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## Introduction

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For international standards, comments will be reviewed by the relevant UK national committee before sending the consensus UK vote and comments to the international committee, which will then decide appropriate action. If the international standard is approved, it is usual for the text to be published as a British Standard.

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| 1  | 2                                          | (3)                          | 4               | 5                                                                                                                                  | (6)                                                                      | 7                                                  |
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| MB | Clause No./ Subclause No./Annex (e.g. 3.1) | Paragraph/ Figure/Table/Note | Type of comment | Comment (justification for change) by the MB                                                                                       | Proposed change by the MB                                                | Secretariat observations on each comment submitted |
|    | 3.1                                        | Definition 1                 | ed              | Definition is ambiguous and needs clarifying.                                                                                      | Amend to read '...so that the mains connector to which no connection...' |                                                    |
|    | 6.4                                        | Paragraph 2                  | te              | The use of the UV photometer as an alternative cannot be supported as serious problems have been encountered in its use in the UK. | Delete reference to UV photometer.                                       |                                                    |



# DRAFT International Standard

## ISO/DIS 33408

### Guidance for the production of pure inorganic substance certified reference materials

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ISO/TC 334

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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](http://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](http://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 of 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 [www.iso.org/iso/foreword.html](http://www.iso.org/iso/foreword.html).

This document was prepared by Technical Committee ISO/TC 334, *Reference materials*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at [www.iso.org/members.html](http://www.iso.org/members.html).

## Introduction

Reference materials (RMs) play an important role in measurement processes and support sound, widely recognized measurement systems. ISO 17034 specifies general requirements to be met by reference material producers (RMPs), including for the production of certified reference materials (CRMs). CRMs play a key role in ensuring that measurements are comparable across time and space and are used by laboratories to establish metrological traceability of their measurement results to appropriate references.

This document outlines recommendations conforming to general requirements of ISO 17034 for production of pure metals or their corresponding crystalline salt CRMs intended for direct use for calibration of appropriate measurement instrumentation or subsequent preparation of solution calibration CRMs. Guidance is provided on key aspects of the production of such CRMs, including assessment of their homogeneity and stability as well as recommended approaches for characterization and assignment of certified purity values.

# Guidance for the production of pure inorganic substance certified reference materials

## 1 Scope

This document provides specific technical guidance for the production of pure metals or their corresponding crystalline salt certified reference materials (CRMs) in accordance with the general requirements of ISO 17034.

In this document, reference to a CRM is limited to solid pure metal and crystalline salt certified reference materials, including candidate materials, unless otherwise noted.

## 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 17034:2016, *General requirements for the competence of reference material producers*

## 3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO/IEC 17000, ISO Guide 30, ISO/IEC Guide 99, ISO 9000, ISO 80000-9 and the following apply.

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

- ISO Online browsing platform: available at <https://www.iso.org/obp>
- IEC Electropedia: available at <https://www.electropedia.org/>

### 3.1

#### **primary component: PC**

principal chemical species of interest in the certified reference material

Note 1 to entry: A perfectly pure material remains an ideal concept because chemical species other than the PC will always be present in a material, even in very small amounts.

Note 2 to entry: the chemical species of interest is either an element or a compound of an element.

Note 3 to entry: for certain elements, unambiguous definition of the chemical species requires the specification of isotopic composition or molar mass.

### 3.2

#### **impurity component: IC**

Any chemical component of the CRM that is not the PC.

### 3.3

#### **purity**

quantity ratio of the primary component in the certified reference material

Note 1 to entry: Purity of metal and metal salt CRMs is usually expressed as the mass fraction of the PC.

Note 2 to entry: Purity of a salt is the sum of the fractions of the cation and the anion. For example,  $w_{\text{NaCl}} = w_{\text{Na}} + w_{\text{Cl}}$ , where  $w_x$  is the mass fraction of component x.

## 4 Technical and production requirements

### 4.1 General

The production of a CRM requires diligent planning, as generally described in ISO 17034:2016, Clause 7 and in ISO 33405.<sup>[1]</sup> Central to this effort is clear specification of the intended uses of the CRM and characterization appropriate for these purposes. The following subclauses provide an overview of considerations relevant to the production of high-purity inorganic CRMs.

### 4.2 Production planning

The production of a CRM requires the following:

- a) specification of the CRM and its measurand;
- b) candidate material sourcing and assessment of suitability, including verification of PC identity and demonstration of adequate purity;
- c) product packaging and specification of conditions for storage and safe handling;
- d) selection of approaches to purity assessment of the CRM;
- e) development and validation of procedures to achieve target measurement uncertainty;
- f) assessment of homogeneity;
- g) assessment and monitoring of stability;
- h) characterization of the CRM;
- i) consideration of metrological traceability of the certified property value;
- j) Preparation of RM documents

### 4.3 Specification of the CRM and its measurand

#### 4.3.1 General

The intended use and relevant properties of the CRM should be clearly specified at the outset of the production process. This can include, but is not limited to, measurement procedures or type of measuring systems for which it is intended to be used, properties to be characterized, target purity, appropriate metrological reference of the certified value and target measurement uncertainty. Special attention is needed for these topics, as described in the following subclauses.

