Terminology in Analytical Measurement

Introduction to VIM 3

Second Edition 2019
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Foreword to the second edition

In line with the Eurachem policy on the development and maintenance of guides, a review of the first edition of this Guide was initiated in 2016, five years after its original publication. The review involved a survey of users of the Guide and, while the feedback was very positive, the responses indicated that there was some scope for revision. In addition, since the publication of the first edition, a number of the key documents used in analytical measurement such as the ISO/IEC 17025 standard have been revised. In this second edition the scope and structure, and the terms and concepts discussed, remain unchanged from the first edition. However, all sections have been reviewed and, where necessary, the text has been revised to improve clarity and ensure consistency with current guidance.
Abbreviations and symbols

The following abbreviations, acronyms and symbols occur in this Guide.

Abbreviations and acronyms

- BIPM: International Bureau of Weights and Measures
- CCQM: Consultative Committee for Amount of Substance – Metrology in Chemistry
- CGPM: The General Conference on Weights and Measures
- CITAC: Cooperation on International Traceability in Analytical Chemistry
- CRM: certified reference material
- ERM®: European Reference Material
- GC-FID: gas chromatography-flame ionisation detector
- GC-MS: gas chromatography-mass spectrometry
- IEC: International Electrotechnical Commission
- IFCC: International Federation of Clinical Chemistry and Laboratory Medicine
- ISO: International Organization for Standardization
- IUPAC: International Union of Pure and Applied Chemistry
- JCGM: Joint Committee for Guides in Metrology
- JCTLM: Joint Committee for Traceability in Laboratory Medicine
- LC-MS: liquid chromatography-mass spectrometry
- LOD: limit of detection
- LOQ: limit of quantification/quantitation
- NIST: National Institute of Standards and Technology (USA)
- NMI: National Metrology (or Measurement) Institute
- p,p’-DDE: p,p’-dichlorodiphenyldichloroethylene
- PT: proficiency testing
- RM: reference material
- SI: International System of Units
- SOP: standard operating procedure
- SRM®: Standard Reference Material (NIST registered trademark)
- VIM: International vocabulary of metrology – Basic and general concepts and associated terms (VIM)
- VSMOW: Vienna Standard Mean Ocean Water
- WHO: World Health Organization
- XRF: x-ray fluorescence

Symbols

- $\alpha$: probability for a Type I error
- $\beta$: probability for a Type II error
- $\rho$: mass concentration
- $k$: coverage factor used to calculate expanded (measurement) uncertainty
- $s$: standard deviation
- $u$: standard (measurement) uncertainty
- $u_c$: combined standard (measurement) uncertainty
- $U$: expanded (measurement) uncertainty
Introduction and scope

Introduction

In the world of metrology – the science of measurement and its application – there is a language which has to be learned. The International Vocabulary of Metrology (VIM) was produced to provide a common language, primarily for physical measurements. The third edition (International Vocabulary of Metrology – Basic and General Concepts and Associated Terms (called VIM 3 in this document)) was produced by WG2 of the Joint Committee for Guides in Metrology (JCGM) and published as JCGM 200:2008 and as ISO/IEC Guide 99 [1]. A revised version of JCGM 200 was published in 2012 which is available free of charge from the BIPM website [2]. This revision included only minor corrections which do not affect the concepts described in this Guide, however ISO/IEC Guide 99 has not been updated. JCGM have also published an online annotated version of the VIM [3]. There are many differences between VIM 3 and earlier editions; one important change is captured in the title with the addition of the word ‘concepts’. VIM 3 is a consistent set of concepts each described by a unique term – the ‘label’ of the concept. It is applicable across all scientific disciplines thus making it relevant to those involved in performing measurements in chemistry and biology. Consistent definitions of concepts with their associated terms and symbols are essential if analysts and customers across the globe are to understand each other.

Scientists from different sectors often attach different words to the same concept, which can make interdisciplinary conversations difficult. There needs to be a common language that is clear and unambiguous. The first thing one does when learning any new language is to acquire a vocabulary, which will grow with time. Anyone learning a new language will know that there are often peculiarities – from words that can have different meanings depending on the context, to words that sound the same but are spelled differently and obviously have a different meaning. In English the word ‘standard’ has often been cited as an example of a word with many meanings. A detailed knowledge of the language is required so as to avoid such words causing mistakes, especially for people who do not have English as a first language. Ambiguous terminology also becomes a problem for translators and can be an indirect barrier to trade.

So why do we need a guide to VIM 3 for analytical scientists? First, VIM is a normative reference in a number of International Standards and Guides that underpin accreditation, including ISO/IEC 17025 [4], ISO 15189 [5], ISO/IEC 17043 [6], ISO Guide 33 [7] and ISO Guide 35 [8]. It is also referenced in ISO 9000 [9] and ISO 17034 [10]. Second, those involved in education and training have realised that there is often confusion about both concepts and terminology. In addition the definitions are often written in a language that is difficult to understand. This is true for analysts even when the definitions are translated from English or French to the local language. Third, in VIM 3 there are some substantial changes to terminology in an attempt to accommodate chemical and biological measurements. Fourth, to make VIM 3 more accessible to analysts working in these sectors there is a need to provide context and additional examples which relate the concepts to chemical and biochemical measurements.

All languages use some words in several different ways which adds confusion when conversations are between different nationalities. As mentioned previously, the word ‘standard’ is one example in English but a more subtle case is the use of the word ‘quantity’. In conversation we may say, e.g. ‘the quantity of sample is 5 g’. This may be acceptable in daily life. However, the VIM 3 usage of the term is more specific. What we should say and write is, ‘the mass of sample is 5 g’. In metrology quantity is not a synonym for amount. Quantity is a generic concept for things we measure, e.g. length, mass, time and amount-of-substance concentration. Validation and verification is another pair of words that have a changed definition in VIM 3 from what is generally used in analytical laboratories, although the actions in the laboratory to carry out these activities will be exactly the same.

This Eurachem Guide gives an explanation of selected concepts and provides examples over and above those in the Notes accompanying the definitions in VIM 3. The words that are defined in VIM 3 are highlighted and a VIM 3 reference number is provided for the concept. In VIM 3 the relations between concepts is displayed in 12 diagrams which have been used to help group concepts into families in this Guide. How the terms and definitions relating to these concepts are linked to each other, either within a family or between families, is illustrated in this Guide. The concepts which appear in this Guide are listed in Table A1 in the Appendix and in the text are organised into the following chapters; General Metrology, Metrological Traceability, Measurement Uncertainty, and Verification, Validation and Method Performance.
**Scope**

The scope of this Eurachem Guide is to cover a selection of the concepts in VIM 3, focusing on those most likely to be encountered in analytical laboratories. It aims to cover chemical, biological and clinical measurements. This Guide is intended for laboratory staff, accreditation bodies, for those commissioning measurements and for those using measurement results. Lecturers and trainers may also find this Guide useful when teaching aspects of metrology.
Notes for the reader

All concepts defined in VIM 3 appear in **bold** in the text. The terms discussed in this Guide are listed in Table A1 in the Appendix. If the full VIM 3 definition is included in this Guide, the VIM 3 reference number is given in the text box where the concept is defined and is not given each time the term is used in the text. When other VIM 3 terms are used in the text without a definition, the VIM 3 reference number is given the first time the term occurs in a section. VIM 3 permits multiple (often shorter) terms for the same concept; these are also included in the Appendix. If more than one term is given in VIM 3, the first term is the preferred one and it is used in this Guide as far as possible. However, a shorter alternative is used where it improves the readability of the text.

Single quotation marks (‘ ’) are used both for emphasis and for quotations. The latter are always referenced. The decimal sign is the point on the line. For the word standard, an upper case S is used when it refers to a norm, e.g. the International Standard ISO/IEC 17025. When the word vocabulary refers to VIM 3 or previous editions, an upper case V is used.

The generic term ‘concentration’ is used on its own, i.e. unqualified, when a generality is required. It represents the family of quantities which includes, mass concentration, amount concentration, number concentration or volume concentration. Note that many other quantities used to express composition, such as mass fraction, substance content and mole fraction, can be directly related to concentration.

It is accepted that the metre is the SI base unit of length, and that volume should be expressed in m$^3$ and multiples or submultiples of this, i.e. 1 litre = 1 dm$^3$. Since litre is an accepted unit it is used in this Guide and is represented by L [11].

A key concept in this Guide is ‘measurement’. However, the core activity of an analytical laboratory is often referred to using wording such as ‘analysis’, ‘test’, ‘examination’ or ‘determination’. Unlike ‘measurement’ which is a quantitative feature, these terms are frequently used, and understood, to involve a qualitative and/or a quantitative aspect.
1 General metrology

1.1 Metrology

Science of measurement and its application (VIM 2.2)

Metrology covers all theoretical and practical aspects of measurement in all sectors, including routine measurement. It applies in analytical science, biological and clinical measurement, whatever the relative magnitude of the measurement uncertainty of the result.

1.2 Quantity

Property of a phenomenon, body, or substance, where the property has a magnitude that can be expressed as a number and a reference (VIM 1.1)

Quantity is a crucial concept in metrology, which applies across all disciplines involved with measurement, and is therefore the first term defined in VIM 3 [1]. The definition identifies a quantity as any property which has size (magnitude) that can be evaluated through measurement. Some of the terms related to quantity are shown in Figure 1.

There are many kinds of quantity including mass, volume, velocity (speed), electric current and flow. In everyday life, we are interested in specific examples of such quantities (formerly referred to as ‘particular quantities’) [12], e.g. the volume of gasoline dispensed into a vehicle, the speed at which my car was travelling when the police stopped me, or the number concentration of red cells in the blood sample taken yesterday from Mr. Smith.

The specification of the (particular) quantity we intend to measure (also called the measurand) is the first part of any measurement.

1.3 Nominal property

Property of a phenomenon, body, or substance, where the property has no magnitude (VIM 1.30)

The current definition of quantity clearly excludes properties that, although carrying valuable information, can only be described in words. Examples include the colour of a spot test in chemistry (e.g. a home pregnancy test), and molecular sequences (e.g. of amino acids in a polypeptide, of nucleotides in a DNA fragment).

