UKAS
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Guidance and policy on the selection and use of reference materials

Contents

Changes since last edition

- ISO standards defined at the start of the document
- Reference to appendices added for extra clarity where required
- 1.6 - clarity added with regards to use of reference material throughout the document
- 3.5 - rewritten to clarify the supplier evaluation needed when distributors are involved
- 3.6 - reference to COMAR moved to Annex 3 and reference to new Annex 3 added
- New section 3.8 added
- 4.1 - examples added to aid clarification
- 4.2(c) - new bullet point added
- Annex A1 - updated to clarify A1.2 and A1.3)
- A2.11 and A2.17 - added as new definitions in Annex 2
- Annex 3 added (list of reference material databases)

1. Introduction

1.1 UKAS considers the use of reference materials and/or calibrated artefacts to be an important tool for demonstrating the validity of test and calibration methods and a potential means of establishing the traceability of measurements produced using said methods. *UKAS recommends the use of accredited reference material producers and calibration laboratories where they exist*.

1.2 ISO/IEC 17025 (*General requirements for the competence of testing and calibration laboratories*) and ISO 15189 (*Medical laboratories – requirements for quality and competence*) require laboratories to establish the traceability of their measurements back to the International System of Units (SI) or appropriate measurement standards. This requirement can be met by the use of fit for purpose certified reference materials and/or calibrated artefacts whose property values have appropriate traceability.

1.3 ISO/IEC 17025 and ISO 15189 also require laboratories to validate methods and confirm that they are fit for their intended purpose and suggest a number of approaches that can be used to achieve this validation. A laboratory can meet this requirement by use of fit for purpose reference materials and/or by the use of calibrated artefacts.

1.4 Reference materials play an important role in underpinning the accuracy and validity of measurements made within testing and calibration laboratories. When selecting and purchasing reference materials and/or calibrated artefacts, to have confidence in the materials/artefacts, laboratories need to ensure that the producer of the material is competent and that the material has been produced using a valid procedure. Some guidance is provided in this document to assist with determining the competence of reference material producers. Further guidance can be found in ISO 17034 (*General requirements for the competence of reference material producers*) and other references in section 5.

1.5 This document describes the steps that laboratories are expected to take in order to demonstrate that they have selected reference materials that are fit for purpose. In particular the laboratory should consider the matrix, concentration, accuracy, traceability, uncertainty, stability and homogeneity of the reference material as key factors that help to determine fitness for purpose. Some guidance is provided in this document to assist with determining fitness for purpose, further guidance can be found in ISO 17034 and other references in section 5.

1.6 It is important at this stage to clearly define reference materials (RMs) and certified reference materials (CRMs). A reference material (RM) is a material, sufficiently homogeneous and stable with reference to one or more specified properties, which has been established to be fit for its intended use in a measurement process. A certified reference material (CRM) is a reference material characterized 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. See Annex 2 below. For the purposes of this publication the term “reference material” is used to cover both RMs and CRMs except where specific differences are to be defined.

2. Scope

2.1 This document applies to applicant and accredited testing and calibration laboratories. This document is also applicable to other accredited bodies (e.g. inspection bodies, proficiency testing providers) that conduct analytical testing or calibration as part of their accredited activities.

3. Policy

3.1 Use of reference materials for method validation/verification.

3.1.1 It is UKAS policy that all accredited testing and calibration laboratories shall use, where available and appropriate, reference materials or calibrated artefacts for the validation/verification of critical steps and processes in their methods.

Note 1: Laboratories should be aware that all stages (e.g. sample preparation, extraction, measurement, etc.) of the testing/calibration process may need to be validated, and the aspects affecting traceability at each stage may need to be considered.

Note 2: Where the method being validated involves the determination of a property value in a matrix (e.g. Arsenic in Soil) then the reference material(s) chosen for validation shall ideally contain the property value in a comparable matrix. If no suitable matrix reference materials are available, then a suitable 'blank' matrix may need to be fortified with an appropriate non matrix reference material. It is important to ascertain whether or not the fortified material represents the same analytical challenges as real (natural) samples.

Note 3: Laboratories should be aware that it is not normally considered appropriate to use the same reference material for the calibration and validation/verification of a method (see ref A1.3).

3.2 Use of reference Materials for Calibration of Equipment/Methods.

3.2.1 It is UKAS policy that all accredited testing and calibration laboratories shall use, where available and appropriate, certified reference materials and/or calibrated artefacts for calibrations within their methodologies.