#### 4.3.2 Classes of inorganic purity reference materials

For industrial applications of high-purity materials, the key quality parameter is the overall purity, which is often denoted as “N”. N refers to the number of 9 s in the purity statement of a metal. For example, 4N nickel corresponds to a purity of 99,99 % (four nines). For reference materials, especially CRMs intended for calibration, the most relevant indicator is the overall uncertainty. As metal purity CRMs represent direct realizations of an SI unit and appear within the chain of subsequent calibrations (or sometimes material preparations), low uncertainties are of paramount importance.

Inorganic reference materials could be classed into the following categories<sup>[27]</sup>:

Class A: target expanded uncertainties below 0,001 %.

Purity determination of metallic element CRMs using the indirect assessment approach (i.e. mass balance), and associated expanded measurement uncertainties, is most adequate. A commercial purity statement above 5N is best for material sourcing.

Class B: target expanded uncertainties between 0,001 % and 0,01 %.

Purity determination of metallic element CRMs using the indirect assessment approach (i.e. mass balance), and associated expanded measurement uncertainties, is most adequate. A commercial purity statement between 4N and 5N is best for material sourcing.

Class C: target expanded uncertainties between 0,01 % and 0,1 %.

Purity determination of metallic elements to be used for preparation of calibration solutions using a direct metal assay approach yielding expanded measurement uncertainties typically above 0,05 % is most adequate. A commercial purity statement above 3N is adequate for material sourcing.

Class D: target uncertainties equal or greater than 0,1 %

Adequate for in-house standard preparation, verified by atomic spectroscopy methods against a solution CRM.

Inorganic purity CRMs intended for calibration purposes should typically be of class C or above.

#### 4.3.3 Specification of purpose

It is important to consider the intended use of the CRM because it can affect various aspects of the CRM production process, including the verification of the suitability of the sourced material. Pure substances constitute the source of primary measurement standards in most traceability chains in chemistry. The demand for such a CRM is usually recognized through engagement with the intended user community. The measurement needs that are commonly served include improved accuracy of relevant measurement procedures, establishment of metrological traceability and regulatory compliance for chemical testing laboratories.

Such CRMs are typically used for the calibration of measuring instruments and measurement systems. Impurities in a CRM used for this purpose may create interferences in a measurement method. While the presence of such interferences (impurities) would not invalidate the certified purity value of the CRM, it may render the CRM suboptimal for use with some measurement methods. When the PC of the CRM is intended to be used as a spike for the preparation of a multiple-component calibration solution, any co-introduced impurity species may lead to biases derived from the gravimetric preparation process of the multi-component calibration solution. Metals in each of these materials, present as either a PC or impurity species, should be comprehensively evaluated during purity assessments. The decision as to which impurities are significant depends on the intended use of the CRM and the producer should include them as part of the specification for the material.

#### 4.3.4 Specification of the measurand

A clear and unambiguous specification of the measurand is key to the production planning. The certified purity value of a CRM is usually expressed as the mass fraction and sometimes as amount fraction or amount content of PC in the material. The definition of the PC can require specification of its molar mass or isotopic composition.

#### 4.3.5 Metrological reference

ISO 17034 requires the metrological traceability of certified values to be established for CRMs in accordance with ISO/IEC 17025[2].

The metrological reference system is principally dependent upon the purpose of the CRM and the measurement community it is intended to serve. The SI, a coherent system widely used in commerce and science, is the most appropriate system of units for most chemical measurements. The certified purity value of a CRM is ideally obtained by, but not limited to, the practical realization of SI measurement units.

#### 4.3.6 Fitness for purpose

Fitness for purpose of a measurement is the extent to which the measurement result meets the stated requirement for which the measurements are being made. Formal definitions can be found in various

sources such as Reference [9]. For the CRM to be fit-for-purpose, the uncertainty in the certified value should be small enough to be useful in the measurement process. This is especially crucial for CRMs intended for calibration.

NOTE 1 A measured property value without associated uncertainty does not conform to the definition of the certified value of a CRM specified in ISO 17034.

#### 4.3.7 Safety considerations

In regard to workplace health and safety considerations, the reference material producer (RMP) should conduct a risk assessment, which can be replaced by the RMP's pre-established standard safety procedures compliant with local regulations, to establish that appropriate facilities and safeguards are in place to process the candidate material.

