

საქართველოს სტანდარტი

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საინფორმაციო ნაწილი. სრული ტექსტის სანახავად შეიძინეთ სტანდარტი.

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

*Dispositifs médicaux de diagnostic in vitro — Exigences pour
l'établissement d'une traçabilité métrologique des valeurs attribuées
aux étalons, aux matériaux de contrôle de la justesse et aux
échantillons humains*





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CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Fax: +41 22 749 09 47
Email: copyright@iso.org
Website: www.iso.org

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Contents

Page

Foreword.....	vi
Introduction.....	viii
1 Scope.....	1
2 Normative references.....	2
3 Terms and definitions, symbols and abbreviated terms.....	2
4 General requirements to be fulfilled by a manufacturer for establishing, validating and documenting metrological traceability of human sample values determined with a specified IVD MD.....	19
4.1 Requirements for documenting metrological traceability of measured quantity values.....	19
4.2 Definition of the measurand.....	19
4.3 Specifications for maximum allowable expanded measurement uncertainty, $U_{max}(y)$	20
4.3.1 General requirements.....	20
4.3.2 Scope of the specification.....	20
4.4 Defining the calibration hierarchy.....	20
4.4.1 General requirements.....	20
4.4.2 Measured quantity.....	21
4.4.3 Highest level of metrological traceability.....	21
4.4.4 Traceability to SI.....	21
4.4.5 Non-SI traceable IVD MDs.....	21
4.4.6 Number of levels in the specified hierarchy.....	21
4.5 Selection and requirements for RMs and calibrators.....	21
4.5.1 General requirements.....	21
4.5.2 Characteristics to be documented.....	21
4.5.3 Higher order RMs that conform with ISO 15194.....	22
4.5.4 RMs not conforming to ISO 15194.....	22
4.5.5 Commutability of RMs.....	22
4.5.6 Exception to commutability assessment requirements.....	23
4.5.7 Application of a non-commutable CRM.....	23
4.5.8 Alternative RMs.....	23
4.5.9 Augmentation of alternative RMs.....	23
4.5.10 Non-commutable end-user IVD MD calibrators.....	24
4.6 Selection and requirements for MPs.....	24
4.6.1 Rationale for selection of MPs and documentation responsibility.....	24
4.6.2 Metrological status of MPs.....	24
4.6.3 Reference measurement laboratories.....	24
4.6.4 Impact of influence quantities.....	25
4.6.5 Changes in the measured quantity within a calibration hierarchy.....	25
4.7 Estimating uncertainty of assigned values for end-user IVD MD calibrators.....	25
4.7.1 General requirements.....	25
4.7.2 Documentation for method of estimating u_{cal}	26
4.7.3 Statistical considerations and scope of u_{cal} estimates.....	26
4.7.4 Expression of u_{cal}	26
4.7.5 Product modifications.....	27
4.7.6 Information to be provided to the end-user.....	28
4.8 Validation of metrological traceability of values assigned to an IVD MD calibrator.....	28
4.8.1 General validation requirements.....	28
4.8.2 Validation strategies.....	28
4.8.3 Test design considerations and acceptance criteria.....	29
4.8.4 Calibration hierarchies with an available RMP.....	29
4.8.5 Calibration hierarchies with no available RMP.....	29
4.8.6 Calibration hierarchies with no RMPs and no CRMs.....	29
4.8.7 Validation of design changes to an end-user IVD MD calibrator.....	30
4.9 Additional calibration hierarchy documentation responsibilities.....	30

