Eurachem

A focus for analytical chemistry in Europe

Terminology in Analytical Measurement

Introduction to VIM 3

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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 ISO Guide 99 [1] and as JCGM 200:2008, which is available free of charge from the BIPM website [2]. A corrigendum to JCGM 200:2008 was published in May 2010 [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’. The VIM 3 is a consistent set of concepts each described by a unique term, the ‘label’ of the concept. VIM 3 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; this makes interdisciplinary conversations very difficult and confusing. 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 many peculiarities in any language, 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, e.g. the standards underpinning laboratory accreditation such as ISO/IEC 17025 [4] and ISO/IEC 17043 [5], and international guides including ISO Guides 34 [6] and 35 [7]. Definitions from the second edition of VIM [8] are given in ISO 15189 [9]. Second, those involved with education and training have realised that often there is confusion about both concepts and terminology. In addition the strict definitions are often written in a language that is difficult to understand. This is true for bench scientists 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 of amount and as such has never been so defined in the earlier editions of VIM. Quantity is a generic concept for things we measure, e.g. length, mass, time and 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 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 terms for the same concept. If more than one term is given in VIM 3, the first term is the preferred one, and it is used throughout this Guide as far as possible.

This Guide takes account of the amendments given in the corrigendum to JCGM 200:2008 [3].

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 terms which includes, mass fraction, mass concentration, amount of substance concentration etc.

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 [10].

The following abbreviations and symbols are used in this Guide.

Abbreviations

BIPM	Bureau International des Poids et Mesures (International Bureau of Weights and Measures)
CCQM	Comité Consultatif pour la Quantité de Matière: Métrologie en Chimie (Consultative Committee for Amount of Substance – Metrology in Chemistry)
CGPM	Conférence Générale des Poids et Mesures (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	detection limit (limit of detection)
LOQ	limit of quantitation/quantification
NIST	National Institute of Standards and Technology (USA)
NMI	National Metrology (or Measurement) Institute
pp'-DDE	*p,p'*-dichlorodiphenyldichloroethylene
PT	proficiency testing
RM	reference material
SI	Système International d’Unités (International System of Units)
SOP	standard operating procedure
SRM®	Standard Reference Material (as used by NIST)

VIM	Vocabulaire international de métrologie – Concepts fondamentaux et généraux et termes associés (VIM) (International vocabulary of metrology – Basic and general concepts and associated terms)
VSMOW	Vienna Standard Mean Ocean Water
WHO	World Health Organization
XRF	x-ray fluorescence

Symbols

α	probability for a Type I error (false positive)
β	probability for a Type II error (false negative)
ρ	mass concentration
k	coverage factor used to calculate expanded measurement uncertainty
s	standard deviation
u	standard measurement uncertainty
U	expanded measurement uncertainty

1.0. General Metrology

1.1 Metrology

> science of **measurement** and its application (VIM 2.2)

Metrology includes 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**.

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') [8], e.g. the volume of gasoline dispensed into a vehicle, the speed at which my car was travelling when the police stopped me(!), the number concentration of red cells in the blood sample taken yesterday from Mr. Smith.

The description of the (particular) **quantity** we intend to measure (also called **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, such as colour of a spot test in chemistry (e.g. a home pregnancy test), or molecular sequences (e.g. of amino acids in a polypeptide, of nucleotides in a DNA fragment). Such important properties, that have no size, are however acknowledged in the Vocabulary 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. However, in ISO 15189 the term 'examination' is used both for the determination of **nominal properties** and for **measurement procedures** [9].

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** (VIM 5.13).

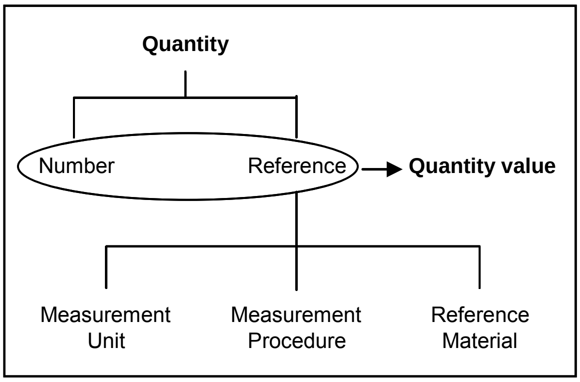

Figure 1 *Some terms related to Quantity. Example: the quantity is mass density. The quantity value could be 1.213 kg L^{-1} where 1.213 is the number and kg L^{-1} is the reference which, in this case, is a measurement unit.*

Consider an example from the field of chemical **measurement**. The mass concentration of lead in a paint sample was reported to be 10 mg L^{-1}. In this case the 'mass concentration of lead in paint' is the specific **quantity** (the **measurand**). The **quantity value** is 10 mg L^{-1}, where 10 is the number and mg L^{-1} (the **measurement unit**) is the reference. If an empirical method is used, e.g. the estimation of the fibre content of a breakfast cereal, then the reference would be both the **measurement unit** and the **measurement procedure** used.