#### 4.3.8 Resources and approaches to purity analysis

Considerations for resource requirements are described in ISO 17034. CRM characterization should be fit-for-purpose and achievable with available laboratory resources, including labour, packaging materials and candidate materials. Allocation of these resources and anticipated cost recovery through CRM distribution are key considerations that govern the practicality of CRM production. Costs largely depend upon the rigour of analytical methods selected for characterization. For CRMs, purity determination can be accomplished through either one or a combination of two basic approaches, "direct" and "indirect", as described in 4.6.

The target measurement uncertainty should be considered prior to characterization<sup>[10],[11]</sup>. If available, the use of two or more independent methods underpinned by different measurement principles can be used to evaluate possible systematic errors. Analyst expertise and preliminary experiments conducted for method development can generally provide realistic expectations of measurement uncertainty associated with specific measurement techniques and assist with experimental design for CRM characterization using either approach to purity analysis.

Statistical methods can also be employed to estimate optimal experiment design for a given set of constraints, including the target measurement uncertainty<sup>[12]</sup>. Such experimental design should take into account sampling that is required to adequately assess homogeneity across the entire lot of candidate CRM<sup>[1]</sup>. As such, the number of units in the production lot should be known prior to development of methods for CRM characterization.

### 4.4 Candidate material sourcing and assessment of suitability, including verification of PC identity and adequate purity

#### 4.4.1 Material sourcing

Candidate materials can be sourced commercially, through custom synthesis or from refinement of materials. Factors that should be considered in screening such materials include affordability, purity, homogeneity and stability.

Impurities can have a significant effect on the accuracy of purity analyses. The RMP can conduct further purification of the candidate material when a sufficiently pure material cannot be sourced. The RMP should weigh the advantages of purification against the cost of the process and any other potential changes to material composition during this process.

High-purity metallic materials are commercially available for a number of elements and represent an ideal starting point for CRM development. RMPs should seek to acquire sufficiently pure material. Metallic materials should be sourced in a form (ingot, pellets, shots, powder etc) most appropriate for future use, taking into consideration the RMPs' capability to further process or subdivide the material. Effort should be invested to acquire candidate materials offering low surface-to-volume ratios to reduce the impact of adsorbed gases and the degree of surface oxidation and contamination; denser forms such as ingots, rods or wires are recommended, powders are to be avoided. Note that even some compact materials may contain higher mass fractions of impurities such as oxides, depending on the production technique; spheres produced by rolling a metal sheet into a ball should be avoided.

When the candidate PC material can only be sourced as a corresponding salt, usually because of the reactivity of the metallic form (e.g., lithium as carbonate or sodium as chloride), the RMP may grind and sieve the bulk material to needed consistency to improve homogeneity. Material with uniform particle size distribution is less prone to spatial stratification during packaging, storage and transportation. [Figure 1](#) shows a flowchart for material sourcing.

Usually, any processing such as cutting, grinding, sieving should be carefully considered from a contamination control point of view and should be kept to minimum.

It is desirable that the estimated PC mass fraction is at least 0,999 (3N, see [4.3.2](#)) in the candidate material, but this requirement is commensurate with its desired fit-for-purpose end use. During material sourcing, commercial certificates claiming various levels of purity should be carefully examined along with the impurity profile of the material to ensure that all possible sources of impurity were considered by the manufacturer for the purpose of purity assignment. It is an industry practice of reporting only functionally relevant impurities, often omitting dissolved gases, halogens, etc., which could be the most significant impurities in high-purity metals.

