General requirements for the competence of Reference Material Producer as per ISO 17034:2016

Technical & Production Requirements

TECHNICAL & PRODUCTION REQUIREMENTS

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7.1 General requirements

RMP shall address the requirements in this clause for the production of RMs, including CRMs.

✓A CRM has at least one certified value.

✓ Clause 7.9 applies only to certified values.

7.2 Production planning

7.2.1 The RMP shall identify and PLAN those processes that directly affect the quality of RM production, and the production plan shall be documented.

A mechanism (e.g. a management/ technical advisory group) can be established to make recommendations on part or all of the production processes, for example, assigning the property values of interest.

7.2.2 Technical input of subcontractors involved shall be specified and the required information documented and regularly reviewed.

7.2 Production planning

7.2.3 The RMP shall address, during the planning stage, the following:

a) material selection (including, where appropriate, sampling);

b) verification of the identity of the material;

c) maintaining suitable environments for all aspects of production (see 6.4);

d) material processing (see 7.5);

e) choice of measurement procedures (see 7.6,);

7.2 Production planning

f) validation of measurement procedures (see 7.6);

g) verification and calibration of measuring equipment (see 7.7);

h) specification of acceptance criteria for, and assessment of, homogeneity, including sampling (see 7.10);

i) specification of acceptance criteria for, and assessment and monitoring of, stability, including sampling (see 7.11);

j) designing and organizing appropriate characterization, including sampling (see 7.12);

7.2 Production planning

k) assessing commutability (where appropriate);

l) assigning property values (see 7.13);

m) establishing uncertainty budgets & estimating uncertainties of certified value(s) (see 7.13);

n) defining acceptance criteria for measurand levels and their uncertainties;

o) establishing metrological traceability of measurement result(s) & certified value(s) (see 7.9);

p) issuing RM documents (see 7.14);

7.2 Production planning

q) ensuring adequate storage facilities and conditions (see 7.4);

r) ensuring appropriate labelling and packaging of the RMs (see 7.14);

s) ensuring appropriate transport arrangements (see 7.15);

t) ensuring post-production stability monitoring, if applicable (see 7.11);

u) ensuring an adequate post-distribution service for RM users (see 7.15).

7.2 Production planning

7.2.4 Where multiple batches of RMs with equivalent properties are produced by using similar starting materials and by applying the same procedures, VERIFICATION shall ensure that information obtained from previous batches remains applicable for the new batch (see 7.2.3).

- ✓Multiple batches can be batches of the same material produced at the same time, or can be successive batches of material produced at substantially different times.
- ✓Further guidance for multiple batch productions is given in ISO Guide 35.
- ✓Where multiple batches are produced, some tests can be omitted or simplified for some batches

Production planning

It is critical that, before the start of the production of reference material, a detailed production plan is available. It is understood that pilot studies may sometimes need to be carried out but the need of any pilot study should be considered at the planning stage. The production plan should be fully documented. There are requirements for each step of the production process given in ISO 17034:2016 and the RMP is required to provide evidence that, at the planning stage, these requirements are given full consideration, and if necessary, recommendations from advisory groups have been sought.

Production planning

Advisory group shall have the expertise to carry out the functions as required in clause 7.2.3 of ISO 17034:2016. Technical experts may be used on an ad-hoc basis either in-house or external (eliminating conflict of interest). The terms of reference and membership criteria of the advisory group shall be documented. Records of the competence of advisory group shall be maintained. Also records of their participation in the planning process shall be maintained, if used.

Production planning

The production plan may need to be reviewed regularly during the production process. If it is necessary to make any change to the plan, the effects of the change on the conformity with the requirements of ISO 17034:2016 should be evaluated. Changes should be approved by the person authorized (in accordance with clause 6.1.6 of ISO 17034:2016), to perform production planning of the reference material. Changes should be fully documented, and should include the reasons and justifications for the changes. If the changes can affect the contract with the customer, the customer should be consulted. Customer's agreement with the changes should be obtained and records maintained as required by clause 4.1.3 of ISO 17034:2016.

Production planning

Production and purchasing of starting material largely depends on the type of CRM. Therefore, when planning to produce matrix CRM, starting material with suitable properties must be obtained in sufficient quantity. The starting material must be checked whether they are suitable for the production of the planned CRM.

7.3 Production control

The RMP shall VERIFY that the production plan has been implemented as specified, and deviations from the plan shall be documented and approved.

