and

— strengthened the documentation requirements for both the certificate and the certification report accompanying a CRM.

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

Reference measurement systems are needed to enable the results produced by end user measurement procedures to be metrologically traceable to measurement standards and/or measurement procedures of the highest metrological level. Such systems exist within a traceability chain/calibration hierarchy as described in ISO 17511:2020. In the context of in vitro diagnostic (IVD) medical devices, they mitigate the risk of harm to patients by avoiding inconsistent results from different measurement systems.

Substances that are used to establish and maintain this metrological traceability of measurement results - over time within one location, between different physical locations or with the application of different measurement procedures - are Reference Materials (RMs). Certified Reference Materials (CRMs) are a category of RMs required at the higher metrological levels of a calibration hierarchy or that underpin the metrological traceability of measurement results.

A given CRM is supported by documentation describing the sources of the material, its processing and production, measurement results, metrological traceability, instructions for use, homogeneity and stability data, commutability data when applicable, and storage conditions, as well as health and safety warnings. When the intended application of the CRM is as a secondary calibrator in the calibration hierarchy of IVD devices, the commutability of the CRM is a critical property to be reported.

This Standard specifies the quality requirements for such materials and the recommended content of their supporting documentation.

CRMs are used for one of three main purposes:

a) calibration of quantity values indicated by a measurement system or assigned to another RM;

b) assessment of measurement trueness of quantity values obtained in a given laboratory, or in a group of laboratories;

c) assessment of measurement trueness of quantity values obtained using a new measurement procedure.

NOTE “Measurement trueness” (ISO 17511:2020 3.47) is the closeness of agreement between the average of an infinite number of replicate measured quantity values and a reference quantity value. It is inversely related to systematic measurement error but is not related to random measurement error.

“Measurement precision” (ISO 17511:202 3.34) is the closeness of agreement between measured quantity values obtained by replicate measurements on the same or similar objects under specified conditions. It is usually expressed numerically by measures of imprecision, such as standard deviation, variance, or coefficient of variation under the conditions of measurement. “Measurement precision” is a measure of random measurement error.

The combined uncertainty of the assigned value of a CRM is determined by the combined uncertainty of the steps above the CRM in the calibration hierarchy and the CRM uncertainties associated with its homogeneity and stability. Suitability of its measurement uncertainty is determined by its intended use in the calibration hierarchy.

Since the proper use of a CRM depends on the provision of detailed information, it is important to apply rules for the documentation of CRMs.

In this Standard, defined concepts are indicated by italicized text.

In vitro diagnostic medical devices — Requirements for certified reference materials and the content of supporting documentation

1 Scope

This standard specifies requirements for producers of CRMs of higher metrological order and the content of their supporting documentation that comply with the requirements of ISO 17511 and the calibration hierarchies described therein. It is applicable to CRMs intended for use as either primary reference materials, secondary calibrators or international conventional calibrators within calibration hierarchies appropriate for measurands used in laboratory medicine, or for applications as trueness controls. Requirements for determining the certified value of a CRM, including evaluation and reporting of the assigned uncertainty, are specified.

This standard applies primarily to CRMs with assigned property values where the property has a magnitude that can be expressed as a quantitative scalar number or ratio to a reference or refers to a counting scale as also described in the scope of ISO 17511:2020. Annex A provides information on CRMs for qualitative nominal properties and ordinal quantities, to provide guidance on important quality attributes for such CRMs, whilst recognizing that they are not within the metrological traceability schemes described in ISO 17511:2020.

When a CRM includes multiple measurands, this Standard is applied to each of the certified quantity values present in the CRM.

Although intended to be applicable to producers of CRMs, this Standard will also be useful for RMs that do not comply with the full metrological requirements of CRMs. For example, this International Standard does not apply to a RM created by IVD MD manufacturers for use as working calibrator or end-user calibrator within a calibration hierarchy traceable to a CRM, although some content may be useful in assessing its performance.

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 80000 (all parts), *Quantities and units*

ISO 17511, *In vitro diagnostic medical devices — Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples*

ISO 17034, *General requirements for the competence of reference material producers*

ISO/IEC Guide 99:2007, *International vocabulary of metrology — Basic and general concepts and associated terms (VIM)*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO/IEC Guide 99 and ISO 17511 and the following apply.

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

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

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

3.1
analyte
component represented in the name of a quantity (3.22)

EXAMPLE In the type of *quantity* (3.22) "mass of protein in 24-hour urine", "protein" is the analyte. In "amount of substance of glucose in plasma", "glucose" is the analyte. In both cases the full phrase describes the *measurand* (3.13).