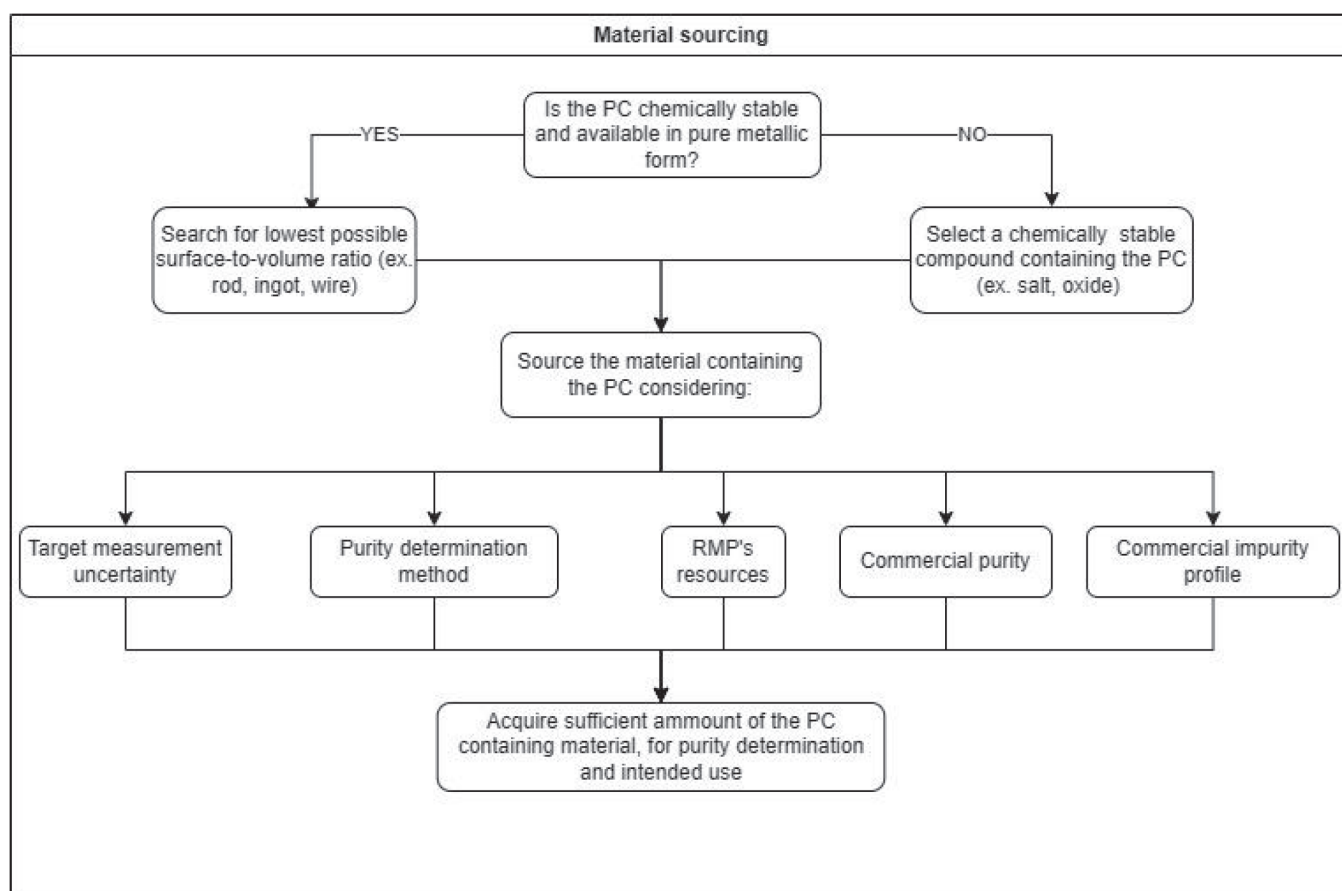


**Figure 1 — Material sourcing flowchart.**

#### 4.4.2 Verification of PC identity

The identity of a PC is critical for any chemical CRM. ISO 17034 requires the RMP to address the verification of the identity of the PC.

The identity of the PC can be specified as an element, metal, or compound with defined composition containing the given metal (i.e., metal halide, oxide, etc.).

When the target uncertainty for purity of the PC is comparable to that of typical variation of its isotopic composition and consequently the molar mass of the PC, definition of the PC may require assessment of the molar mass or isotopic composition of the PC.

The RMP should utilize analytical techniques such as inductively coupled plasma optical emission spectrometry (ICP-OES), inductively coupled plasma mass spectrometry (ICP-MS) or X-ray fluorescence spectrometry (XRF) to confirm the identity of the PC. When isotopic analysis is warranted, isotope ratio mass spectrometry (IR-MS), multicollector ICP-MS or thermal ionization mass spectrometry (TIMS) may be used.

#### 4.4.3 Material suitability

A suitable candidate material is one that is of the correct physical form for its intended use and can be sufficiently characterized to achieve target uncertainties. Overall impurity levels and profiles are often good initial indicators of suitability. A preliminary experimental effort should be made to verify that a candidate material meets acceptance criteria for purity and homogeneity. The suitability assessment should be conducted with an appropriate rigor to provide a go/no-go decision for further processing of the CRM.

### 4.5 Product packaging and specification of conditions for storage and safe handling

#### 4.5.1 General considerations

The nature of the product packaging, especially the primary packaging material, could significantly impact the integrity of the material and the stability of the property values. Therefore, packaging should be selected carefully and its impacts studied under storage and transport conditions.

Factors that can influence the choice of packaging material include, but are not limited to:

- hygroscopicity, air, moisture sensitivity of the CRM material;
- the physical state and form of the CRM material (e.g., liquid vs. solid; ingot vs. powder);
- the amount per unit to be packaged;
- temperature conditions for storage and transport;
- inertness;
- handling aspects at the user laboratory.

#### 4.5.2 Selection and treatment of packaging materials

Preliminary studies to assess candidate packaging materials or different storage conditions are recommended. The CRMs can be packaged in primary containment glass vessels, such as sealed ampoules or vials. In order to protect the material from environmental conditions that could impact the integrity of the CRM (e.g., moisture, contact with oxygen), the following packaging options should be considered:

- amber or clear glass vials;
- screw cap or septum lid with crimped aluminum cap;
- inert gas/nitrogen or air to fill the glass storage vial headspace.