Evidence of verification of critical activities required

Production control

Although effective control of each stage of the production process is needed, there are also certain critical steps in each stage where the quality of the reference material can be significantly affected. An analysis of such critical control points can be carried out and a plan that is designed to ensure that these critical control points are effectively controlled and monitored is a useful means to ensure the quality of reference materials. If the activity for processing has been subcontracted, then RMP should establish the methodology of control over the subcontractor activity. Appropriate records for this purpose shall be maintained.

Records shall be maintained to provide evidence that there is effective control of each stage of reference material production, e.g. records of inspection, testing, etc.

7.4 Material handling and storage

7.4.1 The RMP shall make arrangements to ensure the integrity of its candidate RMs and RMs throughout the production process. Precautions shall be taken against adverse environmental influences and possible contamination of the candidate RM during its processing.

(e.g) packaging of a cement material requires conditions of low humidity, while the processing and characterization of a material in which the content of traces of lead is to be measured requires clean room conditions to prevent contamination from dust containing lead. Clean room conditions can also be required for other types of trace analysis. Proper choice of container material and adequate cleaning PROCEDURES are also important to avoid contamination.

7.4 Material handling and storage

7.4.2 The RMP shall identify, preserve and separate candidate RMs and RMs from chemicals and other samples, from the time of processing through to their distribution to users.

It can be useful to uniquely identify each unit of a (candidate) RM in order to facilitate subsequent sampling, trend analysis, distribution services or complaints investigation.

7.4 Material handling and storage

7.4.3 The RMP shall ensure adequate packaging of all RMs (e.g. where appropriate, use light-shielding, air-free, moisture-free or inert-gas packaging) and provide secure storage areas/stock rooms which prevent damage or deterioration of any item or material between characterization and distribution.

7.4.4 The condition of all RMs shall be assessed at appropriate intervals throughout the storage period, in order to detect possible deterioration.

7.4 Material handling and storage

7.4.5 The RMP shall control packaging and labelling processes to the extent necessary to ensure conformity with safety and transport requirements. PROCEDURES for transport to the customer shall be defined.

7.4.6 The RMP shall take measures to ensure that the integrity of each individual RM unit is maintained until the seal, if any, has been broken or up to the point when first used.

Material handling and storage

It should be emphasized that the requirements of this section apply to all stages of the production - from the receipt of the raw material to the finished reference material. If during some stages of production, the material has to go out of the direct control of the RMP, the RMP should provide necessary written instructions to the party responsible for handling the material. When storing the material, the storage environmental conditions should be specified.

When the same equipment is used for different materials, the facility should ensure that no cross-contamination or carry-over contamination is taking place. Work instructions for cleaning of equipment, change over process, etc. shall be documented.

Material handling and storage

All persons handling the materials (including those of the subcontractor's (if relevant)) shall be trained on the proper handling procedures. They should be aware of the precautions to be taken whilst handling the material, as required by clause 6.1.3 of ISO 17034:2016. It is the responsibility of the RMP to ensure that the packaging and labelling of the reference materials meet the safety and transport related regulatory requirements.

Reference material must be stored separately from the test materials and other materials in such a way that any adverse effects on their quality/integrity as well as misuse and loss are excluded. If particular storage conditions are specified (e.g. cooling) compliance shall be monitored and documented.

Material handling and storage

Where applicable, safety measures for occupational health and environmental protection are taken according to the relevant dangerous properties (toxic, flammable, explosive, radioactive etc).

Access to rooms and facilities where RM are stored as well as withdrawal of RM shall be regulated and documented.

7.5 Material processing

7.5.1 The RMP shall establish procedures to ensure that the material has undergone adequate processing for its intended use. PROCEDURES for material processing shall address at least the following:

a) qualitative analysis for VERIFICATION of material type and/or identity;

b) synthesis, purification (e.g. distillation, extraction), incubation, and transformation into the final form (e.g. machining, grinding, blending, sieving and riffling, extrusion, melting);

c) homogenization;

d) proper handling (e.g. protection from contamination and use of inert equipment) (see 7.4);

7.5 Material processing

e) measurements for control of material processing (e.g. particle size distribution, moisture content);

f) pre-treatment, cleaning or sterilization of processing equipment and sample containers;

g) stabilization of material (e.g. drying, irradiation, sterilization);

h) packaging (e.g. bottling, ampouling) of the material;

i) safety precautions.

7.5.2 Equipment used in material processing shall be operated in accordance with documented procedures.

Manufacturer's instructions are one form of documented procedure

Material processing

Preparation of the material (such as drying, mixing of ingredients, spiking with analytes, etc.) is a form of material processing. The main purpose of further preparation of the starting material is to generate a homogeneous batch of stable material with property levels as required. In addition, the prepared material should be similar to the typical test samples used with the test methods for whose quality assurance the RM is intended.