4.9.1	Obligation to end-users.....	30
4.9.2	Maintaining documentation.....	30
4.9.3	Third party manufacturers of IVD MD calibrators.....	30
4.9.4	Modifications introduced by independent entities.....	30
4.9.5	Calibration hierarchies supporting IVD MDs developed by a single entity for its own use.....	31
4.9.6	RMs other than end-user IVD MD calibrators.....	31
4.9.7	EQA and PT materials with claims of metrologically traceable target values.....	31
5	Model calibration hierarchies for metrological traceability.....	31
5.1	Elements of the description of a calibration hierarchy.....	31
5.2	Cases with RMPs and primary RMs.....	32
5.2.1	General considerations.....	32
5.2.2	Definition of the measurand.....	33
5.2.3	Selecting RMPs.....	34
5.2.4	Primary RMPs.....	34
5.2.5	Primary calibrators.....	35
5.2.6	Assigning a value to a secondary RM or calibrator.....	35
5.2.7	Commutability of secondary RMs.....	35
5.2.8	Manufacturer’s Selected MP.....	35
5.2.9	Working calibrators.....	35
5.2.10	Manufacturer’s standing MP.....	36
5.2.11	Manufacturer’s end-user calibrator.....	36
5.2.12	u_{cal} of the assigned value of the end-user calibrator.....	36
5.2.13	End-user IVD MD.....	36
5.3	Cases with a primary RMP that defines the measurand.....	36
5.3.1	General Considerations.....	36
5.3.2	Definition of the measurand.....	38
5.3.3	Higher order RMP that defines the measurand.....	38
5.3.4	The primary RMP and definition of the measurand.....	38
5.3.5	Documentation of the primary RMP.....	38
5.3.6	Assignment of values to secondary RMs.....	39
5.3.7	Manufacturer’s selected MP.....	39
5.3.8	Manufacturer’s working calibrator.....	39
5.3.9	Manufacturer’s standing MP.....	40
5.3.10	Manufacturer’s end-user calibrator.....	40
5.3.11	End-user IVD MD.....	40
5.4	Cases for measurands defined by a RMP calibrated with a particular primary calibrator.....	40
5.4.1	General considerations.....	40
5.4.2	Definition of the measurand.....	41
5.4.3	Value assignment of the primary RM.....	42
5.4.4	Value assignment of the primary calibrator.....	42
5.4.5	Selection and intended use of the RMP in the calibration hierarchy.....	42
5.4.6	Manufacturer’s selected MP.....	42
5.4.7	Manufacturer’s working calibrator.....	42
5.4.8	Manufacturer’s standing MP.....	43
5.4.9	End-user IVD MD calibrator.....	43
5.4.10	End-user IVD MD.....	43
5.5	Cases with an international conventional calibrator that defines the measurand.....	43
5.5.1	General considerations.....	43
5.5.2	The international conventional calibrator — Material description.....	45
5.5.3	Value assignment of an international conventional calibrator.....	45
5.5.4	Commutability of an international conventional calibrator.....	45
5.5.5	Calibration and selection of the manufacturer’s selected MP.....	46
5.5.6	Characteristics and value assignment of the manufacturer’s working calibrator.....	46
5.5.7	Manufacturer’s standing MP.....	46
5.5.8	End-user IVD MD calibrator.....	46
5.5.9	End-user IVD MD.....	46

5.6	Cases with metrological traceability supported by an international harmonisation protocol.....	46
5.6.1	General Considerations.....	46
5.6.2	International harmonisation protocol.....	47
5.6.3	Assignment of values to harmonisation RMs.....	48
5.6.4	Application of harmonisation RMs.....	48
5.6.5	End-user IVD MD.....	48
5.7	Cases for measurands with metrological traceability only to manufacturer’s internal arbitrarily defined RM(s).....	48
5.7.1	General considerations.....	48
5.7.2	Selection of RMs.....	49
5.7.3	Manufacturer’s Selected MP.....	50
5.7.4	Manufacturer’s Standing MP.....	50
5.7.5	End-user IVD MD calibrators.....	50
5.7.6	End-user IVD MD.....	50
5.7.7	Documentation of the calibration hierarchy.....	50
6	Labelling information to be provided to end-users by the manufacturer.....	51
	Bibliography.....	52

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).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

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For an explanation on 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 the following URL: 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 17511:2003), which has been technically revised. The main changes compared to the previous edition are as follows:

- incorporation of the special requirements for metrologically traceable calibration hierarchies for measurement of catalytic concentration of enzymes (previously covered in ISO 18153:2003);
- to clarify that final reported values on human samples shall be metrologically traceable to the highest order available reference, the title and scope were modified to include metrological traceability of values assigned to human samples;
- updated normative references to remove International Vocabulary of Basic and General Terms in Metrology, 2nd edition, ISO, Geneva (1993) and ISO Guide 35:1989, Certification of reference materials — General and statistical principles;
- revision of [Clause 4](#) to clearly define requirements of a manufacturer of an in vitro diagnostic medical device in establishing and documenting metrological traceability of assigned values (for calibrators, trueness controls and human samples), while incorporating requirements previously addressed in [Clauses 6](#), 7 and 8 (thus eliminating those sections);
- revision of [Clause 5](#) to incorporate additional models of metrologically traceable calibration hierarchies, especially [5.3](#) for measurement of catalytic concentration of enzymes (where the measurand is defined by a primary RMP; previously addressed in ISO 18153:2003), and [5.6](#) for an overview of the concept of assigned values of materials for measurands with metrological traceability to international harmonisation protocols (addressed in detail in ISO 21151).

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

In laboratory medicine, the objective of examining a measurand in a human sample is to produce laboratory results that will enable a clinician to assess the risk of a disease, or to diagnose and make treatment decisions for a medical condition. To be clinically useful, the results obtained from a given human sample examined by different laboratories or among different in vitro diagnostic medical devices (IVD MDs) within a single laboratory should be equivalent, regardless of the measurement procedure employed. Equivalent results allow uniform application of medical decision limits and reference intervals, which can reduce the risk of harm caused by medical decisions based on non-equivalent examination results. Equivalence of results among different IVD MDs for the same measurand is also important for the analysis of results in medical records for the purpose of supporting clinical decisions and for conducting epidemiological investigations.

Equivalent results for human samples for a measurand can be achieved by establishing metrological traceability of the values assigned to the calibrators for a measurement procedure (MP) to the highest available reference system component for the measurand. Metrological traceability describes the calibration hierarchy and the sequence of value assignments, demonstrating an unbroken linkage between the measurement result for a human sample up to the highest available reference system component in the calibration hierarchy. The point at which metrological traceability begins (i.e. the highest level of metrological traceability in the calibration hierarchy) depends on the availability of higher order reference measurement procedures (RMPs), reference materials (RMs) or harmonisation protocols for the stated measurand.

Limitations in implementing metrologically traceable calibrations occur when different IVD MDs intended for the same measurand do not measure the same or very closely related measurable quantities. Some measurands of medical interest may be well-defined elements or molecules. An increasing number of medical decisions depend on measurands that consist of complex and variable mixtures of chemical structures, molecular species and molecular complexes in varying proportions, e.g. glycoproteins with multiple isoforms, variant amino acid sequences, nucleic acid sequences, and other complex molecular forms. When the selectivity of an IVD MD is not fit-for-purpose, sample-specific influence quantities in human samples due to factors including disease, drugs or other pathological conditions may lead to erroneous values for the intended measured quantity. Even with metrological traceability to higher order reference system components, the selectivity of MPs at all levels in the calibration hierarchy for a given IVD MD can influence its ability to achieve results for human samples that are equivalent to the results obtained with other IVD MDs for the same measurand.

This document presents requirements for manufacturers of IVD MDs in documenting the calibration hierarchy for a measured quantity in human samples using a specified IVD MD. The document includes various model calibration hierarchies offering potential technical solutions for different kinds of measurands in establishing metrological traceability of assigned values for human samples, calibrators and trueness control materials. Use of this document as part of a broadly-based risk management program for manufacturers of IVD MDs is consistent with the requirements of ISO 14971 and is expected to assist in the reduction of the risk of harm to patients due to non-equivalence of results among different IVD MDs.

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