Ampoules could be sealed under an inert atmosphere (e.g., nitrogen, argon), whereas with bottles this is not typically the case.

The RMP should also consider any necessary pre-treatment of the packaging materials, e.g., cleaning.

To ensure that the candidate CRM material is properly transferred to a selected packaging material upon production, the process should be controlled and documented, see ISO 17034.

After the establishment of a suitable process for packaging or filling, ISO 17034 requires the RMP to conduct a stability assessment of all relevant properties of the CRM under expected storage and transport conditions, as specified in ISO 17034 and ISO 33405<sup>[1]</sup>.

### 4.5.3 Storage and transport

Containers for CRM storage should sufficiently isolate the material from the environment. Isolation from moisture or air can be key considerations for material selection for the storage conditions for many CRMs.

Equally important is the nature of the transport conditions. The conditions of shipment, including the provision to provide all necessary documents (e.g., permits, statement of origin) for customs clearance, are the responsibility of the RMP.

### 4.5.4 Container Labels

ISO 17034 requires appropriate labels to be applied during product packaging; guidance can be found in ISO 33401<sup>[3]</sup>.

## 4.6 Measurement strategies for assessment of purity

The RMP should plan a measurement strategy for determination of purity of the candidate material that is fit for its intended use and should consider measurement procedures that collectively ensure:

- a) adequate specificity for PC measurement;
- b) an adequate survey of impurities;
- c) sufficient accuracy of measured purity value;
- d) sound evidence for assigning a sufficiently small measurement uncertainty.

NOTE Numerous complementary instrumental techniques are available for purity assessment. Hence, it is possible for the strategy adopted to vary with the instrumentation and other resources available to the RMP.

The use of one or a combination of appropriate measurement procedures can meet the objectives for producing a CRM with metrologically traceable certified values. Direct and/or indirect approaches to the certification of purity may be pursued, as outlined below.

Direct approach: determination of relative quantities, such as mass fraction of the PC, without necessarily quantifying all impurities. This approach commonly implements techniques such as quantitative coulometry, titrimetry, gravimetry or inductively coupled plasma mass spectrometry (ICP-MS) and a number of other atomic spectroscopy methods.

#### NOTE 1

Purity values obtained using the direct approach may require correction for some relevant impurities. For example, argentometry of sodium chloride determines the total halogen content in the material and requires assaying of substances that react with silver to form precipitates such as bromine and iodine to obtain chlorine contents. Further, EDTA titration determines the total EDTA-chelatable elemental content and requires the assessment of EDTA-chelatable impurity content by other means.

Indirect approach: determination of purity through a comprehensive survey of impurity components, where the purity,  $w_{PC}$ , is calculated using [equation \(1\)](#):

$$w_{PC} = 1 - \sum w_{IC_i} \quad (1)$$

where

$w_{PC}$  is the mass fraction of the PC;

$w_{IC_i}$  is the mass fraction of the  $i^{\text{th}}$  impurity component.

A thorough indirect approach requires more resources and varied expertise than a direct approach; however, it could lead to significantly lower uncertainties on purity estimates when the starting material is highly pure. All stable elements of the Periodic Table should be considered as potential impurities and

efforts should be made for their characterization. Carbon, nitrogen, oxygen and hydrogen, and in some cases the halogens, are frequently present in high-purity metals. More than one analytical approach is typically required to detect all potential elemental impurities. Highly sensitive atomic spectroscopy approaches such as glow discharge mass spectrometry (GD-MS) and ICP-MS are used for metallic impurity characterization along with CNOH combustion analysers for carbon, nitrogen, oxygen and hydrogen detection and carrier gas hot extraction for other elements (dissolved gases).

Selection of methods for purity assessment should leverage information about material composition gathered during the initial suitability analysis. A preliminary investigation of impurities should indicate the most appropriate methods for purity assessment. Furthermore, the achievable uncertainty in the certified value is likely larger for materials with high levels of impurities than for those with lower levels of impurities, simply as a result of the quadrature summation of all relative uncertainties of impurities. When applying the indirect approach to assess purity of a candidate material, the time and effort required to identify and quantify each impurity increases as the number of impurities increases. If such an analysis becomes too complicated or costly, the RMP may consider the purification of the candidate material to remove impurities and reduce the effort required for purity assessment, or reassessment of the availability of alternative starting materials. Materials of higher purity are also generally more suitable from the perspectives of the end user.

More detailed information for the assessment of purity can be found in [Annex A](#).

## **4.7 Development and validation of procedures for characterization, including achieving target measurement uncertainty**

### **4.7.1 General**

Specification of acceptable uncertainty in the certified purity value should be made with a clear understanding of the intended use of the CRM.