3.3 Laboratories are required to determine the fitness for purpose of the reference materials and/or calibrated artefacts used for either calibration or validation/verification for methods within their scope of accreditation. Where reference materials are used for the purposes of calibration the traceability of the values assigned to the material shall be a consideration as to the reference materials' fitness for purpose. This can be achieved by, for instance, using a certified reference material from a producer accredited to ISO 17034, as the certificate will include a statement on the metrological traceability of the certified values. Laboratories should review these statements, seeking guidance and/or clarification from the accredited producer if necessary.

Note 1: UKAS accepts that it may not be feasible to establish traceability for measurements as required by ISO/IEC 17025 and ISO 15189 in all cases. However, the use of certified reference materials and/or calibrated artefacts should be employed by laboratories where available and appropriate to the methodology. Additionally, UKAS also acknowledges that:

a) The concept of traceability of measurement in fields such as chemical and biological sciences is still under international debate and progression towards unified understanding and use of this concept is not yet complete.

b) The role of certified reference materials in providing traceability of measurement results has not yet been fully established internationally for all sciences.

3.4 Laboratories shall ensure that reference materials they purchase are obtained from a competent producer of reference materials.

3.5 ISO/IEC 17025 and ISO 15189 require laboratories to evaluate suppliers; this includes producers of reference materials and suppliers of calibration services/items. Therefore, laboratories are required to determine the competence of the producer of the reference materials and/or calibrated artefacts used. Accreditation will demonstrate appropriate competence (see note 1) but if using non accredited suppliers then it is important that not only is the producer evaluated but also any distributors that are included in the initial supply chain (1st reseller only).

The evaluation of distributors will need to ensure that the integrity of the reference materials or artefact remain as expected e.g. storage is appropriate for the materials being held prior to dispatch and that dispatch is controlled as required.

Note 1: UKAS recommends the use of accredited reference material producers and calibration laboratories where they exist. ISO 17034 outlines the general requirements for the competence of reference material producers and should be used as a basis for such an evaluation. UKAS accredits reference material producers to ISO 17034; a list of accredited reference material producers is available on www.ukas.com*. Details of UKAS accredited calibration laboratories can also be found on* www.ukas.com (see ref A1.1).

3.6 Where reference materials are available but not used, the justification for this shall be documented. This information may be requested at the time an application for accreditation is made.

Note 1: Whilst no single source of information on the availability of reference materials currently exists, laboratories are recommended to contact reference material producers and distributors to discuss availability and suitability. There are a number of databases on the internet that contain information on certain reference materials and this can also be a useful starting point (See Annex 3). If no appropriate reference materials or calibrated artefacts are available, then the laboratory shall endeavour to demonstrate that any alternatives used represent the best available practice to ensure that the method and subsequent results can be deemed fit for purpose and relied upon. Guidance and advice on how to achieve this can be found in references 5.3 b) and 5.3 d).

3.7 Mandatory use of a specified reference material may be a requirement for some sector schemes or in support of regulatory activities. In these cases, UKAS may specify the use of a particular reference material where it is deemed necessary to demonstrate the validity of a method or traceability of a measurement. Where use of a specified reference material is a mandatory requirement, this shall be stated in an appropriate UKAS publication (see UKAS publications list on the UKAS website).

3.8 Whilst the reference material producer may assign an expiry date for each RM, possible adulteration of the material may occur once opened and during its period of use. It is good practice to undertake periodic analysis of each batch to establish its suitability for use.

4. Guidance on selecting an appropriate reference material and producer

4.1 Reference materials have many and varied uses within accredited laboratories, each of which will have specific requirements. As such it is important that the laboratory identifies the correct criteria for selection of a reference material to ensure that they obtain one that is fit for purpose. Therefore, laboratories should consider the following questions:

- 'What am I using the reference material for?' (*Has the RMP used the method of choice to assign the property value of the CRM*.)
- 'What is the appropriate uncertainty for my purpose?*'(How much will uncertainty be affected by further modification (dilution)?*
- 'What is the minimum sample size for my analytical method and therefore for the reference material?'
- 'Do I need a matrix reference material, or a pure reference material, or both?'
- 'What do my measurements need to be traceable to?'
- 'Do I have any requirements around the effective life of the materials?' *(If the CRM is used or modified a mistake may occur the first time of use or it may never occur, but probability will increase with use and time. Effective life should be a continuous assessment. A suggested log of use with specific methods should be included.)*
- 'What methods/equipment am I intending to use the reference material with?'
- 'What measurement range do I need to use the reference material in?' *(Selection of CRM that requires simple low ratio dilutions is more appropriate than large or multiple dilutions)*
- Is demonstration of commutability (ref A2.17) required for the reference material being used?
- 'Does the reference material contain anything that may cause an interference with the measurement capabilities of the method?' *(This is particularly important if there is any modification to the matrix when diluting for example)*