Each of the material processing steps as described above may require to be subdivided in to different steps. In that case work instructions additional documentations shall be created.

Material processing

The packaging process generally includes following steps:

- ✓ Specification of packaging units and containers
- ✓ Splitting the batch among the packaging units
- ✓ Filling into the designated containers
- ✓ Labelling

When splitting the batch, homogeneity among the packaging units must be ensured.

Material processing

The requirement of the containers depends on the type of reference material. General requirement are as follows:

- ✓ The container must be such that the reference material is protected against adverse effect of ambient condition (air moisture, oxygen, light etc.).
- ✓ The reference material must be inert against the inner surface of the containers.

Material processing

The requirement of the containers depends on the type of reference material. General requirement are as follows:

- ✓ For storing the packaged material, appropriate storage conditions must be specified and appropriate storage capacity has to be made available. Storage conditions are derived from available information about stability relevant factors and where applicable dangerous properties of reference material according to the relevant regulations of dangerous goods.
- ✓ When the same equipment is used for processing different materials, the equipment should be thoroughly cleaned between uses to prevent possible cross-contamination.

Material processing

All material processing procedures should be carried out by trained personnel and requirements of clause 6.1.3 of ISO 17034:2016 are applicable.

When candidate reference materials are sent to subcontractors for testing, they shall be uniquely labelled, suitably packed and stored in suitable conditions during transport. Instructions on the storage conditions should be given to the subcontractors.

7.6 Measurement procedures

The RMP shall ensure that the relevant requirements of ISO/IEC 17025 are met with respect to calibration and testing. These activities shall, where appropriate, be consistent with the required accuracy of the property values of the RM, and with any standard specifications relevant to the measurement concerned.

7.7 Measuring equipment

The RMP shall ensure that measuring equipment used in RM production is used in compliance with the relevant requirements of ISO/IEC 17025.

7.8 Data integrity and evaluation

7.8.1 The RMP shall ensure that all calculations and data transfers are subject to appropriate checks.

7.8.2 The RMP shall ensure that:

a) computer software developed in-house or off-the-shelf software further developed for specific use is validated and shown to be adequate for use;

b) procedures are established and implemented for protecting the integrity of data; such procedures shall include, but are not limited to, integrity of data entry and capture, data storage, data transmission and data processing;

7.8 Data integrity and evaluation

c) equipment and software are maintained to ensure proper functioning and are provided with the environmental and operating conditions necessary to maintain data integrity;

d) appropriate procedures are established and implemented for the maintenance of data security, including prevention of unauthorized access and changes to records, including computer records.

7.8.3 Statistical PROCEDURES used in monitoring, testing, calibration or value assignment of RMs shall be appropriate for their application.

Data integrity and evaluation

Homogeneity and stability assessments, characterization and assignment of property values and their uncertainties involve evaluation of data. The RMP shall use appropriate statistical techniques for data evaluation. The general and statistical principles for certification of a given reference material in ISO Guide 35, where appropriate, shall be followed.

7.9 Metrological traceability of certified values

7.9.1 When producing CRMs, the metrological traceability of the certified values shall be established in compliance with the relevant requirements of ISO/IEC 17025. The RMP shall provide EVIDENCE of the metrological traceability of the certified value to a stated reference.

- ✓A combination of results obtained by different measurement procedures and/or laboratories all being traceable to the same reference is also traceable to that reference.
- ✓The evidence can be based on evaluation of the measurement process or on confirmation of metrological traceability by comparison of results with independent traceable values.
- ✓Clear identification of the property of interest, traceability of the numerical value and the stated reference contribute to the traceability of results.

7.9 Metrological traceability of certified values

✓ISO/TR 16476 contains additional information on establishment and expression on metrological traceability of certified values

7.9 Metrological traceability of certified values

7.9.2 The stated reference shall be a definition of a measurement unit through its practical realization, or a measurement procedure including the measurement unit, or a measurement standard.

7.9.3 Where it is technically possible, the RMP shall DEMONSTRATE that the stated reference is traceable to the International System of Units (SI).

7.9.4 Where metrological traceability to the SI units is not technically possible, the RMP shall DEMONSTRATE metrological traceability to an appropriate reference (see traceability requirements in ISO/IEC 17025).