Such important properties, that have no magnitude, are however acknowledged in VIM 3 and described with the term nominal property. In analytical chemistry the term, qualitative analysis is often used to describe the examination of nominal properties.

It is possible to measure a quantity (see the definition of measurement), whereas obtaining information about a nominal property is not a measurement. The term examination is appropriate [13]. However, in ISO 15189 the term ‘examination’ is used for both the determination of nominal property values and for measurement [5].

1.4 Quantity value

Number and reference together expressing magnitude of a quantity (VIM 1.19)

The size (magnitude) of a quantity is expressed as a number accompanied by a measurement unit and – if appropriate – by additional reference to a measurement procedure or a reference material (RM) (VIM 5.13).

Consider two examples from the field of chemical chemistry, both concerned with the measurement of lead in paint.

(i) A laboratory is required to determine the total mass concentration of lead in a paint sample. This is reported as 10 mg L\(^{-1}\). In this case the specific quantity (the measurand) is the total mass concentration of lead. The quantity value is 10 mg L\(^{-1}\), where 10 is the number and mg L\(^{-1}\) (the measurement unit) is the reference.
1 (ii) A laboratory is required to determine the mass of extracted lead from the paint on a toy following the measurement procedure described in European Standard EN 71-3 ‘Safety of Toys. Migration of certain elements’ [14]. Since the amount of extracted lead is strictly dependent on the treatment applied (e.g. solvent, time, temperature), the measurand is defined by the measurement procedure applied (often referred to as an ‘empirical method’) and is therefore called an operationally defined measurand (see section 1.11). A different measurement procedure would probably give a different result. Therefore, the 10 is still the number but the reference is both the measurement unit (mg L⁻¹) and the measurement procedure used.

The third case shown in Figure 1 is where the reference is an RM. This can be illustrated using an example from laboratory medicine. The quantity value of the activity of a batch of an anticoagulant factor, Factor VIII, extracted from human blood, is referred to the value of the corresponding RM, periodically prepared and approved by WHO and known as a WHO International standard [15].

1.5 Nominal quantity value

<table>
<thead>
<tr>
<th>Terminology in Analytical Measurement</th>
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<tbody>
<tr>
<td>(VIM 3) the word ‘nominal’ is used in a different sense in nominal quantity value and nominal property (see section 1.3).</td>
</tr>
</tbody>
</table>

A volumetric flask may be marked 100 mL, this is its nominal quantity value (or, more simply, the nominal value). The actual value of the volume of the flask may not be exactly 100.00 mL, but will fall in a range according to the glassware class. For example, if a class A 100 mL volumetric flask has a tolerance of 0.08 mL the actual volume will lie in the interval 99.92 mL to 100.08 mL.

1.6 Reference quantity value

<table>
<thead>
<tr>
<th>Terminology in Analytical Measurement</th>
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<tr>
<td>(VIM 5.18)</td>
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</table>

Many different types of materials and devices may have a reference quantity value and an associated measurement uncertainty. Some examples are:

- The quantity value given on the certificate of a certified reference material (CRM) with its associated measurement uncertainty is a reference quantity value for the particular property to which it relates.
- The values of a set of solutions of known concentration, analysed to build a calibration diagram (VIM 4.30), are reference quantity values used for determining the value of the same quantity in other samples.
- In a calibration laboratory, mercury-in-glass thermometers are calibrated against a measurement standard (thermometer) reproducing specific temperature values (with associated uncertainties): these are reference values of the quantity ‘temperature’.
- Analysts use the value assigned to a CRM as a reference quantity value for the assessment of the trueness of a measurement procedure.
- In order to assess the competence of staff and laboratories, the staff may be required to analyse samples which have assigned values. The value assigned to a sample may be a quantity value obtained either from previous analyses by more experienced staff/laboratories or from PT rounds, or from a certificate if the sample is a CRM. In this context, the value assigned to any of these materials is deemed to be a reference quantity value.

1.7 System of quantities

<table>
<thead>
<tr>
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<tr>
<td>(VIM 1.3)</td>
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</table>

In practice, it is useful to identify a set of quantities from which all other quantities can be derived. Such a set is a system of quantities.

In any system of quantities the base quantities (VIM 1.4) that constitute the set are, by definition, considered to be mutually independent – they cannot be described as a product of other base quantities. The choice of these quantities is by convention. Other choices are equally valid, provided that they satisfy the definition. However, a specific system of quantities has been agreed and adopted. The Metre Convention established a permanent organisational structure for member governments to act in common accord on all matters relating to units of measurement. It led to the creation of the International Bureau of Weights and Measures (BIPM). The seven base...
1.8 International System of Quantities

**system of quantities** based on the seven **base quantities**: length, mass, time, electric current, thermodynamic temperature, amount of substance, and luminous intensity (VIM 1.6)

7 The definition of the units corresponding to the **base quantities** (VIM 1.4) is extremely important since they provide the foundation for the entire system of **units** (VIM 1.13). The **International System of Units** (VIM 1.16), the SI, is recognised by many countries (at the time of writing there are 59 members states of the Metre Convention) and is adopted as the only legal system of units within the European Union [11, 16]. The **base quantities** and their corresponding **base units** (VIM 1.10) are shown in Table 1.

In 2018 it was agreed that four of these **base units** would be redefined – the kilogram, the mole, the ampere and the kelvin. Following the adoption of the revised definitions in May 2019, all the **base units** are defined in terms of fundamental constants which are unchanged with respect to time and location. By definition, these fundamental constants have no uncertainty. The kilogram is defined in terms of the Planck constant \( h = 6.626 \times 10^{-34} \text{ J s} \) and the mole as the specific number of elementary entities (atoms, molecules, ions, etc) given by the Avogadro constant \( N_A = 6.022 \times 10^{23} \text{ mol}^{-1} \). These changes do not affect the way routine **measurements** are made and **metrological traceability** is obtained exactly as before. It is only the definition of the **units** that has changed.

Many other **quantities** within the SI are expressed as relations between those shown in Table 1 and are called **derived quantities** (VIM 1.5). The definitions of the **derived units** (VIM 1.11) in terms of the **base units** follow from the equations defining the **derived quantities** in terms of the **base quantities**. For example, the **derived quantity** mass density is:

\[
\text{mass density} = \frac{\text{mass}}{\text{(length)}^3}
\]

The **measurement unit** (**derived unit**) is obtained by applying the same formula to the **units**, i.e. \( \text{kg/m}^3 \) which is usually written as kg m\(^{-3}\) or kg/m\(^3\).

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**Table 1 – Base quantities and base units.**

<table>
<thead>
<tr>
<th>Base quantity</th>
<th>Base unit (symbol)</th>
</tr>
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<tbody>
<tr>
<td>length</td>
<td>metre (m)</td>
</tr>
<tr>
<td>mass</td>
<td>kilogram (kg)</td>
</tr>
<tr>
<td>time</td>
<td>second (s)</td>
</tr>
<tr>
<td>electric current</td>
<td>ampere (A)</td>
</tr>
<tr>
<td>thermodynamic</td>
<td>kelvin (K)</td>
</tr>
<tr>
<td>temperature</td>
<td></td>
</tr>
<tr>
<td>amount of substance</td>
<td>mole (mol)</td>
</tr>
<tr>
<td>luminous intensity</td>
<td>candela (cd)</td>
</tr>
</tbody>
</table>

A common mistake is to confuse **quantities** and their **measurement units**. It should be kept in mind that whereas a **quantity** is a measurable property of a phenomenon, body or substance (e.g. mass), a **measurement unit** (e.g. the kilogram) is chosen by convention as the reference to which **measurements** of that property refer.

**1.9 Measurement unit**

A **real scalar quantity**, defined and adopted by convention, with which any other quantity of the same **kind** can be compared to express the ratio of the two quantities as a number (VIM 1.9)

We are all familiar with the concept of a **measurement unit**; the method of pricing many products is by showing the cost per agreed unit, e.g. food as cost per kg, price of gasoline quoted per litre (L). If we say the mass of an apple is 0.15 kg, this means that the mass of the apple is 0.15 \( \times \) mass of the kilogram, that is, the **measurement unit**. To obtain the number 0.15 you compare the value indicated for the apple with that indicated for a reference mass, i.e. the mass used to calibrate the balance. The reference mass in turn is compared with a practical realisation of the definition of the kilogram by national metrology institutes (NMIs), or by calibration or testing laboratories. The result of any such comparison is expressed as a ratio of the **indication** obtained to the value of a **quantity** of the same **kind** (VIM 1.2).

**1.9.1 Quantities of the same kind**

The classification of **quantities** of the same **kind** (VIM 1.2) is somewhat arbitrary, but the concept that only similar items can be compared is well understood. **Quantities** of the same **kind** will have
The example of the mass of the apple was easy because quantities of the same kind were compared. Sometimes it is not possible to obtain the quantity value by comparison with a quantity of the same kind, e.g. because of an incomplete understanding of the measurand or the complexity of the factors influencing the measurement process and its result. An example of such a measurand is the mass fraction of fibre in a food product (the "fibre content"). However, it is still possible to compare results for such measurands, provided they are obtained using identical or proven equivalent measurement procedures. In such cases, reference must be made to which measurement procedure (including details such as reagent grade, calibrator, etc.) was used to obtain the quantity value.

1.10 Measurement

A measurement is a series of actions (steps, stages) taking place in a defined manner (i.e. following a measurement procedure). Some measurements are a single step, others have many stages. There is potential for controversy as some regard measurement as the instrument response, often the last stage in a multi-stage process, e.g. for an aliquot of sample extract. What is clear is that measurement relates to the whole process of obtaining a quantity value and should not be used to refer to the numerical value obtained.

1.10.1 What is a ‘measurement’ and what is not?

In analytical sciences, a test sample submitted for analysis often undergoes a series of chemical and/or physical treatments in order to convert it to a form that can be presented to a measuring instrument. These steps are acknowledged to be part of the measurement process. In some cases there may be a particular sampling procedure included in the process.