4.2 When an accredited organisation has determined the selection criteria for their reference material, the organisation will need to obtain the reference material from a producer which they can have confidence in; such that they can be sure that their requirements can be met. Obtaining a reference material from a reference material producer that is accredited to ISO 17034 by a recognised accreditation body will provide the organisation with confidence that the statements that the reference material producer makes about their materials can be relied upon. Where a reference material producer holds accreditation or certification to one of the following standards, the organisation may wish to consider the following points:-

a) When engaging the services of a reference material producer that is accredited to ISO/IEC 17025 as a calibration laboratory:

- 'Does the material I am planning to purchase have the potential for instability, if so, what has the reference material producer done to determine its stability?'
- 'Does the material I am planning to purchase have the potential for heterogeneity, if so, what has the reference material producer done to determine its level of homogeneity?'
- 'How will the material be stored and shipped, and will this ensure its ongoing suitability?'

b) When engaging the services of a reference material producer that is accredited to ISO/IEC 17025 as a testing laboratory:

- ‘Does the material I am planning to purchase have the potential for instability, if so, what has the reference material producer done to determine its stability?’
- ‘Does the material I am planning to purchase have the potential for heterogeneity, if so, what has the reference material producer done to determine its level of homogeneity?’
- ‘What do I need the assigned values to be traceable to, and how has the producer demonstrated the traceability of their assigned values?’
- ‘How will the material be stored and shipped, and will this ensure its ongoing suitability?’

c) When engaging the services of a reference material producer that operates a quality management system certified to ISO 9001:

- ‘Does the material I am planning to purchase have the potential for instability, if so, what has the reference material producer done to determine its stability?’
- ‘Does the material I am planning to purchase have the potential for heterogeneity, if so, what has the reference material producer done to determine its level of homogeneity?’
- ‘How does the producer ensure the quality and consistency of each material that they produce?’
- ‘How has the reference material producer performed the characterisation of the material to determine the assigned values and has this been done using an appropriate process?’
- How have the property values for which the CRM has been characterised been realised, have they been measured, calculated or a combination of both?
- ‘What do I need the assigned values to be traceable to, and how has the producer demonstrated the traceability of their assigned values?’
- ‘How will the material be stored and shipped, and will this ensure its ongoing suitability?’
- ‘What is my requirement for uncertainty, how has it been calculated, and is it acceptable?’

d) When engaging the services of any of the above:

- ‘Does the producer have the competency to organise all aspects of the production of reference materials which will meet my requirements?’ (Competency requirements to consider include; planning of a certification exercise; handling, processing & storage of the materials; choosing of any subcontractors or consultants used; assessment of homogeneity; assessment of stability; characterisation; assignment of property values and their uncertainties; packaging and labelling of the final RM; production of certificates including traceability statements and instructions for users in order to preserve the integrity of the RM; guidance and technical support)

5. References

5.1 References relating to criteria for the competence of reference material producers

a) ISO Guide 31: Reference materials - Contents of certificates, labels and accompanying documentation

b) ISO 17034: General requirements for the competence of reference material producers

c) ISO Guide 35: Reference materials - Guidance for characterization and assessment of homogeneity and stability

5.2 References relating to Guidance on the Use and Selection of reference materials

a) ISO Guide 30: Reference materials - Selected terms and definitions

b) ISO Guide 33: Reference Materials - Good practice in using reference materials

c) EA-4/14 INF: The Selection and use of reference materials

d) Eurachem Guide - The Selection and use of reference materials

5.3 General references

a) ISO/IEC 17025: General requirements for the competence of testing and calibration laboratories

b) ISO 15189: Medical laboratories – requirements for quality and competence

c) ILAC P10: ILAC Policy on the Traceability of Measurement Results

d) TPS 41: UKAS Policy on Metrological Traceability

e) VAM (Valid Analytical Measurement) / LGC - Meeting the Traceability Requirements of ISO/IEC 17025: An Analyst's Guide (Third Edition)

f) ISO/IEC Guide 99International vocabulary of metrology - Basic and general concepts and associated terms (VIM)

Annex 1 - Frequently Asked Questions

A1.1 Do all reference materials purchased by a laboratory need to come from a producer accredited to ISO 17034?