7.9 Metrological traceability of certified values

7.9.5 For studies in which the values need to be traceable to a higher order reference system (e.g. characterization studies with measurements under reproducibility conditions), it shall be ENSURED that the measurements are calibrated with standards with metrologically traceable values.

7.9.6 Secondary parameters that have a significant influence on the certified value or its uncertainty shall have EVIDENCE of metrological traceability.

Examples of secondary parameters are temperature and humidity.

Metrological traceability of certified values

The ILAC P 10 policy in regard to traceability provided by RMPs is:

- ✓ The values assigned to CRMs produced by NMIs and included in the BIPM KCDB or produced by an accredited RMP under its accredited scope of accreditation to ISO 17034 are considered to have established valid traceability (see ILAC General Assembly resolution ILAC 8.12).
- ✓ The values assigned to CRMs covered by entries in the JCTLM (Joint Committee for Traceability in Laboratory Medicine) database are considered to have established valid traceability.
- ✓ Majority of RMs and CRMs are produced by "other RMPs". These can be considered as critical consumables and the laboratory shall demonstrate that each RM or CRM is suitable for its intended use as required by ISO/IEC 17025/ ISO 15189.

Metrological traceability of certified values

Metrological traceability is the 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.

Metrological traceability requires an established calibration hierarchy. For measurements with more than one input quantity in the measurement model, each of the input quantity values should itself be metrological 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.

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.

Metrological traceability of certified values

ILAC P-10 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

The suitability of the metrological traceability utilized by the RMP is important. In cases where the metrological traceability cannot be achieved through an unbroken chain of calibrations, clause 7.9 of ISO 17034:2016 provides other alternative means. If a CRM is used for establishing metrological traceability, the CRM used shall have comparatively small uncertainty and higher in the metrological traceability hierarchy. The uncertainties in the certified values of the CRM used shall be suitable for establishing metrological traceability appropriate to the RMs being produced.

Metrological traceability of certified values

RMP should consider the competence of the producer of any certified reference material it uses to provide the metrological traceability of the assigned value of its CRM. A competent RMP or testing/calibration organization which may be a National Metrology Institute which is a signatory to the CIPM MRA, participates regularly in BIPM (Bureau of Weights and Measures) or Regional Key Comparisons, and has the relevant CMCs been included in Appendix C of the BIPM Key Comparison Database (KCDB).

7.10 Assessment of homogeneity

7.10.1 The RMP shall CARRY OUT AN ASSESSMENT OF THE HOMOGENEITY of any candidate RM in its final packaged form to ensure its fitness for purpose.

- ✓Assessment of homogeneity can include the use of prior evidence (including prior experimental evidence), the conduct of an experimental homogeneity study on the candidate RM or both. In most cases, an experimental study is necessary. Guidance on experimental homogeneity study is provided in ISO Guide 35.
- ✓In most cases, experimental homogeneity tests require measurements of a representative number of randomly chosen units. The units can be chosen for example by random selection, stratified random selection or systematic selection from a random start point.

7.10 Assessment of homogeneity

7.10.2 When the material is produced in multiple batches, the equivalence of the batches shall be DEMONSTRATED or the homogeneity of each batch shall be evaluated separately.

7.10.3 Validated measurement procedures shall be selected so that the precision and selectivity are fit for the purpose required.

7.10 Assessment of homogeneity

7.10.4 Where homogeneity needs to be determined experimentally, the RMP shall determine the homogeneity for every property of interest unless it can be shown, using scientific evidence or previous experience, that particular groups of properties are sufficiently closely associated that measurement of one property in such a group furnishes evidence of homogeneity for other properties in the same group.

Guidance for homogeneity testing is given in ISO Guide 35.

7.10.5 For certified values, homogeneity shall be quantified as an uncertainty contribution to the certified value or shall be shown to be a negligible contribution to the uncertainty of the certified value.

Assessment of Homogeneity

For a CRM it must be ensured that the certified values are valid for all packaging units.

In addition, the certified values must be valid for all samples from a packaging unit.

Under normal circumstances, the degree of homogeneity assessment of a RM with respect to the property of interest should be performed.

It is not acceptable to assume the homogeneity of a property value based on the assessment of another value unless correlation is demonstrated with analytes that are tested for homogeneity.

If homogeneity testing is done only on a subset of the assigned values, the requirement given in clause 7.10.4 of ISO 17034:2016 applies.

Assessment of Homogeneity

When data from assessment of homogeneity are used for assigning the property values, the requirements for metrological traceability (Clause 7.9 of ISO 17034:2016) and characterizations (Clause 7.12 of ISO 17034:2016) apply to the test procedures used.