A quantity value is expressed as a number and a reference, expressing the magnitude of the quantity. Does this mean that the procedure of counting items is a measurement? The answer is yes, because the result is quantitative and the reference is the counting procedure. However, visually inspecting a sample to note its colour is not a measurement, but an ‘examination’, as measurement does not apply to nominal properties. In contrast, using a spectrophotometer to record some property relating to the colour of a sample (e.g. absorbance at a particular wavelength) is a measurement.

1.10.2 Preliminary to making a measurement

Before making a measurement, the quantity must be clearly defined, bearing in mind the purpose for which the experimental result is required. The quantity referred to is the measurand. In addition, for measurement results to be fit for purpose, a validated measurement procedure needs to be available and must be applied using a calibrated measuring system. In this context ‘fit for purpose’ means that, when the measurement procedure is applied, the quantity intended to be measured is measured, and the uncertainty in the measurement results is acceptable. The concept of target measurement uncertainty (VIM 2.34) (see section 3.1.2) is used to describe the maximum measurement uncertainty that can be accepted by the customer for a specific application [17].

1.11 Measurand

There is a great deal behind this apparently simple definition. The measurand is a description of the specific quantity we intend to measure. The specification of the measurand should be sufficiently detailed to avoid any ambiguity. Measurand is not another name for analyte. Analyte is the component represented in the name of a measurable quantity, whereas measurand refers to a specific quantity to which quantity values are expected to be attributed by means of a measurement. Consider two examples of quantities which may be measured:

- mass of protein in a 24-hour urine collection;
In each case the complete statement represents the measurand. The analytes are protein and glucose, respectively.

The specification of the measurand is critical, in the order that the measurement result is suitable for its intended use, and should include all important parameters and conditions. For example, if the volume of the liquid delivered by a pipette is to be determined by weighing, the specification of the measurand should at least include the type of liquid to be used and the temperature at which the measurements should be carried out. In chemical and biological analysis the specification of the quantity (e.g. mass fraction or amount-of-substance concentration), the analyte and where relevant the matrix, even if it is not possible to give a clear chemical definition of the analyte, for example:

- mass fraction (e.g. mg kg\(^{-1}\)) of cadmium in soil;
- amount-of-substance concentration (e.g. mol L\(^{-1}\)) of total cholesterol in blood serum;
- mass fraction (e.g. mg kg\(^{-1}\)) of extractable fat in a meat sample.

In the measurement of the mass fraction of cadmium in a soil sample, the sample drying conditions (e.g. dried to constant mass at (105 ± 5) °C) should be included in the definition of the measurand as they have an influence on the basis for reporting results. It may be necessary to specify the measurement procedure in even more detail and define whether the measurement result will be referring to the laboratory sample or the whole bulk (e.g. a batch of animal feeding stuff, whole lake). In other cases, the measurand can only be defined with reference to an agreed empirical measurement procedure (operationally defined measurand). For example the measurement of extractable fat in a sample of meat will depend strongly on the solvent used and the conditions of extraction. Such ‘operationally defined’ measurands are still fit for the purpose of comparing results and making decisions provided that the agreed measurement procedures are strictly followed.

The description of how measurements are performed involves several levels of detail, with the most comprehensive being the measurement procedure, which encompasses all others.

Performing measurements requires an understanding of the measurement principle (VIM 2.4), that is of the phenomenon underlying the measurement. The same measurement principle can be applied according to different measurement methods (VIM 2.5), e.g. using different techniques (such as flame or electrothermal atomic absorption spectrometry), or different calibration procedures (external calibration or by the ‘method of standard additions’). The measurement method is a generic description of the operations involved. The following are examples of measurement methods, with the measurement principle given in brackets:

- Determining by weighing the amount of a chemical compound precipitated from a liquid test sample using a defined chemical reaction (gravimetry).
- Determining the amount-of-substance concentration of a compound in a given sample, either directly, by measuring its absorbance at a given wavelength, or indirectly, by measuring a so-called ‘surrogate quantity’, such as the absorbance of a complex formed as a result of a defined chemical reaction (spectrophotometry).
- Determining the amount-of-substance concentration of a compound by means of its ability to become permanently linked to a specific antibody carrying a tag (immunochemistry).

Although not defined in VIM 3, the term ‘measurement process’ is used in a number of international Standards. It is defined in ISO 9000 [9] as ‘a set of operations to determine the value of a quantity’. It is the overall process of planning, performing and evaluating measurements and, as such, the measurement principle, method and procedure form part of the measurement process.

The most complete level of description of a measurement is the measurement procedure which should be sufficiently detailed to allow a suitably trained person to perform the measurement. In some laboratories the
1 measurement procedure may be documented in one or more standard operating procedures (SOP).

2 Although ISO/IEC 17025 [4] refers to measurement procedures in some clauses, ‘method’ and ‘test method’ are also used and considered synonymous with measurement procedure as defined in VIM 3. However, it should be noted that the requirements of the Standard apply to both measurements and examinations. As mentioned earlier, ISO 15189 [5] uses the term ‘examination’ to refer both to the determination of nominal properties and to measurement procedures. In ISO/IEC 17025 the method includes, where relevant, aspects of ‘sampling, handling, transport, storage and preparation of items to be tested and/or calibrated’. However, in ISO 15189, examination does not include sampling; the latter is part of the ‘pre-examination’ covered in clause 5.4 of that Standard.

3 A measurement procedure includes a description of how measurement results are obtained and calculated, including any calculation. A measurement result is generally expressed as a single measured quantity value and a measurement uncertainty. The measurement procedure should therefore include an estimate of the measurement uncertainty to be used when reporting measurement results or information on how it should be calculated.

4 There are two types of measurement procedure that are included as two separate concepts; they are reference measurement procedures and primary reference measurement procedures.

1.13 Reference measurement procedure

measurement procedure accepted as providing measurement results fit for their intended use in assessing measurement trueness of measured quantity values obtained from other measurement procedures for quantities of the same kind, in calibration, or in characterizing reference materials (VIM 2.7)

5 Reference measurement procedures are well characterised and will normally provide measurement results with a small measurement uncertainty. For example, in the clinical sector, to comply with the requirements of the In vitro Diagnostics Directive [18] manufacturers are required to use reference measurement procedures or CRMs (VIM 5.14) to establish the metrological traceability of values assigned to calibrators. The Joint Committee for Traceability in Laboratory Medicine (JCTLM) lists a number of

47 reference measurement procedures [19], e.g. NIST LC-MS reference method for the determination of the mass concentration of cortisol in blood serum [20].

51 In the hierarchy of metrological order, the highest level is occupied by a primary reference measurement procedure.

54 1.14 Primary reference measurement procedure

reference measurement procedure used to obtain a measurement result without relation to a measurement standard for a quantity of the same kind (VIM 2.8)

56 Primary reference measurement procedures (also known as primary methods of measurement or, more simply, ‘primary methods’) allow a quantity value to be determined with direct reference to the definition of its measurement unit or to fundamental constants. Because there are no other intermediate steps, they provide, under the stated conditions, metrologically traceable measurement results with the highest levels of accuracy. Examples of such procedures are the determination of the amount-of-substance concentration by coulometry, gravimetry or by isotope dilution mass spectrometry.

58 1.15 Measurement result

set of quantity values being attributed to a measurand together with any other available relevant information (VIM 2.9)

72 The measurement result is the outcome of any measurement activity and is what is reported to the customer, be it a regulatory body, the accreditation body or a commercial client.

76 In the past, the term ‘measurement result’ has been used to mean different things. A measuring instrument gives a number, i.e. an indication; the number can be converted into an uncorrected result using a calibration curve (VIM 4.31). In some cases, due to measurement bias (VIM 2.18), this value is corrected and the corrected result reported to the customer along with, e.g. a recovery factor with its measurement uncertainty. This is what constitutes a measurement result in the VIM 3 definition. Historically often a single number was all that was given to the customer. The VIM 3 definition aims to eliminate this lack of consistency, by clearly identifying a measurement result as the final
outcome of the process of determining the quantity value(s) of a measurand, i.e. providing an answer to the customer's request. In this context, all the relevant information relating to the measurement is also part of the measurement result.

A measurement result is generally expressed as a single measured quantity value and a measurement uncertainty. This can be interpreted as a 'set of quantity values', meaning that any value, within the interval defined by the measurement uncertainty is a possible value for the measurand. This provides the customer with information on the reliability of the measurement result which should be taken into account if, for example, it is compared with a stated limit.

The measurement uncertainty and the level of confidence associated with it are part of a measurement result. The measurement uncertainty may not always be explicitly reported if it is considered to be negligible in terms of interpreting the result, or if it is not relevant in the interpretation, or not required by the customer. Examples of where this normally holds true are a) the volume delivered by a petrol station pump, b) the mass of groceries weighed on a modern balance in a supermarket, and c) the examination results delivered to the physician by a hospital laboratory. However, the uncertainty is still taken into account, since the pump, the balance and the clinical tests must fulfil certain stated performance criteria before they can be put into use.

The requirements of ISO/IEC 17025 [4] are that information on measurement uncertainty should be presented in test reports when it is relevant to the validity or application of the test results, when the customer's instruction so requires or when the uncertainty affects conformity to a specification.

1.16 Measured quantity value

Measured quantity values are an essential part of a measurement result. In the simplest cases, e.g. when weighing bread or potatoes on a commercial weighing scale, the measured quantity value is the measurement result as the measurement is a simple single step process and no intermediate measurements or calculations are required. However, more often, in analytical sciences, a measurement involves different quantities and indications, to be combined according to the measurement model (VIM 2.48), to obtain the measured quantity value. The final value is usually calculated as the average of the set of values obtained from repeated measurements, which will have a lower measurement uncertainty than the individual values. In many cases, the measurand requires more than one measured quantity value, obtained with separate measurement procedures.

For example if the measurand is to be defined as the mass fraction of an analyte on a dry weight basis, the mass of the sample after drying and the mass fraction of the analyte of interest are both required.

1.17 Measurement error

No measurement is perfect; the very action of measuring introduces changes in the system subjected to measurement. It is convenient to describe this scenario in terms of a measurement error, affecting each individual measurement. In principle, the measurement error is represented by the difference between the measured quantity value and a reference quantity value. In practice, for a measurement on a test sample, the measurement error is unknowable. This is because, in this case, the reference quantity value is the unknown true quantity value (VIM 2.11) for the measurand. The measurement error consists of two components, systematic measurement error (VIM 2.17) and random measurement error (VIM 2.19), which represent respectively, the constant or predictable variation and the unpredictable variation in a series of replicate measurements. Well known parameters describing the performance of analytical methods are associated with the estimate of the random and systematic components of measurement error (see chapter 4).