In clinical chemistry 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 **reference material**, periodically prepared and approved by WHO and known as a WHO International Standard.

1.5 Nominal quantity value

rounded or approximate **value** of a characterizing **quantity** of a **measuring instrument** or **measuring system** that provides guidance for its appropriate use (VIM 4.6)

In VIM 3 the word 'nominal' is used in a different sense in **nominal quantity value** and **nominal property** (see section 1.3).

A volumetric flask may be marked 100 mL, this is its **nominal quantity value** (in general use this is called the nominal value). The actual value of the volume of this particular 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 0.10 mL the actual volume will lie in the range 99.90 mL to 100.10 mL.

1.6 Reference quantity value

quantity value used as a basis for comparison with values of **quantities** of the same **kind** (VIM 5.18)

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

- The **quantity value** given on the certificate of a **certified reference material (CRM)** (VIM 5.14) with its associated **measurement uncertainty** is a **reference quantity value** for the particular property to which it relates. Such a value may be used in the **calibration** of a **measuring instrument** which may then be used for determining the value of **quantities** of the same **kind** (VIM 1.2) (see section 1.9.1).
- When a mercury-in-glass thermometer is calibrated against a standard thermometer in a calibration laboratory using a **reference measurement procedure**, the values provided by the standard thermometer are **reference quantity values**.
- Analysts use the value assigned to a **CRM** as a **reference quantity value** for the assessment of the **trueness** of a **measurement procedure**.
- The values of a set of solutions of known concentration, analysed to build a **calibration diagram** (VIM 4.30), are **reference quantity values**.
- 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 **certified reference material**. In this context, the value assigned to any of these materials is deemed to be a **reference quantity value**.

1.7 System of quantities

set of **quantities** together with a set of non-contradictory equations relating those quantities (VIM 1.3)

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 quantities**, which are agreed and defined by The General Conference on Weights and Measures (CGPM), are shown in Table 1. This is called the **International System of Quantities** [11].

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)

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 adopted as the only legal **system of units** within the European Union [11, 12]. The **base quantities** and their corresponding **base units** (VIM 1.10) are shown in Table 1. The definitions of the **base units** can be found in references 11 and 12.

Many other **quantities** within the **SI** are expressed as relations between those shown 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. $\frac{\text{kg}}{\text{m}^3}$ which is usually written as kg/m^3 or kg m^{-3}.

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

Base quantity	Base unit (symbol)
length	metre (m)
mass	kilogram (kg)
time	second (s)
electric current	ampere (A)
thermodynamic temperature	kelvin (K)
amount of substance	mole (mol)
luminous intensity	candela (cd)

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

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, gasoline by volume and price quoted per litre (L) [10]. If we say the mass of an apple is 0.15 kg, this means that the mass of the apple is 0.15 x mass of the international prototype kilogram. '*The mass of the international prototype kilogram*' is the **measurement unit**. To obtain the number 0.15 you have to compare the value indicated for the apple with the value indicated for a reference mass, i.e. the mass used to calibrate the balance. The reference mass in turn is compared with the kilogram. 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** is somewhat arbitrary, but the concept that only similar items can be compared is well understood. **Quantities** of the same **kind** will have the same unit but two **quantity values** having the same unit do not have to be of the same **kind.** The unit of mass density and of mass concentration is kg m^{-3} but these are not **quantities** of the same **kind**. The **measurement unit** of both frequency and activity of radio nuclides is s^{-1} but they are not **quantities** of the same **kind**. In this example the unit in each case is given a special name, namely hertz (Hz) and becquerel (Bq), respectively.

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 fibre content of food. 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

process of experimentally obtaining one or more **quantity values** that can reasonably be attributed to a **quantity** (VIM 2.1)

A **measurement** is a series of actions (steps, stages) taking place in a defined manner. Some **measurements** are a single step, others have many stages. There is potential for controversy as some regard **measurement** as the amount indicated by an instrument, 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 the **measurement procedure** measures what it is intended to measure and the **uncertainty** in the **measurement results** is acceptable.

1.11 Measurand

quantity intended to be measured (VIM 2.3)

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. The analyst should realise that **measurand** is not just 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 in clinical chemistry [13]:

- mass of protein in 24-hour urine
- amount of substance concentration of glucose in plasma.

In each case the complete statement represents the **measurand**. The analytes are protein and glucose, respectively.