Note: Assessment of Homogeneity need to be done by RMP; however other related activities like testing, etc. as per initial planning may be sub-contracted.

7.11 Assessment and monitoring of stability

7.11.1 The RMP shall: (Please refer ISO Guide 35)

a) assess, by experimentation if necessary, the stability of all relevant properties of an RM under proposed storage conditions and choose pre-treatment, packaging and storage conditions in accordance with the results of the assessment;

b) assess, by experimentation if necessary, the stability of all relevant properties of an RM under proposed conditions of transport, and choose transport conditions to maintain stability during transport;

c) establish any necessary advice on storage and use of the material to maintain stability at the user's premises;

7.11 Assessment and monitoring of stability

d) select a scheme for monitoring the stability of materials held in long term storage that permits prompt detection of change, taking into account the possible rate of change;

e) where the stability of a certified value cannot be ensured, make due allowance in the stated uncertainty for possible change in the value prior to use or, where the change with time can be predicted, provide a means of correcting the certified value and its uncertainty for the expected change over time;

f) where repeated sampling from an RM unit or repeated use of an entire RM unit is permitted by the instructions for use, assess the possible effects on the stability of the material and take appropriate action.

7.11 Assessment and monitoring of stability

7.11.2 The RMP shall conduct an experimental assessment of stability before release unless the RMP has EVIDENCE of stability or prior experience of stability from closely similar materials held for an extended period under the same planned storage conditions.

"Closely similar" materials are materials characterized for the same properties, which share the same matrix composition, processing conditions, similar or less effective packaging, etc.

7.11 Assessment and monitoring of stability

7.11.3 Where an RM is produced in multiple batches that are not individually tested for stability, the RMP shall VERIFY the stability of a sufficient number of different batches experimentally to provide confidence in the stability of all batches.

Verification can be a simple test to confirm that different batches behave similarly or, for successive batches, do not change over their lifetime. Experimental assessment of stability typically involves an extended study aimed at determining rates of change.

Assessment and monitoring of stability

For a CRM it must be ensured that the certified values are valid until the end of utilization period (expiry date) specified in the certificate. This validity applies to unopened packaging units under proper storage. Under normal circumstances, stability assessment for each and every certified property value should be performed. It is not acceptable to assume the stability of a property value based on the assessment of another value unless correlation is demonstrated with analytes that are tested for stability.

Prediction of stability using a model is generally not acceptable unless such model is well established and widely accepted in the discipline concerned.

Assessment and monitoring of stability

In cases where data from assessment of stability are used for assigning the property values, the requirements for metrological traceability (Clause 7.9 of ISO 17034:2016) and characterization (Clause 7.12 of ISO 17034:2016) apply to the test procedures used.

Stability assessment should include assessment of the effects of shipment. This includes studies with actual shipping under maximum stress conditions, e.g., distance, and temperature.

Assessment and monitoring of stability

Stability assessment should include assessment of the effects of use. This includes studies with multiple subsamples and any requirements for changed temperature for storage before sub sampling. In stability testing the temporal change (changes with time) of certified values is investigated over an appropriate period. Any associated uncertainty could be expressed within the long term stability assessment or as considerations described in the certificate.

Note: Assessment of Stability need to be done by RMP; however other related activities like testing, etc. as per initial planning may be sub-contracted.

7.12 Characterization

7.12.1 Where the RMP assigns property values, characterization of the RM is required.

7.12.2 The RMP shall clearly define whether a quantitative or a qualitative property will be characterized and, if quantitative, whether the measurand is operationally defined or is defined independently of any specific procedure.

7.12.3 The RMP shall select a characterization STRATEGY appropriate for the intended use of the RM

7.12 Characterization

Such characterization can include, but is not limited to, the following approaches: (Please refer ISO Guide 35)

a) using a single reference measurement procedure in a single laboratory;

b) characterization of a non-operationally defined measurand using two or more methods of demonstrable accuracy in one or more competent laboratories;

c) characterization of an operationally-defined measurand using a network of competent laboratories;

d) value transfer from an RM to a closely matched candidate RM performed using a single measurement procedure performed by one laboratory;

e) characterization based on mass or volume of ingredients used in the preparation of the RM.