- No, but they are strongly encouraged to do so. The laboratory must have confidence in the competence of the producer from whom it obtains reference materials and must be able to demonstrate the basis of its confidence in this respect to UKAS. Using an ISO 17034 accredited supplier demonstrates this competence

A1.2 If an accredited reference material producer is used, does the accreditation of the reference material producer to ISO 17034 need to be provided by UKAS? No, if an accredited producer is used then ISO 17034 accreditation is covered under the scope of the European cooperation for Accreditation Multilateral Agreement (EA MLA) and International Laboratory Accreditation Cooperation Mutual Recognition Arrangement (ILAC MRA). Accreditation by signatory accreditation bodies is recognised as equivalent. Lists of signatories and scopes are available on the EA and ILAC websites.

A1.3 Do the reference materials that a laboratory uses for calibration and quality control need to come from separate sources/batches?

Ideally Yes. However, it is acknowledged that this is not always practically possible and therefore the follow pragmatic steps can be taken to enhance confidence in the quality control proceedings when independent sources are not feasible.

- Participation in external proficiency testing schemes.
- Splitting the reference material into two portions.
- Having independent analysts prepare the calibrators and controls or implement checking procedures.
- QC charting to identify any change over time.
- Use of, and comparison with isotopic labelled variants

Note: Some regulations and Government schemes operated within the United Kingdom require the use of separate source/batch calibration and quality control solutions.

Annex 2 - Terminology

A2.1 ***Reference material (RM)***, material, sufficiently homogeneous and stable with reference to one or more specified properties, which has been established to be fit for its intended use in a measurement process.

Note 1: RM is a generic term.

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

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

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

A2.2 ***Certified reference material (CRM)***, reference material, as above, accompanied by an RM certificate that provides the value of the specified property, its associated uncertainty, and a statement of metrological traceability.

Note 1: 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: Metrologically valid procedures for the production and certification of RMs are given in, among others, ISO 17034 and PD ISO Guide 35.

Note 3: PD ISO Guide 31 gives guidance on the contents of RM certificates.

Note 4: ISO/IEC Guide 99 has an analogous definition (5.14).

A2.3 ***Matrix reference material***, reference material that is characteristic of a real sample. Examples are soil, drinking water, metal alloys, blood.

Note 1: Matrix reference materials may be obtained directly from biological, environmental, or industrial sources.

Note 2: Matrix reference materials may also be prepared by spiking the component(s) of interest into an existing material.

Note 3: A chemical substance dissolved in a pure solvent is not a matrix material.

Note 4: Matrix materials are intended to be used in conjunction with the analysis of real samples of the same or a similar matrix.

A2.4 ***Primary measurement standard****,* measurement standard that is designed or widely acknowledged as having the highest metrological qualities and whose property value is accepted without reference to other standards of the same property or quantity, within a specified context.

Note 1: See also ISO/IEC Guide 99:2007.

A2.5 ***Secondary measurement standard****,* measurement standard whose property value is assigned by comparison with a primary measurement standard of the same property or value.

Note 1: See also ISO/IEC Guide 99:2007.

A2.6 ***Calibration****,* operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by measurement standards and corresponding indications with associated measurement uncertainties and, in a second step, uses this information to establish a relation for obtaining a measurement result from an indication *(ISO/IEC Guide 99:2007 International vocabulary of metrology - Basic and general concepts and associated terms (VIM)).*

Note 1: A calibration may be expressed by a statement, calibration function, calibration diagram, calibration curve, or calibration table. In some cases, it may consist of an additive or multiplicative correction of the indication with associated measurement uncertainty.

Note 2: Calibration should not be confused with adjustment of a measuring system, often mistakenly called "self-calibration", nor with verification of calibration.

Note 3: Often, the first step alone in the above definition is perceived as being calibration.

A2.7 ***Metrological Traceability***, property of a measurement result whereby the result can be related to a reference through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty *(ISO Guide 99:2007 International vocabulary of metrology - Basic and general concepts and associated terms (VIM)).*

Note 1: For this definition, a 'reference' can be a definition of a measurement unit through its practical realisation, or a measurement procedure including the measurement unit for a non-ordinal quantity, or a measurement standard.