CRM purity and associated uncertainty should be fit for intended use when used to establish metrological traceability for a measurement procedure. Note that the uncertainty of the certified purity value should also realistically reflect the homogeneity and stability of the production batch. General guidance for the evaluation of measurement uncertainty is provided in ISO/IEC Guide 98-3 (GUM)<sup>[4]</sup> and its supplements. <sup>[5]</sup><sup>[6]</sup> Assessment of batch homogeneity and stability for CRM production is discussed in ISO 33405<sup>[1]</sup>. These sources of uncertainty should be evaluated during material suitability tests and considered when planning experiments.

An optimal experimental design is one which uses a minimum amount of resources to provide a sufficient amount of information. For CRMs, this means efficiently conducting measurements to achieve results with suitably small uncertainty. Expert judgement should ultimately decide the combination of appropriate analytical procedures best suited to the nature and composition of the material. In addition to achieving the smallest practical measurement uncertainty of a certified value, the execution of a plan for adequate characterization is contingent upon resources available to the RMP. Batch size is an important factor in sampling schemes and experimental design. General guidance on approaches to experimental design and adequate material sampling to achieve target measurement uncertainty under these criteria is available<sup>[1]</sup><sup>[8]</sup><sup>[12]</sup>.

Examples of purity analyses for characterization of CRMs are provided in [Annex B](#).

### **4.7.2 Use of Multiple methods for purity determination**

When well-characterized CRMs are needed, the use of multiple, uncorrelated methods for characterization is recommended. This is often challenging, considering the scope, especially when indirect approaches are used that require the determination/assessment of all possible elemental impurities.

When multiple measurement results are consistent, confidence gained through this corroboration can be reflected in the evaluation of uncertainty of a certified purity value. Information collected through several procedures should be combined in a way that is chemically and metrologically justifiable<sup>[13]</sup>. This is crucial when results from different methods are inconsistent or the composition of the material is complex. When

a direct approach is used for purity determination, a survey of key elemental impurities (representing a minimum of 90 % of total impurities) should be conducted and reported along with the PC mass fraction in the CRM.

#### 4.7.3 Property value boundaries

The RMP should consider the natural limit of chemical purity, 1 kg/kg (i.e., 100 %), during the characterization of CRMs. This is particularly relevant to candidate materials with very few low-level impurities. Generally, the entire coverage interval defined by the uncertainty of a certified value should lie between 0 kg/kg and 1 kg/kg.

When a material is known to contain a small mass fraction of total impurities, the variability of data from a direct measurement (e.g., coulometry) can yield purity estimates that are not entirely within this interval. For such cases, the measurement function or coverage interval can be constrained to observe the natural limits. This can be achieved in accordance with approaches described in the GUM and other documents<sup>[14]-[18]</sup>. Additional resources for the practical treatment of asymmetric coverage intervals near natural limits are available<sup>[14],[18]</sup>.

Similar considerations should be made for measurements  $w_{li}$  that are near limits of detection. If the uncertainty of a high-purity value determined by an indirect mass balance method is expected to be small, it should be substantiated by evidence from appropriately sensitive procedures used to determine  $w_{li}$ .

### 4.8 Assessment of homogeneity

#### 4.8.1 General

Candidate materials selected for CRM preparation are expected to have a high degree of homogeneity. Certified values for such materials are often expected to have very small uncertainties, making even a small amount of heterogeneity potentially impactful.

Generally, only the homogeneity of the PC should be assessed. Depending on the circumstances, other aspects should be assessed; e.g., if the content of an impurity is also certified in the CRM, the homogeneity of the impurity should be assessed as well.

#### 4.8.2 Preliminary assessment of homogeneity

Before packaging, it is recommended that a preliminary assessment of homogeneity be performed to ensure that the candidate material is suitably uniform. This may be particularly beneficial if the sample is an agglomerated powder or granular. In the event that the candidate material demonstrates a significant degree of heterogeneity, the RMP can consider further homogenization of the sample. To avoid unnecessary risk of contamination and exposure to reactive environments, homogenization should only be performed when the variance due to heterogeneity would otherwise be too large to achieve a target uncertainty in the certified purity value. If there is an unacceptable risk of contamination or environmental exposure expected during homogenization, a new candidate material should be sought.

#### 4.8.3 Sampling strategy

When sampling crystalline solids or agglomerated powders, the position of the samples within the material container should be considered to address impurity content stratification throughout the unit, in addition to the need for adequately representative sampling across units of the produced batch. For example, the material should be collected from the upper, middle and lower portions of the container, from the inside and outside portions of the bulk, or from portions of the container having disparate particle size. For metallic solids in the form of wire or ingots, sampling approaches should be developed considering intended use. Subdivision, cutting/sawing samples could introduce significant sources of contamination and should be carefully considered.