7.12 Characterization

7.12.4 The RMP shall specify the characterization study so that the properties of interest are each characterized with appropriate traceability and sufficient reliability whether or not traceability and measurement uncertainty are reported on the RM documentation. To this end, the RMP shall:

a) DOCUMENT A MEASUREMENT PLAN that clearly describes the tasks to be performed and communicate this to all personnel responsible for measurements used in characterization;

b) for certified values, DEMONSTRATE the competence of each involved laboratory by using data from each laboratory that was not obtained on the material to be characterized.

7.12 Characterization

7.12.5 When EVALUATING THE CHARACTERIZATION DATA, the RMP shall perform a technical evaluation of the data and documents involved in characterization to confirm adherence to the measurement plan as defined in 7.12.4, bullet a), and, in the case of deviations from the plan, assess whether the deviation necessitates exclusion of the data from characterization.

7.13 Assignment of property values and their uncertainties

7.13.1 The RMP shall use documented procedures for the assignment of property values.

7.13.2 These procedures shall include, as appropriate:

a) details of experimental designs & statistical techniques used;

b) policies on treatment and investigation of anomalous results, including outliers;

c) whether weighting techniques are used for contributions to assigned property values derived from different procedures or laboratories with different measurement uncertainties;

d) the approach used to assign uncertainties to the property values;

e) any other significant factors that may affect the assignment of property values.

7.13 Assignment of property values and their uncertainties

7.13.3 The RMP shall take due account of technical information on test methods and equipment, including reported uncertainty information, and of any evidence of laboratory performance when assigning the property values of interest.

ISO Guide 35 provides guidance on valid approaches for value assignment.

7.13.4 Outliers shall not be excluded solely on statistical evidence until they have been investigated and, where possible, the reasons for the discrepancies identified. Robust statistical methods may be applied where appropriate.

✓ An apparent outlier can be the only technically valid result in the data set.

✓ISO Guide 35 provides guidance on the use of robust statistical methods.

7.13 Assignment of property values and their uncertainties

7.13.5 For certified values, the RMP shall identify the uncertainty contributions to be included in the assigned uncertainty.

7.13.6 For certified values, the RMP shall consider, at a minimum, uncertainty contributions of each of the following:

a) characterization, including any difference between multiple procedures used for characterization;

b) between-unit and within-unit in-homogeneity;

c) changes of property values during storage;

d) changes of property values during transport.

Other uncertainty contributions can be important such as changes of property values in use or on repeated sampling.

Assignment of property values and their uncertainties

As CRMs are often used by laboratories for establishing their metrological traceability, it is important that the uncertainties of the assigned values are estimated using methods which are generally more rigorous than for other purposes. The uncertainties include not just the measurement uncertainty of the characterization procedure but also other contributions.

Uncertainty in this Section covers both "measurement uncertainty" of a quantity value and "uncertainty" associated with a nominal property (i.e. property of a phenomenon, body, or substance, where the property has no magnitude e.g. colour chart, DNA sequence, etc).

The estimate of uncertainty should include at least the effects of characterization, homogeneity, transport and long term storage. In case, the effects of any of the above are known to be zero then the same can be mentioned / recorded.

7.14 RM documents and labels

7.14.1 The RMP shall issue and make available an RM certificate for CRMs & product information sheet for other RMs.

7.14.2 The contents of RM certificates and product information sheets shall include the following:

a) title of the document;

b) unique identifier of the RM;

c) the name of the RM;

d) name and contact details of the RMP;

e) intended use;

f) minimum sample size (whenever applicable);

7.14 RM documents and labels

g) period of validity;

h) storage information;

i) instructions for handling and use that are sufficient to ensure the integrity of the material;

j) page number and the total number of pages;

k) document version;

l) information on commutability of the material (where appropriate).

7.14 RM documents and labels

7.14.3 In addition to the minimum requirements given in 7.14.2, RM certificates shall contain the following additional information: (Further information is given in ISO Guide 31)

a) description of the CRM;

b) property of interest, property value and associated uncertainty;

c) measurement procedure for operationally defined measurands;

d) metrological traceability of the certified values;

e) name and function of RMP's approving officer.

Sector-specific requirements for RM certificates and product information sheets can exist and can be considered (e.g. ISO 15194 for *in vitro* diagnostic medical devices).

7.14 RM documents and labels

7.14.4 The RM label shall be securely attached to the product container of an individual RM unit, and shall be designed to remain legible and intact under the defined storage and handling conditions within the lifetime of the RM, i.e. the period during which the RM is available from the RMP extended by the period of validity of its certificate. The label shall identify the material, the RMP, its batch, and any other information necessary to enable the material to be uniquely distinguished and referenced (such as the individual sample number), where appropriate, to its product information sheet or RM certificate.

