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In vitro diagnostic medical devices — Requirements for international harmonisation protocols establishing metrological traceability of values assigned to calibrators and human samples

Dispositifs médicaux de diagnostic in vitro — Exigences relatives aux protocoles d'harmonisation internationaux établissant la traçabilité métrologique des valeurs affectées aux étalons et aux échantillons humains

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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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Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

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*.

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

Results for a measurand in a human sample should be numerically equivalent, within clinically meaningful limits, among different laboratories using different in vitro diagnostic (IVD) medical devices (MDs). Clinical practice guidelines for diagnosis and treatment decisions that use fixed decision limits for interpreting laboratory results can only be appropriately applied when results are equivalent irrespective of the IVD MD used. Laboratory medicine has adopted the principle of metrological traceability of IVD MD calibration to higher order references as the basis to achieve equivalent results for the same measurand that are independent of the IVD MD, location or time the measurements were made.

ISO 17511:2020, describes 6 calibration hierarchies of reference measurement systems (referred to as cases in 5.2 to 5.7 of ISO 17511:2020) that fulfil the requirement for metrological traceability of a calibration to higher order references. Metrological traceability of calibrator assigned values for particular IVD MDs for measurands in cases 5.2, 5.3 and 5.4 are based on the availability of a reference measurement procedure. Case 5.5 includes measurands for which a certified reference material or an international conventional calibrator with a consensus-based protocol for value assignment is available but there is no reference measurement procedure. Cases 5.6 and 5.7 include measurands for which neither a reference measurement procedure nor a certified reference material or international conventional calibrator is available. Case 5.6 achieves standardization based on a consensus harmonisation protocol. The requirements for such a harmonisation protocol are described in this document. Case 5.7 includes measurands that are not addressed by traceability schemes in the preceding categories. For such measurands, metrological traceability is to the calibrator chosen by the manufacturer of an IVD MD but there is no traceability to a common reference. In case 6 the results from different IVD MDs can be different and not comparable to each other or to decision limits used in guidelines for making medical decisions.

Higher order references for measurands in case 5.6 have been technically difficult to develop thus requiring an approach for standardization based on a protocol for achieving equivalence of results among two or more IVD MDs. Research to develop suitable processes for harmonisation of case 5.6 measurands forms the basis for the requirements in this document[5][11]. Standardization of results based on a harmonisation protocol provides metrological traceability of particular IVD MD calibrators to that protocol. A harmonisation protocol is developed and administered by an international body to achieve equivalence among results for different IVD MDs thus meeting requirements for use of the results in medical decisions.

Annex A provides a worked example to illustrate the principles of a harmonisation protocol and one possible approach to implementing a harmonisation protocol. Other approaches are also possible and will likely be developed for particular measurands and IVD MDs.

In vitro diagnostic medical devices — Requirements for international harmonisation protocols establishing metrological traceability of values assigned to calibrators and human samples

1 Scope

This document specifies requirements for a protocol implemented by an international body to achieve equivalent results among two or more IVD MDs for the same measurand for cases where there are no reference measurement procedures and no fit-for-purpose certified reference materials or international conventional calibrators. In this case, the harmonisation protocol defines the highest level of metrological traceability for the stated measurand.

This document can be applied in cases when certified reference materials or international conventional calibrators exist but are not fit-for-purpose because, for example, they are not commutable with human samples.

NOTE This document addresses one case of traceability of assigned and measured values described in 5.6 in ISO 17511:2020.

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).

ISO 17511:2020, *in vitro diagnostic medical devices — Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples*

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
aliquot
known amount of a homogeneous material, assumed to be taken with negligible sampling error

[SOURCE: ISO 11074:2015]

3.2
calibration verification control
control provided by a manufacturer for use with a stated IVD MD to confirm that a satisfactory calibration was achieved using the end-user calibrator(s) intended for use with that IVD MD