Note 2: Metrological traceability requires an established calibration hierarchy.

Note 3: Specification of the reference must include the time at which this reference was used in establishing the calibration hierarchy, along with any other relevant metrological information about the reference, such as when the first calibration in the calibration hierarchy was performed.

Note 4: For measurements with more than one input quantity in the measurement model, each of the input quantity values should itself be metrologically traceable and the

calibration hierarchy involved may form a branched structure or a network. The effort involved in establishing metrological traceability for each input quantity value should be commensurate with its relative contribution to the measurement result.

Note 5: Metrological traceability of a measurement result does not ensure that the measurement uncertainty is adequate for a given purpose or that there is an absence of mistakes.

Note 6: A comparison between two measurement standards may be viewed as a calibration if the comparison is used to check and, if necessary, correct the quantity value and measurement uncertainty attributed to one of the measurement standards.

Note 7: ILAC considers the elements for confirming metrological traceability to be an unbroken metrological traceability chain to an international measurement standard or a national measurement standard, a documented measurement uncertainty, a documented measurement procedure, accredited technical competence, metrological traceability to the SI, and calibration intervals (see ILAC P10).

Note 8: The abbreviated term "traceability" is sometimes used to mean 'metrological traceability' as well as other concepts, such as 'sample traceability' or 'document traceability' or 'instrument traceability' or 'material traceability', where the history ("trace") of an item is meant. Therefore, the full term of "metrological traceability" is preferred if there is any risk of confusion.

A2.8 ***Homogeneity***, the degree to which a property or constituent is uniformly distributed throughout a quantity of material or between separate units of the same material.

A2.9 ***Stability***, characteristic of a reference material, when stored under specified conditions, to maintain a specified property value within specified limits for a specified period of time.

A2.10 ***Artefact****,* for the purposes of this document "artefact" shall be taken to mean, either a single item (e.g., calibration weight) or a material (Solid, Liquid or Gas).

A2.11 ***Calibrated Artefact:*** An item as detailed in A2.10 that through a measurement process has assigned values to the property of the artefact so that it can be used as a reference standard

A2.12 ***Property Value***, value corresponding to a quantity representing a physical, chemical, or biological property of an RM.

A2.13 ***Property Attribute****,* value or non-numerical *descriptor corresponding to a qualitative characteristic representing a physical, chemical, or biological property of an RM.*

A2.13 ***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.

A2.14 ***Indicative value***, value of a quantity or property, of a reference material, which is provided for information only.

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

A2.15 ***Quality control material***, reference material used for quality control of a measurement.

A2.17 ***Commutability***, a critical property that ensures the reference material behaviour, as a calibrator, and the test sample will be consistent between different measurement procedures or methods so that the result of one determination can reliably be used to calibrate another method

A2.18 ***Interlaboratory comparison***, ***interlaboratory study***, ***interlaboratory test***, ***collaborative study***, organisation, performance and evaluation of measurements or tests on the same or similar items by two or more laboratories in accordance with predetermined conditions.

A2.19 ***Reference method***, ***reference procedure***, measurement method that has been shown to have the appropriate trueness and precision for its intended use and has been officially defined as reference method by a competent body.

A2.20 ***Recognised Accreditation Body***, an accreditation body that is a signatory to the ILAC (International Laboratory Accreditation Cooperation) MRA (Mutual Recognition Arrangement) or IAF (International Accreditation Forum) MLA (Multi-Lateral Recognition Arrangement), or to the EA (European cooperation for Accreditation) MLA (Multilateral Agreement), for the relevant accreditation standard.

Note 1: Details of mutual recognition arrangement signatories can be found on the relevant websites - EA and ILAC

Annex 3 - Reference material databases

The following table provides an overview of some of the databases available that can be accessed to check for reference materials in different areas of testing.

Name	Link
JCTLM database	Home - JCTLM
COMAR	COMAR | Materials (bam.de)
European Virtual Institute for Speciation Analysis (EVISA)	EVISA: The premier source of information for speciation analysis
Brammer Standard Co	Brammer Standard Home Page
GeoReM	GeoReM - Database on geochemical, environmental and biological reference materials (gwdg.de)
WHO	NIBSC - WHO international standards
RM Producer databases / catalogues	