1.18 Indication

Most measurements are based on indications provided by measurements or measuring systems. An indication (e.g. an instrument signal or response) and a corresponding value of the quantity being measured are not necessarily values of quantities of the same kind (VIM 1.2). In many cases, the indication provided by the measuring instrument or measuring system will be a value related to a quantity different from the measurand.
1. In most cases in analytical science, analysts rely on the measurement of physical quantities such as mass of precipitate, volume of titrant, or the change in electrical signal produced by the absorption of radiation of a particular wavelength. These indications are then converted, using well known stoichiometric relationships or a calibration curve (VIM 4.31), to quantities related to the amount of substance. In chemical analysis it is quite common to observe an instrument response for a series of reference solutions and then for the test sample, so in this context the term ‘instrument response’ is generally used for indication. Similarly blank indication (VIM 4.2) refers to the instrument response for a test material where the analyte of interest is believed to be absent (in VIM 3 the phrase ‘supposed not to be present’ is used).

1.19 Measuring instrument

device used for making measurements, alone or in conjunction with one or more supplementary devices (VIM 3.1)

Measuring instrument is closely related to the concept ‘measuring system’.

1.20 Measuring system

set of one or more measuring instruments and often other devices, including any reagent and supply, assembled and adapted to give information used to generate measured quantity values within specified intervals for quantities of specified kinds (VIM 3.2)

In some cases, when the measuring instrument can be used alone (e.g. mercury-in-glass thermometer) the measuring system consists of one measuring instrument. However, for the majority of analytical methods the measuring system consists of several measuring instruments and associated equipment and reagents.

VIM 3 defines three types of measuring instruments:

- **Indicating measuring instruments** (VIM 3.3) provide an output signal directly, for example a number (e.g. an electronic balance) or a visual/acoustic signal. The output may be transferred to another device, e.g. a computer with software providing data integration.

- **Displaying measuring instruments** (VIM 3.4), a particular type of indicating instrument, display the result of a measurement on a scale, e.g. mercury-in-glass thermometer, a spring balance. For instruments with analogue outputs, the indication is given by the position of a pointer on the display.

- **Material measures** (VIM 3.6) are intended to reproduce an assigned quantity value, e.g. volumetric flasks, standard weights or CRMs (VIM 5.14).

Distinguishing between these categories of measuring instruments is not normally a concern in analytical measurement.

1.21 Metrological comparability of measurement results

VIM 3 uses the word comparability in the sense of ‘ability to compare’ not in the sense of being ‘similar in magnitude’. Hence, to be comparable the measured quantity values or the measurement uncertainties do not have to be of the same order of magnitude. For example, measurement results for the determination of the mass fraction of chromium in an alloy and in a sample of contaminated soil are metrologically comparable when they are traceable to the same measurement unit.

The purpose of making measurements is often to enable a comparison to be made between a measurement result obtained and another value for a quantity of the same kind (VIM 1.2), e.g. a legal limit or a reference interval. Examples of possible questions asked by a customer are, ‘Is the mass fraction of lead in this sample of soil greater than the allowed limit?’ or ‘Is the mass fraction of lead in two samples of soil significantly different?’ A question which often arises, for instance, in a legal context is, ‘Are the results provided by the two laboratories different?’ In order to be able to answer these questions, measurement results need to be metrologically comparable.

A comparison is only meaningful if the results are traceable to the same reference (preferably internationally accepted) which may be, e.g. the metre or the quantity value of a CRM (VIM 5.14).

The concept ‘ comparability’ is associated with the concept ‘compatibility’.
1.22 Metrological compatibility of measurement results

Property of a set of measurement results for a specified measurand, such that the absolute value of the difference of any pair of measured quantity values from two different measurement results is smaller than some chosen multiple of the standard measurement uncertainty of that difference (VIM 2.47)

For a set of two results to be metrologically compatible the difference between them should be smaller than the expanded uncertainty (VIM 2.35) of their difference. With knowledge of the value of the measurement uncertainty of the quantity values it is possible to calculate a permissible difference \( d \) between a pair of independent results which refer to the same measurand. A difference between \( x_1 \) and \( x_2 \) greater than \( d \) suggests a possible failure of the measuring system, a change in the measurand or that the measurement uncertainty of one or both results has been estimated incorrectly.

The standard uncertainty (VIM 2.30) of the difference \( u(d) \) between two completely independent measurement results \( x_1 \) and \( x_2 \) (obtained, for example, from two different laboratories) is given by the equation:

\[
u(d) = \sqrt{u(x_1)^2 + u(x_2)^2}\]

where \( u(x_1) \) and \( u(x_2) \) are the standard uncertainties associated with \( x_1 \) and \( x_2 \) respectively. Therefore, for two measurement results to be considered metrologically compatible, the difference \( d \) must be less than \( k \cdot u(d) \), where \( k \) is the coverage factor (VIM 2.38) appropriate for the required level of confidence.

For a larger set of results metrological compatibility cannot be determined so easily. The ‘chosen multiple’ in the definition would depend on the level of confidence required and the number of paired comparisons involved.

Correlation between the measurements influences metrological compatibility of measurement results. The standard uncertainty of the difference will be lower for positive correlation and higher for negative correlation.
2 Metrological traceability

This chapter describes the terminology relating to metrological traceability. Further information on how to establish the traceability of measurement results is given in a Eurachem/CITAC Guide [21] and an IUPAC Technical Report [22].

2.1 Metrological traceability

Metrological traceability is essential for meaningful measurement results as it helps demonstrate that such comparisons are scientifically valid. It is meaningful to compare the length of a football field with the distance between street lights so long as they are both expressed in metres – the same unit of measurement. However, just because results are metrologically traceable does not mean they are fit for purpose as it does not ensure that the measurement uncertainty is adequate. For example, the measurement result obtained when weighing a certain mass of sodium chloride using a calibrated technical (2-figure) balance is metrologically traceable to the kilogram. This may be fit for purpose for preparing reagents such as buffers but may not be sufficiently accurate for the preparation of calibration solutions for the determination of low concentrations of sodium in water. In addition, to ensure that measurement results are fit for purpose, the measurement procedures used must be validated (see chapter 4) and adequate on-going quality control procedures must be in place.

2.1.1 Reference points

According to VIM 3 there are three types of metrological traceability.

- A measurement unit, e.g. mol L⁻¹, g, mg kg⁻¹, °C, µkat L⁻¹, through its practical realisation (see section 2.1.2).

- A measurement procedure, which is fully defined and internationally agreed upon, e.g. the procedures defined in the IFCC primary reference procedure for the measurement of catalytic activity concentration of alkaline phosphatase in human serum [23] or the procedures defined in the ISO Standard method for the determination of the fat content of dried milk and dried milk products [24].

- A measurement standard, e.g. the CRM (VIM 5.14) SRM® 2193a CaCO₃ pH standard which, when prepared according to the instructions given in the certificate, has a certified pH value of 12.645 at 20 °C with an expanded uncertainty (VIM 2.35) of 0.011 (k = 2).

For many measurement results the reference will be a measurement unit but in some cases additional metrological references, such as a measurement procedure, will also be required (see section 1.11). In such cases the references are used in combination.

The ‘unbroken chain of calibrations’ is a traceability chain (VIM 2.42), consisting of the sequence of measurement standards and calibrations used to relate a measurement result to a reference. A generic flow chart of metrological traceability is shown in Figure 2. The direction of increasing measurement uncertainty and the calibration hierarchy (VIM 2.40) are illustrated. The calibration hierarchy is a sequence of calibrations from the chosen reference to the final measuring system where the outcome of each calibration depends on the outcome of the previous calibration. The traceability chain is defined by the chosen calibration hierarchy.

The result should always be traceable to an appropriate reference point and accredited laboratories must be able to demonstrate this. The laboratory can draw its own traceability chains by studying the documentation for its routine procedures, equipment and calibrators. Examples of generic traceability chains can be found in the Standard ISO 17511 [25]. The IUPAC Technical Report on establishing traceability in chemistry contains the following seven illustrated examples of traceability chains [22]:

- Amount-of-substance concentration of an acid in a solution;
- pH of a solution;
1. mass concentration of ethanol in breath;
2. number-ratio of isotopes of an element in a material;
3. mass fraction of glyphosate in an agricultural chemical;
4. amount-of-substance concentration of creatininum in blood plasma;
5. mass fraction of protein in grain.

2.1.2 Practical realisation of a measurement unit

In the case of metrological traceability to a measurement unit (VIM 2.43), the reference is the definition of a unit through its practical realisation. What does this mean in practice? The realisation of the definition of a unit is the procedure by which the definition may be used to establish the value and associated measurement uncertainty, of a quantity of the same kind (VIM 1.2) as the unit.

Mass and amount of substance are two base quantities (VIM 1.4). They correspond to the base units (VIM 1.10) of the kilogram and the mole respectively. Although the definition of the kilogram is changed and there is no longer an international prototype kilogram (see section 1.8) the realisation of the unit will still be made using a Kibble balance [11]. The measurement unit, or multiples of it, are embodied in calibrated weights.

The embodiment (realisation) is achieved by measurement using a primary reference measurement procedure and a measuring system to assign a quantity value and a measurement uncertainty.

The revised definition of the mole is discussed in section 1.8. A common realisation of the mole is achieved through weighing. The amount of substance \( n \) in a pure sample is measured by determining the mass \( m \) of the sample and dividing by the molar mass \( M \) according to: \( n = \frac{m}{M} \). This approach is only possible when the chemical entity or entities, specified in a measurand, can be defined. If this is not the case then amount of substance cannot be measured. In such cases, other quantities, such as mass, which do not need entities to be specified, can be chosen. To report measurement results in the SI (VIM 1.16) unit mole, the embodiment of the definition of the mole would require a primary measurement standard (VIM 5.4) for each of the millions of chemical compounds. To overcome this problem the Consultative Committee for Amount of Substance (CCQM) has selected measurement principles (VIM 2.4) and measurement methods (VIM 2.5) that have the potential to assign quantity values in mole, or its derived units (VIM 1.11), for the quantities carried by materials which then become primary calibrators, e.g. CRMs (VIM 5.14).