7.14.5 Where the physical size of the RM unit limits the amount of information that can be contained on the label, the information shall be included elsewhere (e.g. in an RM document). A unique identifier shall be given

RM documents and labels

Instructions for the handling and use of the RM shall be stated. Examples of instructions for handling and use of an RM are:

- ✓ **appropriate instructions to ensure homogenization of the container contents before use;**
- ✓ **prescribed instructions for the opening of the container;**
- ✓ **the exact conditions for the drying of the material and/or the dry mass correction;**
- ✓ **where necessary, instructions for further particle size reduction;**
- ✓ **appropriate instructions for the reconstitution of a solid RM to prepare a solution;**
- ✓ **appropriate mathematical expression for the calculation of the value of the property at the time of use, e.g. in the case of materials which are inherently unstable, such as radioactive substances.**

RM documents and labels

The RM producer may include indicative values. Examples are:

- ✓ **the approximate concentration of an analyte in a complex matrix that does not fulfil the criteria for a certified property value;**
- ✓ **individual results from each laboratory or analyst, where results from several laboratories or analysts were used to assign the property value(s).**
- ✓ **Documentation for non-certified reference materials shall include information on homogeneity and stability and on the period of validity of the stated information. It shall also contain information for the user on the proper application and storage conditions of the reference material.**

RM documents and labels

Internal reports of the RMP should not be confused with a Reference Material certificate or product information sheet which is supplied with a reference material to the customer.

An RMP is allowed to contract out some of its tasks to competent subcontractors. It may not be necessary to indicate which parts of the production process have been subcontracted in the certificate of CRMs or the documentation for RMs.

7.15 Distribution service

7.15.1 The distribution PROCESS shall be specified including precautions needed to avoid deterioration of the RM (see 7.11.1). The RMP shall determine the conditions of shipment and ensure that appropriate documentation is provided to allow customs clearance.

- ✓The conditions of shipment can include for example shipping temperature, packaging, duration of transport and other precautions necessary for integrity of the material.
- ✓For some RMs, additional documentation related to, for example, origin and, conformity of the material to safety requirements, might be required for customs clearance.

7.15 Distribution service

7.15.2 The RMP shall maintain up-to-date RECORDS of all RM sales and distribution.

7.15.3 The RMP shall offer to users reasonable guidance and technical support related to the RMs it produces.

7.15.4 The RMP shall employ best efforts to notify users of any change to the property value or uncertainty for any RM within the validity period of the RM certificate or product information sheet.

7.15 Distribution service

7.15.5 Where RMs are subject to resale through a distributor with whom the RMP has a contractual relationship, the RMP shall pass on to the authorized distributor all necessary information to ensure that an effective post-distribution service is maintained and make arrangements with the distributor to ensure that its activities are executed in accordance with the relevant clauses of this International Standard.

Where RMs are subject to resale by other organizations, the RMP has no control over these organizations' activities after the RMs have been purchased. The requirements regarding distribution service to such resellers are limited to the first reseller.

7.16 Control of quality & technical records

7.16.1 The RMP shall establish and maintain PROCEDURES for identification, collection, indexing, access, storage, maintenance and disposal of quality and technical records.

Quality records are records providing objective evidence of the extent of the fulfilment of the requirements for quality or the effectiveness of the operation of the management system. They include reports from internal audits and management reviews, and corrective action and improvement records.

Technical records are accumulations of data and information which result from carrying out RM production, measurement, testing and calibration procedures and which indicate whether specified quality or process parameters are achieved. They include forms, contracts, work sheets, work books, check sheets, control charts/graphs, calibration reports/certificates, reports, certificates and other statements to users.

7.16 Control of quality & technical records

7.16.2 The RMP shall ENSURE THAT IT HAS RECORDED such information that might be needed in a future dispute situation.

7.16.3 All records shall be legible and shall be stored and retained in such a way that they are readily retrievable and in facilities that provide a suitable environment to prevent damage, deterioration or loss. Retention time of records shall be established in accordance with customer or other relevant requirements, and shall be documented.

Records can be in the form of any type of media, such as hard copy or electronic media.

7.16 Control of quality & technical records

7.16.4 When mistakes occur in records, each mistake shall be crossed out, not erased, made illegible or deleted, and the correct information entered alongside. All such alterations to records shall be signed or initialled, and dated by the person making the correction. In the case of records stored electronically, equivalent measures shall be taken to avoid the loss or change of original information.

