

HOW TO SELECT (CERTIFIED) REFERENCE MATERIALS

XXXX 2020

Reference Materials (RMs) and Certified Reference Materials (CRMs) are limited, sometimes expensive and not always appropriate for all purposes in a measurement process.

This application note aims to acquaint end-users with the selection of the proper (C)RMs, thus supporting their correct use.

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INTRODUCTION

Reference Materials (RMs) and/or Certified Reference Materials (CRMs) are not highly available due to the limited number of reference material producers. Furthermore, a given (C)RM can only be used for one single purpose in a specific measurement and its suitability should always be checked. This explains why the selection process of a (certified) reference material is difficult and sometimes requires making compromises.

However, there exist some guidelines to facilitate this choice and this application note tries to highlight them. These can be summarised in the following three steps:

1. Define the intended use of the (C)RM
2. Check all available information
3. Verify the availability of the selected (C)RM in your region.

1. DEFINE THE INTENDED USE OF THE (C)RM

RMs and/or CRMs can be used for several purposes in a measurement process. These include calibration and establishment of metrological traceability, method validation (trueness and precision), quality control, and assigning values to other materials.

The first step in the selection of a (C)RM is, therefore, to identify the intended use, especially because not all materials are appropriate for all the different applications. The key questions are the definition of the measurand, quantity value with its uncertainty and traceability and the kind of material (matrix or pure substance).

Definition of the measurand

While some measurands are structurally defined (lead is lead), others are defined by a specific method (e.g. enzymatic activity as measured by the IFCC reference procedure at 37 °C; impact toughness of steel as measured by ISO-148). How the measurand is defined is described in the document accompanying the (C)RM. The definition of the measurand in the (C)RM must match the definition of the method for which the C(RM) should be used.

Quantity value, uncertainty and traceability

Standards for quality systems of laboratories like ISO/IEC 17025 or ISO 15189 require measurement results to be metrologically traceable. For the establishment of metrological traceability, a CRM having a statement concerning the metrological traceability is required. The statement includes the definition of the identity (the measurand) and the quantity value. This links the CRM to a metrological standard, which could be either the SI (International System of Units) or any other conventional scales (arbitrary scales based to assigned values of CRMs stated in standard specifications, international recommendations or other reference documents).

Once verified that the CRM is suitable for the intended use, it is important to verify that the quantity value and its uncertainty are the desired ones. The quantity value must be within the working range of the method and its uncertainty appropriate for the purpose for which the CRM will be used. It is always important to keep in mind that the uncertainty of the CRM will be included in the final uncertainty of the result obtained by that method. Hence, if the CRM is used for applications such as calibration, assigning values to other materials or trueness assessment, the uncertainty should be as small as possible or ideally smaller than any other uncertainty contribution. For other applications, such as precision assessment or

quality control, it is enough to have a (C)RM with sufficient homogeneity.

Pure substance or matrix (C)RM

For the calibration of the measurement stage of a method or for assigning values to other materials (widespread practices that include methods of preparation of calibrants), normally, a pure substance CRM is used. Pure substances are characterised by their chemical purity and other physical properties. Sometimes, for some techniques such as XRF or ICP-AES, a matrix-CRM is required. This happens when the matrix has an impact during the measurement process of the analytes.

For other purposes such as method validation (trueness and precision assessment) and quality control, metrologically traceable certified values are needed. In avoiding breaking the traceability chain, in most of the operations, a matrix-CRM is the preferred option. Ideally, the scope of the method used includes the matrix of the CRM. If this is not the case, some tools exist to guide end-users in the identification of a correct matrix-CRM. One of these is the AOAC fat-protein-carbohydrate triangle that can be used for assessing the similarity of different food matrix CRMs (Wolf and Andrews 1995; Philips et al., 2013).

2. CHECK ALL AVAILABLE INFORMATION

The second step in the selection of a (C)RM is to check all available information. Information about CRM uncertainty, (C)RM stability, traceability statement, quality assurance, production process, measurements and data treatment should be included in the (C)RMs certificate, in the certification report or both.

All the information reported is essential and must be checked carefully before acquiring any (C)RM.