2.1.3 Route to establishing metrological traceability

Establishing and demonstrating metrological traceability in chemistry is often not straightforward. One reason is that there may be several ways of obtaining the measurement result for the same measurand. For example, the quantitative analysis of copper in a water sample can be carried out using various types of spectrometric instrumentation, with or without digestion, separation, and pre-concentration steps. In addition, the complexity of test materials means that extensive sample pre-treatment and clean-up is often required which makes straightforward comparisons between measurement standards and test samples difficult.

The secondary measurement standard (VIM 5.5) shown in Figure 2 serves to calibrate the measuring system, within the given reference measurement procedure. This reference measurement procedure is the one used to assign a value to the calibrator, e.g. a CRM (VIM 5.14), used in the laboratory during the analysis of routine samples. The choice of calibrator will depend on the measurement procedure and the purpose for which the measurement is being made. Analysts must assess the influence of the entire measurement process, and sampling if appropriate, on the metrological traceability of the measurement result.

Manufacturers normally offer various materials for the preparation of working measurement standards (VIM 5.7) for calibration of routine measurements. There are, e.g. pieces of copper metal with stated purity, and solutions with specified amount-of-substance concentration and matrix composition. The uncertainty in the value of the calibrator will directly influence the measurement uncertainty of the final result so here the analyst may have a choice.

Fewer standards qualify as secondary measurement standards, and there are an even smaller number of primary measurement standards (VIM 5.14).
standards (VIM 5.4) and primary procedures available. So although the lower parts of the chain shown in Figure 2 will differ, measurements of the concentration of copper made in different laboratories will be traceable to a stated endpoint reference via the same primary calibrator or procedure. Many of the measurements of the protein transferrin in serum performed in medical laboratories are traceable to the SI unit (VIM 1.16) g L\(^{-1}\) via the CRM ERM\(^{\circledR}\) DA 470k/IFCC [26]. The laboratory has to ensure the metrological traceability of the steps shown below the dotted line in Figure 2.

Metrological traceability is the property of a result. In the generic example in Figure 2 the measurement result is the quantity value and its measurement uncertainty, together with any other relevant information relating to the sample.

Figure 2 – Example of a generic traceability chain. The traceability chain relates the measurement result for a routine test sample to the reference point (here the SI) via a sequence of calibrations (the arrows). Uncertainties, present in all procedures and calibrators, are propagated to the final result. The arrows to the left illustrate the direction of the traceability chain (upwards) and the direction of the calibration hierarchy (downwards). The arrow on the right indicates the measurement uncertainty increasing from the metrological reference to the measurement result.
2.1.4 Practical demonstration of metrological traceability

Examples of how to achieve metrological traceability can be found in a number of guides [21, 56, 22, 27]. For routine testing most of the information that the laboratory needs to establish and demonstrate metrological traceability is available in-house.

- Definition of the measurand: Includes at least the type of quantity (e.g. mass concentration), the analyte (e.g. methyl mercury), and type of samples (e.g. freshwater, dairy products ...), but may require additional specifications (e.g. dry mass and drying temperature), see also section 1.11 for details.

- A description of the measurement procedure: Includes details of all steps, equipment and materials required, the measuring system and a model (VIM 2.48) showing how the result is calculated.

- The target measurement uncertainty (VIM 2.34): The maximum uncertainty that is acceptable. This depends on the application (the intended use) and, ideally, the customer knows this, or can refer to specifications. In order to choose appropriate references knowledge of the target measurement uncertainty is required.

- Reference: The top of the traceability chain (VIM 2.42), (e.g. a measurement unit, a material with a specified quantity value (CRM (VIM 5.14)) or a measurement procedure).

- Calibration hierarchy (VIM 2.40) and traceability chain: The laboratory can perhaps choose between several working calibrators, each one provided with its own different, fixed traceability chain. The documentation accompanying the calibrator describes the sequence of steps (involving measurement standards, measuring systems and measurement procedures), each with increasing uncertainty, between the calibrator and its reference (calibration hierarchy) which define the traceability chain for the calibrator of choice. If the working calibrators are prepared in the laboratory, this step is added to the traceability chain and its uncertainty evaluated according to established procedures.

Many measurements involve multiple input quantities (VIM 2.50) and influence quantities (VIM 2.52). These should all be metrologically traceable resulting in the calibration hierarchy having a branched structure. The metrological traceability of all relevant input quantities and influence quantities must be demonstrated by the laboratory by means of documented calibrations. The effort involved in establishing metrological traceability for each quantity should be commensurate with its relative contribution to the measurement result. Any corrections (VIM 2.53) applied before presenting the measurement result must also be traceable, for example when correcting results for measurement bias (VIM 2.18).

- Check that the relevant properties of the calibrators – quantity values, uncertainties and metrological traceability – are fit for purpose and fully documented.

2.1.5 Appropriate equipment and degree of control

Knowing the target measurement uncertainty (see section 2.1.4) the analyst can select appropriate equipment and measurement standards. It is important to identify the input and influence quantities (VIM 2.50 and 2.52) which have a significant effect on the measurement result so that the uncertainty associated with the measurement of these quantities can be controlled appropriately.

For example, when measuring a volume of liquid there is a choice of apparatus available (measuring cylinder, volumetric flask, pipette, etc.). The measurement uncertainty associated with volumes measured using these devices will differ. When preparing a reagent, where the concentration is not critical to the measurement result, using a measuring cylinder may be acceptable. In contrast, the concentration of a calibration solution will have a direct influence on the measurement result so a higher degree of accuracy (smaller measurement uncertainty) in volume measurements is required.

In addition, when preparing a calibration solution different grades of chemical substances are often available. The appropriate grade (quality) should be selected for a particular application. For example, a commercial grade chemical with stated purity expressed as a mass fraction >95 %; a CRM (VIM 5.14) with certified purity expressed as a mass fraction of (99.6 ± 0.4) %.
The measurement uncertainty associated with the stated purity of the commercial grade chemical may be sufficient in a screening exercise to assess the degree of contamination. However, the CRM, which has documented metrological traceability and a smaller measurement uncertainty associated with the stated purity, would be more appropriate to use if the intention is to determine if a specific test sample complies with a legal limit. As mentioned above, the choice of calibrator fixes the calibration hierarchy (VIM 2.40), and thereby the traceability chain (VIM 2.42).

As a rule of thumb, the measurement uncertainty for those steps in the measurement procedure that have a significant effect on the result should be ≤1/5 of the target measurement uncertainty for the final result. When this condition is met, the individual steps concerned will make a negligible contribution to the overall measurement uncertainty.

When selecting measurement standards, certificates of analysis and calibration certificates should be considered in the light of the accuracies or approvals held by the issuing body. Values given on a certificate from a non-accredited facility may not have the degree of metrological traceability that the customer would anticipate. Producers of CRMs should comply with the requirements of ISO 17034 [10], as documented by their accreditation or otherwise verified by external assessment by customers or by self-assessment.

2.2 Calibration

Calibration in chemical analysis is frequently associated with calibrating a measuring instrument or measuring system. Typical features of these are:

- they contain chromatographic and/or spectrometric equipment;
- they need frequent (daily, weekly, monthly) calibration;
- the indication, i.e. the signal from the instrument or system, corresponds to a quantity other than that intended to be measured, e.g. an electric charge or potential, rather than amount-of-substance concentration or mass fraction.

The VIM 3 definition of calibration is divided into two parts. Figure 3 illustrates the first part as a calibration diagram (VIM 4.30).

As a function of an operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by measurement standards and corresponding indications with associated measurement uncertainties and, in a second step, uses this information to establish a relation for obtaining a measurement result from an indication (VIM 2.39).

In a calibration experiment, the analyst typically prepares a set of calibration solutions (also known as ‘calibrators’, ‘calibrants’, ‘standard solutions’ or ‘working standards’ (VIM 5.7)), i.e. a set of measurement standards. When measured, each of them gives rise to an indication (‘signal’, ‘response’). The relation \( y = f(x) \) between the indication and the corresponding quantity value is called a calibration curve (VIM 4.31). The uncertainty of the calibration will include contributions from the uncertainty of the measurement standards, variation in indications, and limitations in the mathematical model when establishing the relation \( y = f(x) \).

The analyst then analyses the unknown sample and uses the indication \( y_i \) to calculate a corresponding quantity value \( x_i \) from the calibration curve using the function \( x = f^{-1}(y) \). This second part of the definition is illustrated in the calibration diagram shown in Figure 4. If, for example, \( f(x) \) is defined as \( y = ax + bx \), where \( b \) is the slope of the curve and \( a \) is the \( y \)-axis intercept when \( x = 0 \), then \( f^{-1}(y) = (y - a)/b \).
Uncertainties arising from the indication, the calibration, and other corrections (VIM 2.53), contribute to the uncertainty of the measurement result.

Figure 4 – Schematic calibration diagram illustrating the second clause of the definition of calibration. The indication (‘signal’ $y_s$) from a sample corresponds to a quantity value $x_s$. The vertical and horizontal arrows indicate the standard uncertainty of the indication and of the quantity value respectively.

**2.3 Instrumental drift**

Instrumental drift is the gradual change over time (in either direction) in the indication provided by an instrument. Drift will affect the trueness of results if the true calibration parameters have changed between the time the instrument was calibrated and the time test samples are analysed. The extent to which an indication drifts therefore determines the required frequency of recalibration of the instrument. In analytical chemistry, a ‘drift correction standard’ with a known quantity value can be measured regularly to monitor the state of calibration of an instrument and determine whether adjustment to the configuration of the instrument or recalibration is required.

**2.4 Measurement standard**

A commercial laboratory regularly monitors the level of cadmium in drinking water. Legislation has specified that the quantity measured should be the mass concentration. For instrument calibration the laboratory uses a CRM (VIM 5.14) for which, according to the certificate, the value of the mass concentration of cadmium is $(1005 \pm 3) \text{ mg L}^{-1}$. In this case the quantity value is $1005 \text{ mg L}^{-1}$ and the value of the measurement uncertainty is $3 \text{ mg L}^{-1}$.