[SOURCE: ISO 17511:2020, 3.1]

3.2
calibrator
CRM (3.3) or a *RM* (3.23) with a traceable assigned *quantity* (3.22) value used in calibration of a *measurement system* (3.16) according to a specified *measurement procedure* (3.15)

[SOURCE: ISO 17511:2020, 3.6, modified – "CRM or a RM with a traceable assigned quantity value" replaced "measurement standard"]

3.3
certified reference material (CRM)
reference material (3.23), accompanied by documentation issued by an authoritative body and providing one or more specified property values with associated *uncertainty* (3.29) and *traceability* (3.17) using valid procedures

Note 1 to entry: "Documentation" is given in the form of a *reference material certificate* (3.24) and a *certification report* (3.4).

Note 2 to entry: Requirements for the production of a CRM are given in ISO 17034. ISO Guide 35 provides technical guidance on the characterization and the assessment of the homogeneity and stability of a CRM.

Note 3 to entry: In this definition, "uncertainty" covers both '*measurement uncertainty*' (3.29) and 'uncertainty associated with the value of a nominal property', such as for identity or sequence. "Traceability" covers both '*metrological traceability* (3.17) of a *quantity* (3.22) value' and 'traceability of a nominal property value'.

Note 4 to entry: Specified *quantity* (3.22) values of CRMs require *metrological traceability* (3.17) with associated *measurement uncertainty* (3.29).

Note 5 to entry: ISO 17034 has an analogous definition.

Note 6 to entry: Specific additional requirements for CRMs and the content of supporting documentation required in the field of *IVD medical devices* (3.11) are given in this Standard.

Note 7 to entry: For a specified material, a calibration certificate provided by an accredited calibration laboratory is not by itself sufficient to confer the status of CRM on these types of materials.

EXAMPLE Human serum with an assigned *quantity* (3.22) value and associated *measurement uncertainty* (3.29) for concentration (amount of substance per unit volume) of cholesterol inherently present in the serum and used as a *calibrator* (3.2) or as a *trueness control material* (3.28) is an example of a CRM.

See also *primary calibrator* (3.18) and *secondary calibrator* (3.27).

[SOURCE: ISO 17511: 2020, 3.9 – modified. Note 1 to entry includes a certification report in addition to a reference material certificate as "documentation" required for a CRM to meet the Scope of this Standard]

3.4
certification report
additional information on a *CRM* (3.3), supplementary to that contained in a reference material certificate (3.24) that describes the production, characterization and certification of a *CRM* (3.3) intended for use in laboratory medicine and with *IVD devices* (3.11)

3.5
commutability of a reference material
commutability
property of a *reference material* (3.23), demonstrated by the closeness of agreement between the relation among the measurement results for a stated *quantity* (3.22) in this material, obtained according to at least two *measurement procedures* (3.15), and the relation obtained among the measurement results for other specified materials

Note 1 to entry: The *RM* (3.23) is usually a *secondary calibrator* (3.27) and the other materials are usually clinical *samples* (3.26).

Note 2 to entry: For the commutability assessment of a *CRM* (3.3) it is desirable to measure the clinical *samples* (3.26) with as many *measurement procedures* (3.15) as feasible.

Note 3 to entry: Closeness of agreement is defined in terms of fitness for purpose as appropriate for the intended use of the *RM* (3.23).

Note 4 to entry: The validity of a commutability statement is restricted to the *measurement procedures* (3.15) specified in a particular comparison.

[SOURCE: ISO 17511:2020 3.10]

Note 5 to entry: The IFCC Working Group Recommendations for Assessing Commutability and CLSI Document EP30-A provide guidance on how to undertake a commutability study.

[SOURCE: Bibliography - Refs. 15, 16, 17, and 18]

3.6
control material
substance, material or artefact intended by its producer to be used to verify the performance of an *IVD medical device* (3.11)

[SOURCE: ISO 17511: 2020, 3.11]

3.7
examination
set of operations having the objective of determining the numerical value, text value or characteristics of a property

[SOURCE: ISO 15189: 2022, 3.8]

3.8
higher-order reference material
higher-order RM
CRM (3.3) that meets internationally accepted quality requirements and provides a common metrological reference within a calibration hierarchy by which a manufacturer can establish *metrological traceability* (3.17)

[SOURCE: ISO 17511: 2020, 3.14]

3.9
higher-order reference measurement procedure
higher-order RMP
RMP (3.25) meeting internationally accepted quality requirements and providing a common metrological reference within a calibration hierarchy by which a producer can establish *metrological traceability* (3.17) and accepted as providing measurement results fit for their intended use in assessing measurement trueness

Note 1 to entry: Quality requirements for higher-order RMPs are defined in ISO 15193.

[SOURCE: ISO 17511:2020, 3.15 - modified]