The final uncertainty of the CRM must have been calculated following the Guide to the expression of uncertainty in measurements – GUM (ISO/IEC Guide 98-3) as foreseen in ISO Guide 35. This document also provides specific guidance for homogeneity, stability and characterisation studies during the certification of (C)RMs.

Stability is an important parameter to consider if the (C)RM is to be used for quality control purposes, such as control charts, as in this case a material is used over a longer period of time.

The traceability statement must have been clearly reported and it should allow end-users to identify the definition of identity and quantity value of the particular CRM.

Quality assurance information should allow end-users to verify that a competent RM Producer produced the (C)RM. According to ISO/IEC 17025, accreditation of the RM Producer to ISO 17034, (the standard that sets the requirements for the competence of reference material producers), is regarded as evidence of competence. For non-accredited producers, additional proof, of at least adherence to ISO 17034, should be obtained to allow end-users to make their assessment on the manufacturer's quality system.

Finally, details of the production process, as well as of measurements and data treatment, should be transparent because they may influence the choice of the material.

3. VERIFY THE AVAILABILITY IN THE REGION

The last important step in the selection of a (C)RM is to verify the availability in the region. This should always be checked with the reference material producer and/or the local distributor. Some materials, in particular those produced from genetically modified organisms or livestock, could be restricted in certain countries and/or be blocked at customs in non-optimal storage conditions.

WHERE TO FIND (CERTIFIED) REFERENCE MATERIALS

RMs and/or CRMs can be found in:

- Reference material producer catalogues, e.g. <https://crm.jrc.ec.europa.eu>
- Chemical distributors catalogues
- Online databases, e.g. www.comar.bam.de

SUMMARY

The table below gives an overview about which RM properties are required for the different application of an RM:

	Method calibration	Method validation: trueness	Method validation: Precision	Routine quality control	Assigning values to other materials
Measurand definition	Same as for method used	Same as for method used	Not relevant ¹⁾	Not relevant ¹⁾	Same as for method used
Quantity value	Within method working range	Within method working range	Within method working range	Within method working range	Within method working range
Uncertainty	As small as possible	Ideally smaller than other uncertainty contributions	Homogeneity better than between-run variation	Homogeneity better than between-run variation	As small as possible
Traceability of assigned value	Same as for method used	Same as for method used	Not relevant ¹⁾	Not relevant ¹⁾	Same as for method used
Matrix	Pure substance Matrix RM	Matrix-RM	Matrix-RM	Matrix-RM	Pure substance Matrix RM
CRM required or non-certified RM sufficient?	CRM required	CRM required	Non-certified RM sufficient, CRM possible	Non-certified RM sufficient, CRM possible	CRM required
Certificate or Product Information Sheet available?	Essential	Essential	Beneficial	Beneficial	Essential
Other information available?	Very useful	Very useful	Very useful	Very useful	Very useful

¹⁾ The basis of the comparison in routine quality control and evaluation of precision is to compare the average value obtained by the laboratory. Therefore, the definition and traceability of potential values given by the producer of the RM are not relevant.

REFERENCES - FURTHER READINGS

ISO Guide 33:2015, Reference materials – Good practice in using reference materials, International Organization for Standardization, Geneva, Switzerland

ISO/IEC 17025:2017, General requirements for the competence of testing and calibration laboratories, International Organization for Standardization, Geneva, Switzerland

ISO 15189:2012, Medical laboratories – Requirements for quality and competence, International Organization for Standardization, Geneva, Switzerland

W. R. Wolf and K. W. Andrews, A system for defining reference materials applicable to all food matrices. *Fresen J Anal Chem* (1995) 352:73-76

M. M. Phillips et al., Standard reference materials for food analysis. *Anal Bioanal Chem* (2013) 405:4325-4335

ISO/IEC Guide 98-3, Uncertainty of measurements – Part 3: Guide to the expression of uncertainty in measurement (GUM:1995), International Organization for Standardization, Geneva, Switzerland

ISO Guide 35:2017, Reference materials – Guidance for characterization and assessment of homogeneity and stability, International Organization for Standardization, Geneva, Switzerland

ISO 17034:2016, General requirements for the competence of reference material producers, International Organization for Standardization, Geneva, Switzerland

J. S. Kane, The Use of Reference Materials: A Tutorial. *Geostand Geoanal Res* (2001) 25:7-22