The CRM is an example of a measurement standard.

Measurement standards are used in all scientific areas. Material measures (VIM 3.6), e.g. volumetric flasks and CRMs, as well as measuring system (e.g. a reference thermometer) can function as measurement standards. When analytical scientists talk about calibrators or calibrants they simply mean measurement standards used in calibration.

**2.4.1 A hierarchy of measurement standards**

Various terms are used to indicate properties or uses of measurement standards. Figure 5 shows the relationship between the types of standard.

The ‘Vienna Standard Mean Ocean Water’ (VSMOW2) is an international measurement standard (VIM 5.2) for differential stable isotope
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1 ratio measurements. Many NMIs have a copy of the 51 This is done when the manufacturer or the user 1 former international prototype kilogram serving as a 52 investigates the commutability of a reference 3 national measurement standard (VIM 5.3) for 53 material (see section 2.6).
4 mass. According to VIM 3, by accurately weighing 5 and dissolving glucose of known purity to a known 6 volume, a chemist can prepare a primary standard 7 in the form of a solution of known concentration.
8 The standards mentioned above and secondary 9 measurement standards (VIM 5.5) as well as other 10 reference measurement standards (VIM 5.6) are 11 needed by producers of RMs (VIM 5.13), 12 instrument manufacturers and reference laboratories.
13 In addition, for routine applications laboratories may 14 use working standards (VIM 5.7) to check 15 measuring systems.
16 Two other types of measurement standard are 17 shown in Figure 5. An intrinsic measurement 18 standard (VIM 5.10) is a measurement standard 19 based on an inherent physical constant or inherent 20 physical property. For example, the triple point of 21 water is an intrinsic standard of 22 thermodynamic temperature. A travelling 23 measurement standard (VIM 5.8) is simply a 24 measurement standard intended for transport 25 between locations.

2.5 Calibrator

measurement standard used in calibration 27 (VIM 5.12)

Analytical scientists frequently use the term 28 calibrant, calibrator or standard when referring to 29 measurement standards used in calibration. Many 30 measurements are made using measuring 31 instruments and systems that require regular 32 calibration. An inherent part of the daily work for 33 the analyst is, therefore, preparation and/or 34 maintenance of this type of measurement standard.

Measurement standards are produced and used for 36 different purposes. There are a number of documents 37 which provide guidelines on choosing appropriate 38 measurement standards, for example reference 28.
39 Not all materials described by suppliers and 40 producers as measurement standards can be used 41 for calibration. The user needs to exercise caution 42 when purchasing ‘standards’ as the producer may 43 not interpret the requirements in the same way as the 44 VIM 3.

Many routine measuring systems are designed to 46 handle samples, without isolation or pre- 47 concentration of the analyte. In such cases it is also 48 necessary to demonstrate that the calibrator behaves in the same way as the routine samples.

Below are some examples of materials frequently 54 used by analysts when carrying out calibration.

• Materials produced by manufacturers and 56 intended to be used for calibration or 57 verification of a commercial measuring system, 58 e.g. a working measurement standard (VIM 5.7) with assigned quantity value and 59 measurement uncertainty for amount-of- 60 substance concentration of glucose in human serum, supplied as part of an in vitro diagnostic 61 medical device.

• RMs (VIM 5.13) and CRMs (VIM 5.14).

• Materials produced by authoritative bodies, e.g. a national or international pharmacopoeia, and intended to be used within a limited specified scope.

• Materials produced and characterised by the laboratory in-house, e.g. in the absence of commercial products.

For practical purposes materials used as calibrators 73 should have a statement of measurement 75 uncertainty and metrological traceability.

2.5.1. Check the ‘intended use’!

The content and layout of the documentation 77 supplied with RMs (VIM 5.13) shows considerable 79 variability. The headings may be adapted to meet the 80 requirements of a particular sector. It is not always 81 obvious to the user if the material can be used for 82 calibration.

A description of the ‘intended use’ is an essential 83 part of the certificate for a CRM (VIM 5.14) [29].
85 The primary purpose for which a CRM is issued by 86 the producer should be stated. Many materials are 87 not described as CRMs but still qualify as 88 calibrators. Check the documentation and your own 89 needs, e.g. in the case of medical laboratories the In 90 Vitro Diagnostics Directive 98/79/EC applies [18].

Some materials could very well qualify as 92 calibrators but the intention of the manufacturer of 93 the material and/or measuring system is different, 94 e.g. due to legislative restrictions. For instance, the 95 manufacturer of a measuring system will only take 96 responsibility if the prescribed calibrator is used. 97 The laboratory may, however, wish to check the 98 results by using other measurement standards, and 99 therefore be looking, e.g. for an appropriate
‘trueness control’ to check for measurement bias (VIM 2.18) during verification.

Below are three examples of statements from certificates, indicating their intended use.

- ‘The primary use of this material is for checking the calibration of automatic density meters used in industry to determine alcoholic strength ...’.
- ‘The material is primarily intended to be used to calibrate serum-based protein standards and control products of organisations which offer such preparations for the quantification of C-reactive protein by immunoassay.’
- ‘The material is primarily intended to be used to control the performance of the IFCC reference procedure ... When the material is used as a calibrator in a particular assay, the commutability should be verified for the assay concerned.’

2.6 Commutability of a reference material

The wording of the definition is slightly different from ones that appear in some ISO Standards and Guides but the principle is the same. As mentioned in section 2.5 it is important to check that the RM (VIM 5.13) chosen as a calibrant behaves in the same way as the samples. This is termed the commutability of a reference material. Commutability is of particular concern where methods are very sensitive to the sample matrix or ‘physical form’ of the analyte of interest.
Figure 6 – Schematic to illustrate the commutability of a reference material, showing the measurement results and their associated confidence intervals. In case (a) the reference material is considered to be commutable – the relation between the indication obtained for the reference material (M1) and the indication obtained for the sample (S1) is independent of the measurement procedure. In case (b) the reference material is not commutable – the relation between the indication obtained for the reference material (M2) and the indication obtained for the sample (S1) is different for the two measurement procedures.
3 Measurement uncertainty

This chapter describes the terminology relating to measurement uncertainty. The Guide to the expression of uncertainty in measurement (GUM (published as JCGM100 [33] and ISO/IEC Guide 98-3 [34]), describes the principles of uncertainty evaluation. Further information on how to evaluate measurement uncertainty can be found in the Eurachem/CITAC Guide, Quantifying uncertainty in analytical measurement [35]. An overview of the different approaches is given in a Eurolab report [36]).

3.1 Measurement uncertainty

Measurement uncertainty provides a quantitative indication of the quality of a measurement result. Synonyms are ‘uncertainty’ and ‘uncertainty of measurement’.

This definition expresses the fact that parameters estimates of measurement uncertainty can be used to describe the dispersion of distributions, e.g. expressed in a number of different ways, e.g. as a standard deviation, are usually positive. The standard deviation or a confidence interval. why it is necessary to declare what is included in the estimates they must be expressed in the same form, estimate of measurement uncertainty. This does so some conversion may be necessary. Following not mean we can choose what to include and what to ISO guidelines, uncertainty estimates should be leave out. There are many approaches to evaluating measurement uncertainty and these are described (see below) before they are combined [34].

Calculating the measurement result may involve reagent concentrations and values from measuring instruments, calibrators and RMs (VIM 5.13). All of these values have some uncertainty; and their uncertainties will make the calculated result uncertain. Incompletely known properties of the sample itself – such as possible interferents, matrix effects and effects on analyte recovery – as well as sampling and the manual operations carried out during the measurement, also contribute to measurement uncertainty. This means that, for a specific calculated result, there is not one but a whole range of quantity values (VIM 1.19) that could reasonably have given rise to the measured quantity value. Measurement uncertainty describes the dispersion of these possible values.

The result of a measurement consists of two quantitative parts: i) the measured quantity value and ii) the measurement uncertainty. When the result is reported with the uncertainty, it can be presented in the format (value ± uncertainty) and unit. For example, (5.5 ± 0.5) mL corresponds to the interval (5.0 – 6.0) mL (see Figure 7). The uncertainty is interpreted as providing an interval within which the value of the measurand is believed to lie. The uncertainty is usually reported as the expanded uncertainty (VIM 2.35) (see section 3.1.1).

In certificates of analysis, test reports etc., the letter u denotes uncertainty. However, there are different forms of uncertainty:

- $u(x_i)$ – the standard uncertainty for quantity $x_i$, is an uncertainty expressed as a standard deviation;
- $u(y,x_i)$ – the contribution to the standard uncertainty of the measurand caused by the quantity $x_i$;
- $u_c$ – the combined standard uncertainty (VIM 2.31) for the measurand, is a mathematical combination of several individual standard uncertainties;
- $U$ – the expanded uncertainty (VIM 2.35) is normally what the laboratory reports to the customer. The expanded uncertainty provides an interval within which the value of the measurand is believed to lie with a higher level.
of confidence. The value of $U$ is obtained by multiplying the combined standard uncertainty $u_c$ by a coverage factor $(VIM\ 2.38)$ $k$, i.e. $U = k \cdot u_c$. The choice of the factor $k$ is based on the level of confidence desired.

It follows that $u(y, x) < u_c < U$. These uncertainties are often expressed in relation to the value, e.g. as the relative standard measurement uncertainty $(VIM\ 2.32)$.

### 3.1.2 Uncertainty evaluation

The overall performance of a measurement procedure is studied during method development and method validation (see chapter 4). Individual sources of uncertainty will be identified during this process and studied in detail if they are found to be significant compared to the overall requirements. The laboratory will aim to remove sources of significant uncertainty until the measurement procedure is deemed to be fit for purpose. This means that the laboratory should know the maximum measurement uncertainty that can be accepted by the customer for a specific application. This is called the target measurement uncertainty $(VIM\ 2.34)$. For example, the EU legislation regarding the official control for monitoring the status of surface waters and groundwater states that laboratories performing measurements should use measurement procedures capable of providing results with an ‘uncertainty of measurement of 50 % or below ($k = 2$) estimated at the level of the relevant environmental quality standard [40]. For example, the environmental quality standard for lead in surface waters is 7.2 µg L$^{-1}$ so the target measurement uncertainty is 3.6 µg L$^{-1}$ [41]. A Eurachem/CITAC Guide [17] provides an overview of the possible approaches to setting the target measurement uncertainty in various different scenarios.