#### 4.8.4 Minimum sample size

The minimum sample size can be specified based on use of other data or by experience<sup>[1]</sup>. The stated minimum sample size for the CRM should satisfy the requirements of the intended use of the CRM, which should not be smaller than the sample intake size for which homogeneity has been demonstrated. For metallic samples, it is often advantageous to package CRM unit sizes which promote direct use of the sample without further subdivision.

#### 4.8.5 Experimental method of homogeneity assessment

Generally, one of the methods used for characterization (direct or indirect approaches) is selected as the experimental method for the assessment of homogeneity. A method with suitable repeatability and selectivity should be utilized. Experimental design enabling evaluation of inhomogeneity sources should be implemented. More detailed discussions and recommendations are described in ISO 33405<sup>[1]</sup>.

### 4.9 Assessment and monitoring of stability

#### 4.9.1 General

ISO 33405<sup>[1]</sup> states the importance of demonstrated stability under long-term storage conditions, under transport conditions and, where applicable, the storage and usage conditions likely to be encountered in the user laboratory. For the assessment of the stability, including subsequent stability monitoring of CRMs, the following should be considered in addition to the requirements stated in ISO 17034:2016, 7.11 and recommendations described in ISO 33405<sup>[1]</sup>.

#### 4.9.2 Sources of instability

For metallic solids, the primary consideration for the stability of the material is oxidation and potential atmospheric gas adsorption. Depending on the intended use and definition of the measurand, this might impact the validity of certified values in the CRM and should be assessed.

##### NOTE 1

If an effective cleaning procedure can be provided to the users to remove surface contamination, such a stability component could be considered negligible

Both appropriate short- and long-term stability assessment protocols should be developed and uncertainty components contributing to the final certified values accounted for.

For metallic salts, adsorption or desorption of water is a common cause of instability. This is dependent upon the hygroscopicity of the material and how well the potential effect is controlled by selected methods of packaging and storage conditions. For bulk material packaged in sample bottles, vials or jars, the RMP should monitor the uptake/loss of water. Hygroscopicity should be monitored under appropriate conditions of use and can be measured through experimental determination of moisture sorption isotherms.

NOTE 1 Demonstrated stability of moisture content in the chosen packaging does not guarantee that the material is stable when opened and used under laboratory conditions.

NOTE 2 Statistical treatments of stability data are detailed in ISO 33405<sup>[1]</sup>.

#### 4.9.3 Repeated use stability

When the RMP designates a CRM unit is suitable for repeated use, ISO 17034 requires the RMP to assess stability of the material during repeated use. Such study should simulate routine use of the CRM unit, with repeated cycles of opening, closing, weighing and storing the vial under long-term storage conditions as adsorption or desorption of water is a common cause of instability. The assessment of stability after repeated sampling can be run in parallel with classic/isochronous stability studies, or the RMP can adopt another suitable design for this evaluation.

#### 4.9.4 Stability monitoring

The recommended storage temperature depends on the stability of the element in question. Most metals can be securely stored at room temperature ( $\leq 25\text{ °C}$ ). Storage at lower temperatures for less stable compounds should be considered. In general, high surface area materials such as metal powders and salts require more attention due to increased potential reactivity.

Stability should be monitored during the lifetime of the CRMs. Effort should be commensurate with the likelihood of changes occurring, as many of these matrices are deemed inherently stable.

NOTE Comprehensive guidance on stability monitoring can be found in ISO 33405<sup>[1]</sup>. Monitoring of stability throughout the period of certificate validity provides insight into the long-term impact of the storage and, where applicable, usage conditions.

### 4.10 Characterization of the CRM

#### 4.10.1 General

ISO 17034 requires the RMP to clearly specify the measurand and perform the respective quantitative characterization of the PC in the candidate material. ISO 17034 requires the RMP to select a characterization strategy appropriate for the intended use of the CRM.

When the potential use of the CRM is to utilize it in combination with other such CRMs, e.g., for the preparation of multiple-component calibration solutions, as a minimum, the contribution of any elemental impurities from such PC to that of the other CRMs contributing to such a preparation should be quantified. Generally, this implies needed characterization of all elemental impurities in such CRMs.

ISO 17034 requires the RMP to use documented procedures for the assignment of property values. For certified purity values, ISO 17034 requires the RMP to identify all uncertainty contributions to be included in the assigned uncertainty. ISO 17034 further requires the RMP to define the probability or level of confidence for calculating the expanded uncertainty.

NOTE ISO 33405<sup>[1]</sup> and the GUM can provide guidance on uncertainty evaluation.

#### 4.10.2 Direct determination

Direct methods allow for the determination of the PC without the need to quantify all impurities. These procedures can yield purity results that are metrologically traceable to a reference, usually the SI, and thus offer relatively simple, low-cost approaches to inorganic purity determination. However, direct methods (coulometry, titrimetry, gravimetry) for purity assignment frequently lack the required specificity or are unable to realize a relative target uncertainty of  $\leq 0,01\%$  desired for primary calibrants<sup>[19]</sup>. Moreover, these methods cannot be used universally for all elements and, due to their lack of selectivity, often require additional confirmatory measurements to validate any bias which further contributes to combined uncertainties. For this reason, these methods may suffer numerous application issues. When these direct methods are used, purity uncertainty should not be simply the measurement uncertainty derived from titration or gravimetric procedure, but should explicitly consider uncertainties due to potential poor specificity.

