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Reference materials — Guidance for characterization and assessment of homogeneity and stability

Matériaux de référence — Lignes directrices pour la caractérisation et l'évaluation de l'homogénéité et de la stabilité

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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).

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).

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/REMCO, the Reference Materials Committee of ISO.

This fourth edition cancels and replaces the third edition (ISO Guide 35:2006).

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Introduction

The production of reference materials (RMs) is a key activity for the improvement and maintenance of a worldwide coherent measurement system. As detailed in ISO Guide 33[1], RMs with different characteristics are used in measurements, such as calibration, quality control, proficiency testing and method validation, as well as for the assignment of values to other materials. Certified reference materials (CRMs) are also used to confirm or establish metrological traceability to conventional scales, such as the octane number, hardness scales and pH.

To be comparable across borders and over time, measurements need to be traceable to appropriate and stated references. CRMs play a key role in implementing the concept of traceability of measurement results in chemistry, biology and physics among other sciences dealing with substances and materials. Laboratories use these CRMs as readily accessible measurement standards to establish traceability of their measurement results to International Standards. The property values carried by a CRM can be made traceable to the International System of Units (SI) or other internationally agreed references during production. This document explains how approaches can be developed that will lead to well established property values, which are made traceable to appropriate stated references.

For reference material producers (RMPs), there is an International Standard and three ISO Guides that support the production and certification of RMs to ensure that the quality of the RMs meets the requirements of the end users.

— ISO 17034 outlines the general requirements to be met by an RMP to demonstrate competence.

— ISO Guide 35 provides more specific guidance on technical issues and explains the concepts for processes such as the assessment of homogeneity, stability and characterization for the certification of RMs.

— ISO Guide 31[2] describes the contents of certificates for CRMs, and of accompanying documents for other RMs, respectively.

— ISO Guide 30[68] contains the terms and definitions related to reference materials.

Alongside developments in RM production approaches, the range of classes of RMs is growing with advances in technology, increasing the need for more widely applicable technical guidance in RM production. In addition, increasing use of ISO/IEC 17025[52] and ISO 15189[71] by laboratories has led to greater demand for clear statements of metrological traceability.

This document provides detailed guidance on a larger range of homogeneity study designs, and describes a wider range of stability management strategies than ISO Guide 35:2006. It also contains specific provisions concerning the establishment of metrological traceability in RM production.

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Reference materials — Guidance for characterization and assessment of homogeneity and stability

1 Scope

This document explains concepts and provides approaches to the following aspects of the production of reference materials:

— the assessment of homogeneity;

— the assessment of stability and the management of the risks associated with possible stability issues related to the properties of interest;

— the characterization and value assignment of properties of a reference material;

— the evaluation of uncertainty for certified values;

— the establishment of the metrological traceability of certified property values.

The guidance given supports the implementation of ISO 17034. Other approaches may also be used as long as the requirements of ISO 17034 are fulfilled.

Brief guidance on the need for commutability assessment (6.11) is given in this document, but no technical details are provided. A brief introduction for the characterization of qualitative properties (9.6 to 9.10) is provided together with brief guidance on sampling such materials for homogeneity tests (Clause 7). However, statistical methods for the assessment of the homogeneity and stability of reference materials for qualitative properties are not covered. This document is also not applicable to multivariate quantities, such as spectral data.

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 3534-2, *Statistics — Vocabulary and symbols — Part 2: Applied statistics*

ISO 3534-3, *Statistics — Vocabulary and symbols — Part 3: Design of experiments*

ISO Guide 30, *Reference materials — Selected terms and definitions*

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

NOTE The *International vocabulary of metrology* will hereafter be referred to as the “VIM”.

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO Guide 30, ISO/IEC Guide 99, ISO 3534-2, ISO 3534-3 and the following apply. The definitions in ISO Guide 30 take precedence where more than one definition for the same term exists.

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

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

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

3.1
reference material
RM
material, sufficiently homogeneous and stable with respect to one or more specified properties, which has been established to be fit for its intended use in a measurement process

Note 1 to entry: RM is a generic term.

Note 2 to entry: Properties can be quantitative or qualitative, e.g. identity of substances or species.

Note 3 to entry: Uses may include the calibration of a measurement system, assessment of a measurement procedure, assigning values to other materials, and quality control.

Note 4 to entry: ISO/IEC Guide 99:2007[3] has an analogous definition (5.13), but restricts the term "measurement" to apply to quantitative values. However, ISO/IEC Guide 99:2007, 5.13, Note 3 (VIM), specifically includes qualitative properties, called "nominal properties".

[SOURCE: ISO Guide 30:2015, 2.1.1]

3.2
certified reference material
CRM
reference material (RM) characterised by a metrologically valid procedure for one or more specified properties, accompanied by an RM certificate that provides the value of the specified property, its associated uncertainty, and a statement of metrological traceability

Note 1 to entry: The concept of value includes a nominal property or a qualitative attribute such as identity or sequence. Uncertainties for such attributes may be expressed as probabilities or levels of confidence.

Note 2 to entry: Metrologically valid procedures for the production and certification of RMs are given in, among others, ISO 17034 and ISO Guide 35.

Note 3 to entry: ISO Guide 31[2] gives guidance on the contents of RM certificates.

Note 4 to entry: ISO/IEC Guide 99:2007[3] has an analogous definition (5.14).

[SOURCE: ISO Guide 30:2015, 2.1.2]

3.3
measurement model
mathematical relation among all quantities known to be involved in a measurement
[SOURCE: ISO/IEC Guide 99:2007, 2.48[3]]

3.4
property value
<of a reference material (RM)> value corresponding to a quantity representing a physical, chemical or biological property of an RM

[SOURCE: ISO Guide 30:2015, 2.2.1]

3.5
certified value
value, assigned to a property of a reference material (RM), that is accompanied by an uncertainty statement and a statement of metrological traceability, identified as such in the RM certificate

[SOURCE: ISO Guide 30:2015, 2.2.3]

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3.6
indicative value
information value
informative value
value of a quantity or property of a reference material, which is provided for information only

Note 1 to entry: An indicative value cannot be used as a reference in a metrological traceability chain.

[SOURCE: ISO Guide 30:2015, 2.2.4]

3.7
calibrant
reference material used for calibration of equipment or a measurement procedure

[SOURCE: ISO Guide 30:2015, 2.1.21]

3.8
quality control material
reference material used for quality control of a measurement

[SOURCE: ISO Guide 30:2015, 2.1.22]

3.9
isochronous stability study
experimental study of reference material stability in which units exposed to different storage conditions and times are measured in a short period of time

3.10
production
<of a reference material (RM)> all necessary activities and tasks leading to the release and maintenance of an RM (certified or non-certified)

Note 1 to entry: Activities include, for example, planning, control, material handling and storage, material processing, assessment of homogeneity and stability, characterization, assignment of property values and their uncertainties, authorization and issue of RM certificates or other statements.

[SOURCE: ISO Guide 30:2015, 2.3.7]

4 Symbols

a	number of reference material units in a homogeneity study
d	measurement bias
k	coverage factor or (as subscript) index
L_d	a limit of detection (minimum detectable value of the net state variable) calculated using the methods of ISO 11843-1[48]
N_{min}	minimum number of RM units for a homogeneity study for batch sizes over 100 units
N_{prod}	number of RM units produced in a single batch
n_r	number of runs in a blocked or nested homogeneity study design
p	number of laboratory means in an interlaboratory certification exercise
s_{bb}	between-unit component of variance from a homogeneity study, expressed as a standard deviation

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