7.16.5 All records shall be held securely and, where appropriate, in confidence.

7.16.6 The RMP shall have PROCEDURES to protect electronically held data at all times and to prevent unauthorized access to, or amendment of, such data.

7.16 Control of quality & technical records

7.16.7 The RMP shall arrange for all individual measurement observations, appropriate calculations and derived data (e.g. statistical treatments and uncertainty budgets), calibration records and preparation reports to be retained for a defined period beyond which it is no longer probable that they will be referred to, taking into account the period for which the RM remains valid.

7.16.8 The results of each calibration or measurement (or series of either) carried out by the RMP or by a subcontractor shall be reported in accordance with ISO/IEC 17025.

7.17 Management of non-conforming work

7.17.1 The RMP shall have PROCEDURES that shall be implemented when it establishes that any aspect of its production activities does not conform to its own specified production procedures or the agreed requirements of the customer.

7.17.2 The procedures shall ensure that:

a) responsibilities and authorities for the management of non-conforming work are designated;

b) the actions to be taken when any non-conforming work and/or RMs are identified including root-cause analysis and a system that ensures that they are effectively implemented;

c) an evaluation of the significance of the non-conforming work is made and identification and implementation of correction and corrective action;

7.17 Management of non-conforming work

d) where necessary, work is halted and, if appropriate, issue of the affected RM and its certificates and other appropriate documentation is withheld;

e) remedial actions such as customer notifications are taken within a defined time-frame;

f) where necessary, best efforts are employed to notify the users of the possible effects, within an appropriate period and, where necessary, non-conforming RMs and/or their certificates and other appropriate documentation already distributed, are recalled;

g) the responsibility for authorization of the resumption of work is defined;

h) where necessary, an internal audit is conducted to verify the closure and effectiveness of the corrective actions taken.

7.17 Management of non-conforming work

7.17.3 The decision on recall of RMs shall be taken in a timely manner to limit the use of non-conforming RMs.

The identification of non-conforming RMs or problems with the management system or with production activities can occur at various places within the management system, such as

- ✓complaints,
- ✓quality control,
- ✓checking of consumable materials,
- ✓staff observations or supervision,
- ✓certificate & other appropriate documentation checking,
- ✓management reviews and
- ✓internal or external audits.

7.18 Complaints

7.18.1 The RMP shall have a documented PROCESS to receive, evaluate and make decisions on complaints.

7.18.2 A description of the handling process for complaints shall be available to any interested party on request.

7.18.3 Upon receipt of a complaint, the RMP shall confirm whether the complaint relates to conformity assessment activities that it is responsible for and, if so, shall deal with it.

7.18.4 The RMP shall be responsible for all decisions at all levels of the handling process for complaints.

7.18 Complaints

7.18.5 Investigation and decision on complaints shall not result in any discriminatory actions.

7.18.6 The process for handling complaints shall include at least the following elements and methods:

a) a description of the process for receiving, validating, investigating the complaint, and deciding what actions are to be taken in response to it;

b) tracking and recording complaints, including actions undertaken to resolve them;

c) ensuring that any appropriate action is taken.

7.18 Complaints

7.18.7 The RMP receiving the complaint shall be responsible for gathering and verifying all necessary information to validate the complaint.

7.18.8 Whenever possible, the RMP shall acknowledge receipt of the complaint, and provide the complainant with progress reports and the outcome.

7.18.9 The decision to be communicated to the complainant shall be made by, or reviewed and approved by, individual(s) not involved in the original RM activities in question.

7.18.10 Whenever possible, the RMP shall give formal notice of the end of the complaint handling process to the complainant.

Road map for RMP accreditation – part 1

1) Identify the matirx (product), measurand (test/ property) and level of measurand of RM to be produced
2) Define acceptance level of measurands and MU for the RM
3) Prepare plan as per cl. 7.2.3 of ISO 17034 – (a to u)
4) Pilot study / Feasibility study :
   - Identify specs of raw material to be procured
   - Identify source of raw material supply
   - Identify subcontractors (processing/ production etc.,)
   - Determine processing conditions & equipment required
   - Determine testing procedure for Homo, Stab and characterization
   - Identify labs to be used for ILC

Road map for RMP accreditation – part 2

5) Conduct preliminary ILC
6) Conduct preliminary homogeneity study
7) Calculate U_{bb} and U_{wb}
8) Produce RM on large scale
9) Conduct homogeneity study
10) Commence stability study – immediately, after 1 month, 3 months, 6 months, 9 months and 12 months
11) Characterization by ILC/ Single Lab approach
12) Assign property values and MU