Additionally, when the direct approach is used for purity determination, a survey of key elemental impurities (representing a minimum of 90 % of total impurities) should still be conducted and reported along with the PC mass fraction in the CRM.

[Annex B](#) describes the direct determination of purity of candidate materials.

#### 4.10.3 Indirect determination

Attaining the lowest level of uncertainty for purity assignment can be achieved using indirect methods which rely on a mass balance, whereby the relative amount of each impurity is determined and subtracted from 1 kg/kg. For a metrologically valid approach, it is paramount that all impurities are considered when

using this methodology. Ideally, all stable elements of the Periodic Table should be assessed and a value and associated uncertainty assigned.

Indirect purity determination approaches are capable of achieving the desirable target of  $10^{-4}$  relative uncertainty for inorganic purity CRMs, at least one order of magnitude lower than that typically deliverable using the most precise comparator methods, such as isotope dilution mass spectrometry,<sup>[20]</sup> and 'high-performance' inductively coupled plasma (ICP) optical emission spectrometry for value assignments of measurands in real samples <sup>[11,22]</sup>.

The indirect approach relies on quantitation of impurity components utilizing any number of individual analytical methods, each providing its own associated traceability chain for a given impurity.

The effort associated with the characterization of individual impurity components should be commensurate with their contribution to the overall PC uncertainty. Generally, highest levels of impurities contribute the most to the PC uncertainty.

With the exception of the PC matrix element, all elements of the Periodic Table are regarded as impurity components. Use of ICP-MS, ICP-OES, spark optical emission spectrometry (OES), XRF, GD-MS, combustion (for C,N,O, S) and carrier gas hot extraction techniques ( $H_2$  and inert gases) or other more esoteric methodologies [instrumental neutron activation analysis (INAA) or prompt gamma neutron activation analysis (PGNAA)] are heavily relied on for comprehensive characterization of CRMs. In addition to their selectivity, these methodologies often provide quantitative multi-element surveys of most impurities that could be present. Although relative measurement uncertainty of quantity estimates for individual ICs in high-purity ( $> 99,9\%$ ,  $>3N$ ) PC candidate materials can be relatively large (30 % - 100 %) depending on analytical methodology and IC mass fraction, their impact on the combined uncertainty assigned to the PC remains small ( $\approx 0,001$  kg/kg), which is the hallmark of the advantage of utilizing the indirect approach and initial selection of  $> 3N$  purity candidate materials for CRM characterization<sup>[23,24]</sup>.

There are three categories of ICs present in candidate materials:

- (a) measured and quantified with an associated assigned measurement uncertainty using validated, traceable measurement methodologies;
- (b) measured but present below a limit of detection (LOD) /quantitation (LOQ) in the sample using validated, traceable measurement methodologies;
- (c) not measured, only assessed, for which no validated measurement procedures are available to examine the material or for which no attempt has been made to do so given historical trends with similar materials or informed prior knowledge of the metallurgy/history of such materials. Value and uncertainty for these elements should still be assigned based on contextual information and used in the computation of final purity. Assumptions used for such ICs should be clearly stated on the CRM certificates.

NOTE (a) and (b) should be the largest proportion of impurities, (c) should be used sparingly and only when there is ample evidence that the content of a given impurity in this category is marginal compared to the overall uncertainty in assigned purity.

Multiple determinations of ICs using different analytical techniques will provide a pool of data that is self-validating. It is recommended that any IC contributing 10 % or more to the total impurity mass fraction be determined using at least two independent validated measurement techniques.

The isotopic composition of the PC should be verified. It is often useful to report when the material corresponds to the IUPAC accepted isotopic composition and atomic weight. When the PC isotopic composition and atomic weight differs from that of the IUPAC value, it should be determined and reported on the certificate. This mainly concerns elements prone to isotopic fractionation such as Li, B and Pb.

Depending on the measurement capabilities and the purity of the material, only estimated values for some ICs may be available, as noted when using method (b) above. These values are derived from limits of detection. For ICs that are below detectable/quantitation limits using the most sensitive technique(s) available to the RMP they are assumed present at a mass fraction that may be conveniently accounted for using a rectangular distribution within which the assumed mass fraction lies in the range zero to the LOD, i.e., averaged value =  $LOD/2$  <sup>[25]</sup>, which is likewise subtracted from the idealized PC purity of 1 kg/kg and has a standard uncertainty component of  $u = LOD/(2\sqrt{3})$ .