During validation/verification of a measurement procedure the overall measurement precision of the method and the uncertainty of the measurement bias $(VIM\ 2.18)$ are often evaluated. In many cases combining these two uncertainty components using the law of propagation gives a reasonable estimate of the standard uncertainty of the results obtained when using the measurement procedure [35-39]. Since measurement uncertainty can be estimated in different ways, the resulting value should be accompanied by an explanation, or by reference to available information, of how the uncertainty was evaluated. The customer is then in a position to interpret the uncertainty (see also section 3.2).

The minimum level of uncertainty associated with a given measurement result is implicit in the definition of the measurand (definitional uncertainty, $(VIM\ 2.27)$). For example, the measurand, ‘volume of liquid contained in a volumetric flask’ has a larger definitional uncertainty than the measurand, ‘volume of water contained in a volumetric flask at 20 °C’. In the case of the former neither the nature of the liquid nor the temperature of liquid are specified. The definitional uncertainty depends on the analyst’s ability to define the measurand adequately. No matter how much effort is put into the measurement, the definitional uncertainty cannot be reduced unless a new, more detailed definition of the measurand is given. For example, the definitional uncertainty associated with the measurement of the total amount of protein in a milk sample will be larger than the definitional uncertainty associated with the distribution of individual protein fractions in the milk sample. It is good practice to define the measurand in such a way that the definitional uncertainty is negligible for the purposes of the measurement.

### 3.2 Uncertainty budget

A statement of a measurement uncertainty, of the components of that measurement uncertainty, and of their calculation and combination $(VIM\ 2.33)$.

All known sources of measurement uncertainty have to be evaluated and information about them summarised in an uncertainty budget. The word budget is used in a different sense from that in common usage; it is not an upper limit of measurement uncertainty; it is a statement of the sources of uncertainty and their values. The budget should also include the measurement model $(VIM\ 2.48)$ and type of uncertainty evaluation. Two types of uncertainty evaluation are defined in VIM 3 and the ISO Guide to the expression of uncertainty in measurement [34]. An uncertainty contribution based on statistical analysis of quantity values obtained under defined conditions is a Type A evaluation $(VIM\ 2.28)$. A contribution obtained by any other means, is a Type B evaluation $(VIM\ 2.29)$. An example of Type A evaluation is the standard deviation of the mean of the results from ten replicate measurements performed under repeatability conditions $(VIM\ 2.20)$. An uncertainty value taken from an RM $(VIM\ 5.13)$ certificate is an example of a Type B evaluation. The uncertainty budget may also include the applied probability density function and degrees of confidence.
freedom for each uncertainty contribution, and the of the metal is obtained from the accompanying coverage factor (VIM 2.38) used to calculate the information available from the producer and expanded uncertainty (VIM 2.35).

An example of an uncertainty budget for the mass concentration of a cadmium calibration standard is shown in Table 2. It is based on an example from the Eurachem/CITAC Guide [35]. The mass concentration of cadmium, \( \rho_{Cd} \) (mg L\(^{-1}\)) is given by:

\[
\rho_{Cd} = \frac{(1000 \cdot m \cdot P)}{V}
\]

where \( m \) is the mass in mg of cadmium, \( P \) its purity, \( V \) the volume of the flask in mL. Each of these terms will introduce uncertainty in the calculated concentration of the solution, as shown in the uncertainty budget in Table 2. The uncertainty in the mass is obtained from the calibration certificate provided by an accredited calibration laboratory and their recommendations on the estimation of the uncertainty under the conditions of use. The purity of the metal is obtained from the accompanying information available from the producer and converted to a standard uncertainty (VIM 2.30) assuming a rectangular distribution. The uncertainty in the volume of the flask consists of three components – calibration \( (u_{cal}) \), repeatability \( (u_{rep}) \), and the difference between the temperature at which the calibration was made and the temperature when the flask is used \( (u_{temp}) \).

An example of an uncertainty budget for a test method for the determination of the mass concentration of ammonium nitrogen NH\(_4\)-N in water, validated in a single laboratory, is shown in Table 3.

The mass is obtained from the calibration certificate and the volume of the flask in mL. Each of these terms will introduce uncertainty in the calculated concentration of ammonium nitrogen NH\(_4\)-N in water, validated in a single laboratory, is shown in Table 3.

**Table 2 – Uncertainty budget for the mass concentration of a cadmium calibration standard; values taken from the Eurachem/CITAC Guide [35].** The standard uncertainty in \( \rho_{Cd} \) was calculated by combining the relative standard measurement uncertainties and then multiplying by the value for \( \rho_{Cd} \).

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Value</th>
<th>Standard uncertainty, ( u(x_i) )</th>
<th>Unit</th>
<th>Relative standard uncertainty ( u(x_i)/x_i )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( m )</td>
<td>100.28</td>
<td>0.050</td>
<td>mg</td>
<td>0.00050</td>
</tr>
<tr>
<td>( P )</td>
<td>0.9999</td>
<td>5.8 \times 10^{-5}</td>
<td>g/g</td>
<td>5.8 \times 10^{-5}</td>
</tr>
<tr>
<td>( V^* )</td>
<td>100.00</td>
<td>0.066</td>
<td>mL</td>
<td>0.00066</td>
</tr>
<tr>
<td>( \rho_{Cd} )</td>
<td>1002.70</td>
<td></td>
<td>mg/L</td>
<td></td>
</tr>
<tr>
<td>( \rho_{Cd} ), combined standard uncertainty</td>
<td>0.84</td>
<td></td>
<td>mg/L</td>
<td></td>
</tr>
<tr>
<td>Expanded uncertainty ( k = 2 )</td>
<td>1.7</td>
<td></td>
<td>mg/L</td>
<td></td>
</tr>
</tbody>
</table>

*Volume contributions

| \( u_{cal} \) | 0.041 | mL |
| \( u_{temp} \) | 0.048 | mL |
| \( u_{rep} \) | 0.020 | mL |
| Volume, combined standard uncertainty | 0.066 | mL |

TAM 2019
Table 3 – Uncertainty budget for the mass concentration of ammonium nitrogen NH$_4$-N in water. Values taken from the Nordtest Handbook [39]. The relative standard measurement uncertainty for the intermediate precision ($u(P)$) is combined with the relative standard measurement uncertainty associated with the bias estimate ($u(bias)$). The expanded uncertainty is given with a coverage factor of $k = 2$.

<table>
<thead>
<tr>
<th>Concentration range (µg/l)</th>
<th>Estimate of intermediate precision</th>
<th>$u(P)$</th>
<th>Estimate of uncertainty associated with bias</th>
<th>$u(bias)$</th>
<th>Combined uncertainty</th>
<th>Expanded uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-500</td>
<td>Control sample covering the whole analytical process</td>
<td>1.67 %</td>
<td>Proficiency tests</td>
<td>2.73 %</td>
<td>3.20 %</td>
<td>7.0 %</td>
</tr>
</tbody>
</table>
4 Verification, validation and method performance

4.1 Verification and validation

This chapter describes the terminology relating to verification, validation and method performance. Further information on method validation can be found in the Eurachem guide on the fitness for purpose of analytical methods [42].

4.1.1 Verification of a validated method

In the case where a method that has been validated previously (e.g. a standard method) is being used, the laboratory has to provide objective evidence that the stated performance characteristics of the method can be achieved. Consider the following example.

A laboratory is asked by a customer to perform a measurement of the mass fraction of acrylamide in bakery products, such as bread and biscuits. As a first step, the laboratory agrees with the customer the measurement requirements in terms of working range and expanded uncertainty (VIM 2.35). Then, it checks if a standard method exists, that has been proven, by interlaboratory studies, to fulfil the requirements for the intended use. It finds that the method EN 16618:2015 ‘Determination of acrylamide in food by liquid chromatography tandem mass spectrometry (LC-ESI-MS/MS)’ covers bakery products in its scope, and that both the working range and the expanded uncertainty fulfil the agreed requirements for the intended use. The laboratory must then verify, via an experimental assessment, that the stated method performance can be achieved.

The following sections describe the performance characteristics defined in VIM 3 which are commonly studied during verification/validation.

4.3 Selectivity of a measuring system

The definition of selectivity in VIM 3 is consistent with the more familiar definition proposed by IUPAC: ‘the extent to which the method can be used to determine particular analytes in mixtures or matrices without interferences from other components of similar behaviour.’ [43]. For example, gas chromatography using a mass spectrometer as the detector (GC-MS) would be considered more selective than gas chromatography using a flame ionisation detector (GC-FID), as the mass spectrometer provides additional information which assists with confirmation of identity. The use of the term specificity is not recommended by IUPAC and is not defined in VIM 3.
4.4 Measuring interval

Within the measuring interval, quantities (e.g., mass concentration) can be measured with a specified uncertainty using a stated measurement procedure. The other phrases commonly used for this concept are: ‘working range’ and ‘measurement range’ (the latter is used in ISO/IEC 17025 [4]). The common usage of the term ‘measurement range’ or ‘measuring range’ to denote measuring interval is acknowledged in Note 1 of the VIM definition. However, it should be noted that in VIM 3, the term ‘interval’ denotes a set of numbers defined by its end values whereas the term ‘range’ or ‘range of interval’ is restricted to the difference between the highest and the lowest values of an interval.

Following these conventions, in the example shown in Figure 8 the measuring interval is 0.3 to 0.9, written as [0.3, 0.9], and the range is 0.6.

The lower limit of the measuring interval is often considered to be the limit of quantification (LOQ) (a concept not defined in VIM 3). The upper limit is usually determined by the unacceptance change in measurement uncertainty or in the sensitivity (VIM 4.12), for example the plateauing effect observed at high absorbance values in UV/VIS spectroscopy. Figure 8 illustrates the relationship between some of the key terms related to ‘measuring interval’. The LOD is below the LOQ.

The measuring interval should be compatible with the analytical requirement and, therefore, fit for the purpose. If, for example, the analyte level in samples is expected to be well above the LOQ, the laboratory may not need to cover the entire interval illustrated in Figure 8.

Many methods rely on the test sample received in the laboratory being processed (digested, extracted, diluted, for example) before it can be presented to the measuring instrument and a signal recorded. In such cases there are two measuring intervals to consider – the instrument measuring interval (described in the VIM definition) and the measuring interval for the measurement procedure as a whole (including any sample preparation steps). The evaluation of these different measuring intervals is discussed in detail in the Eurachem guide [42].

The sensitivity of a measuring system is, in the case of linear dependence, given by the slope of the calibration curve (VIM 4.31).

4.5 Detection limit

measured quantity value, obtained by a given measurement procedure, for which the probability of falsely claiming the absence of a component in a material is β, given a probability α of falsely claiming its presence (VIM 4.18).

VIM defines detection limit in terms of a measured quantity value.

This is not consistent with the IUPAC (and other) definitions currently used in analytical chemistry which refer to a true quantity value (VIM 2.11) rather than a measured value. It is not clear whether the difference is intentional or, if so, how it can be implemented. The description below therefore follows recommendations made by IUPAC for establishing detection capability for analytical methods [44].

Many analysts will be familiar with calculating the limit of detection (LOD) for a measurement procedure by multiplying a standard deviation, s (obtained from the results of the analysis of a blank sample or a sample containing a low level of the analyte) by an appropriate factor (typically between 3 and 5). The multiplying factor is based on statistical reasoning. The following text explains the background to the commonly used factor of 3.

The discussion deals with LOD in terms of concentration but it applies equally to other quantities, e.g. mass fraction. The aim when determining the LOD is typically to establish the lowest concentration of the analyte present in a
sample that can be detected, using a given measurement procedure, with a specified level of confidence. Defining the LOD is a two-step process. First a ‘critical value’ is established. This value is set so that the probability of obtaining a measurement result that exceeds the critical value is no greater than $\alpha$, if a sample actually contains none of the analyte. The critical value sets a criterion for declaring a sample to be ‘positive’. A false positive probability of $\alpha = 0.05$ is generally used; this leads to a critical value of approximately $1.65s$ (where $s$ is the standard deviation of a large number of results for a blank sample or a sample containing a low concentration of the analyte, and $1.65$ is the one-tailed Student $t$-value for infinite degrees of freedom at a significance level, $\alpha = 0.05$). The critical value is indicated on the vertical axis in Figure 9 to emphasise the fact that it is a measured value. The critical value is most conveniently expressed in terms of concentration, though in principle it may be any observation, such as peak area. Any result exceeding the critical value should be considered as indicating an analyte level that is significantly different from zero.

However, if the true value for the concentration in a sample were exactly equal to the critical value (expressed in terms of concentration), approximately half of the measurement results would be expected to fall below the critical value, giving a false negative rate of 50%. This is illustrated by the distribution shown with the broken line in Figure 9. A false negative rate of 50% is obviously too high to be of practical use; the method does not reliably give results above the critical value if the true value for the concentration is equal to the critical value.

The LOD (also known as ‘minimum detectable value’) is intended to represent the true concentration for which the false negative rate is acceptable given the critical value. The false negative error, $\beta$, is usually set equal to the false positive error, largely for historical reasons (IUPAC recommends default values of $\alpha = \beta = 0.05$). Using $\alpha = \beta = 0.05$, the LOD is therefore located $1.65s$ above the value specified for the critical value. This is illustrated by the shaded distribution on the horizontal axis in Figure 9. The factor for calculating the LOD with $\alpha = \beta = 0.05$ is thus $1.65 + 1.65 = 3.30$, which is frequently rounded to 3.0. This is based on several approximations which are described in the literature [44].

4.6 Measurement trueness

Measurement trueness expresses the hypothetical ability of a measurement procedure to yield results close to expected reference quantity values, such as the value of a CRM (VIM 5.14). Trueness is not a quantity and therefore cannot be expressed numerically. However, trueness is inversely related to systematic measurement error (VIM 2.17) which may be estimated as measurement bias (VIM 2.18). An example of the estimation of bias as the difference between the mean value of several measurement results and a reference quantity value is shown in Figure 10. Bias can also be reported as the ratio of measured and reference quantity values.

![Figure 9 – Illustration of the statistical basis for detection limit calculations.](image)

![Figure 10 – Schematic illustration of the estimation of measurement bias. The mean of several measurement results is compared with a reference quantity value (note that the uncertainty in the reference value is not shown).](image)
A measurement bias may be due, e.g. to inappropriate calibration or lack of selectivity. VIM 3 defines three measurement conditions: repeatability (see section 4.5), Where appropriate, the effect of known systematic errors on measurement results can be removed by introducing a correction. (VIM 2.53) Based on the estimated bias, e.g. the reading of a digital thermometer can be corrected on the basis of the bias observed during calibration. However, any factor used to make a correction will also have an associated uncertainty. An estimate of the bias in measurement results produced by a laboratory can be obtained by measuring the quantity value of one or more RMs under conditions over a short time period. Measurement (VIM 5.13) several times under repeatability is often used to provide an estimate of conditions (VIM 2.20) or under intermediate within-run (also known as within-batch or intra-precision conditions (VIM 2.22), and calculating assay variability in results. Under intermediate the mean value. The estimate of bias is then the expanded uncertainty (VIM 2.35) of 0.21% (k = 2). The measurement bias determined under intermediate conditions using this CRM is therefore estimated as 63.53 – 63.23 = 0.3%. The bias can also be expressed as a relative value (percent), i.e. 0.3/63.23 × 100 = 0.47%. The measurement error (VIM 2.19) and is a measure of how close results are to one another. Measurement results cannot be corrected to remove the effect of random error but the size of the random error can be reduced by making replicate measurements and calculating the mean value.

Measurement precision is expressed numerically using measures of imprecision such as the standard deviation calculated from results obtained by carrying out replicate measurements on a suitable

### 4.7 Measurement precision

#### Closeness of agreement between indications or measured quantity values obtained by replicate measurements on the same or similar objects under specified conditions (VIM 2.15)

The measurement precision is related to random measurement error (VIM 2.19) and is a measure of how close results are to one another. Measurement results cannot be corrected to remove the effect of random error, but the size of the random error can be reduced by making replicate measurements and calculating the mean value.

Measurement precision is expressed numerically using measures of imprecision such as the standard deviation calculated from results obtained by carrying out replicate measurements on a suitable
Figure 11 illustrates the relationship between measurement repeatability, intermediate measurement precision and measurement reproducibility in terms of the observed imprecision, which is estimated as a standard deviation, $s$. In the figure, ‘between-injections’ refers to replication of only the end measurement step of a multistage measurement procedure (e.g. repeat injections of portions of a test solution onto a gas chromatograph). Replicating this action would give the measurement repeatability of the final measurement stage, but would exclude the effect of random errors associated with any sample pre-treatment or clean-up steps. ‘Within-run replicates’ represents replication of the whole measurement procedure under repeatability conditions.

As the conditions of measurement become more variable (e.g. moving from replicating only part of the measurement procedure (‘between-injections’) to replicating the entire measurement procedure under repeatability, intermediate precision or reproducibility conditions) the observed imprecision of measurement results generally increases.

The ‘shots’ on the target represent individual measurement results; the reference quantity value is the centre of the target. The best accuracy (lowest measurement uncertainty) is achieved in case d) where the individual results are all close to the reference value. In cases c) and d) there is no significant bias as the results are all clustered in the centre of the target. However, the precision is poorer in case c) as the results are more widely scattered. The precision in case b) is similar to that in case d). However, there is a significant bias in case b) as all the results are off-set from the centre in the same area of the target. The accuracy is poorest in case a) as the results are widely scattered and are off-set to the right of the target.

Measurement accuracy cannot be used to give a quantitative indication of the reliability of measurement results. Here an estimate of measurement uncertainty is required (see chapter 3).

**4.8 Measurement accuracy**

closeness of agreement between a measured quantity value and a true quantity value of a measurand (VIM 2.13)
Appendix

Table A 1 Concepts discussed in this Guide, synonyms and the VIM reference. Concept in bold is the preferred term. The VIM reference is shown in bold for concepts where the full definition is given in this Guide.

<table>
<thead>
<tr>
<th>Concept</th>
<th>Synonym</th>
<th>VIM Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>base quantity</td>
<td></td>
<td>1.4</td>
</tr>
<tr>
<td>base unit</td>
<td></td>
<td>1.10</td>
</tr>
<tr>
<td>blank indication</td>
<td>background indication</td>
<td>4.2</td>
</tr>
<tr>
<td>calibration</td>
<td></td>
<td>2.39</td>
</tr>
<tr>
<td>calibration curve</td>
<td></td>
<td>4.31</td>
</tr>
<tr>
<td>calibration diagram</td>
<td></td>
<td>4.30</td>
</tr>
<tr>
<td>calibration hierarchy</td>
<td></td>
<td>2.40</td>
</tr>
<tr>
<td>calibrator</td>
<td></td>
<td>5.12</td>
</tr>
<tr>
<td>certified reference material</td>
<td>CRM</td>
<td>5.14</td>
</tr>
<tr>
<td>combined standard measurement uncertainty</td>
<td>combined standard uncertainty</td>
<td>2.31</td>
</tr>
<tr>
<td>commutability of a reference material</td>
<td></td>
<td>5.15</td>
</tr>
<tr>
<td>correction</td>
<td></td>
<td>2.53</td>
</tr>
<tr>
<td>coverage factor</td>
<td></td>
<td>2.38</td>
</tr>
<tr>
<td>definitional uncertainty</td>
<td></td>
<td>2.27</td>
</tr>
<tr>
<td>derived quantity</td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td>derived unit</td>
<td></td>
<td>1.11</td>
</tr>
<tr>
<td>detection limit</td>
<td>limit of detection</td>
<td>4.18</td>
</tr>
<tr>
<td>displaying measuring instrument</td>
<td></td>
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19. JCTLM Database of higher-order reference materials, measurement methods/procedures and services. Available at www.bipm.org/jctlm/.