The definition of the **measurand** is critical, in 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 **measurand** requires at least the description 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:

- Example 1: mass fraction (mg kg^{-1}) of dimetridazole in animal feeding stuffs;
- Example 2: amount of substance concentration (mol L^{-1}) of sodium in serum.

In the **measurement** of the mass fraction of cadmium in a soil sample, the sample drying conditions (e.g. dried at 105 °C, for 2 h) 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** (standard method), e.g. 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.

1.12 Measurement procedure

detailed description of a **measurement** according to one or more **measurement principles** and to a given **measurement method,** based on a **measurement model** and including any calculation to obtain a **measurement result** (VIM 2.6)

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 principle is the bracketed word in the following examples.

- 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).

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** requires a generic description of the operations involved.

The last and 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 **measurement procedure** may be one or more standard operating procedures (SOP). In ISO/IEC 17025 [4] a different term, 'test method', is used for **measurement procedure** but it should be noted that the requirements of the Standard apply both to **measurements** and examinations. As mentioned earlier, ISO 15189 [9] uses the term 'examination' to refer both to the determination of **nominal properties** and to **measurement procedures**. In ISO/IEC 17025 the test method also 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 the Standard.

A **measurement procedure** includes a description of how **measurement results** are obtained and reported, including any calculation. A **measurement result** is generally expressed as a single **measured quantity value** and a **measurement uncertainty**. The **measurement procedure** should include an estimate of the **measurement uncertainty** which may be used when reporting **measurement results**.

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)

Reference measurement procedures are well characterised and will normally have a very small **measurement uncertainty**. For example, in the clinical sector, to comply with the requirements of the *In vitro* Diagnostics Directive [14] manufacturers are required to use **reference measurement procedures** or **certified reference materials** (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 **reference measurement procedures** [15], e.g. NIST LC-MS reference method for cortisol in blood serum [16].

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

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)

Primary reference measurement procedures (also known as primary methods of measurement) 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.

1.15 Measurement result

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

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

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 end-user 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 end-user. 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 end-user'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 information provides the end-user with sufficient information on the reliability of the **measurement result**, to be taken into account when for example it is to be 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.

The requirements of ISO/IEC 17025 [4] are that information on **measurement uncertainty** is required in test reports only when it is relevant to the validity or application of the test results, when the end-user's instructions so requires or when the **uncertainty** affects compliance to a specification limit.

1.16 Measured quantity value

quantity value representing a **measurement result** (VIM 2.10)

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 replicate **indications** Although each **indication** provides a corresponding **measured quantity value**, the final value is usually calculated from the set of values as an average or median which will usually have a lower **measurement uncertainty** than the individual values. In many cases, a **measurement result** requires more than one **measured quantity value**. For example if the **measurement result** is to be expressed on a dry weight basis the mass of the sample after drying and the mass fraction of the analyte(s) of interest are both required.

1.17 Measurement error

measured quantity value minus a **reference quantity value** (VIM 2.16)

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 an individual 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** (VIM 2.17) and **random** (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

quantity value provided by a **measuring instrument** or a **measuring system** (VIM 4.1)

Most **measurements** are based on **indications** provided by **measuring instruments** 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**. In most cases in analytical science, analysts rely on the **measurement** of physical **quantities** such as mass of precipitate, volume of titrant, or 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 an 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 it states 'supposed to be absent').

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 a digital output in the form of a number, e.g. an electronic balance. The **indication** may be presented in visual/acoustic form or be transferred to another device, e.g. 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 or **certified reference materials** (VIM 5.14).

These categories of **measuring instruments** are not normally distinguished in chemistry.

1.21 Metrological comparability of measurement results

comparability of **measurement results,** for **quantities** of a given **kind,** that are metrologically traceable to the same reference (VIM 2.46)

VIM 3 uses the word comparability in the sense of ‘able to be compared’ **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.

The purpose of making **measurements** is often to enable a comparison to be made between the **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 parties 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 **certified reference material** (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 measurement 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 measurement uncertainty** (VIM 2.30) of the difference u_d between two completely independent uncorrelated **measurement results** x_1 and x_2 (obtained, for example, from two different laboratories or two different portions of the same sample) is given by the equation:

$$u_d = \sqrt{(u_1)^2 + (u_2)^2}$$

where u_1 and u_2 are the **standard measurement 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 ku_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 measurement uncertainty** of the difference will be lower for positive correlation and higher for negative correlation.

2.0. 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 the Eurachem/CITAC Guide on traceability in chemical measurement [17].

2.1 Metrological traceability

> property of a **measurement result** whereby the result can be related to a reference through a documented unbroken chain of **calibrations**, each contributing to the **measurement uncertainty** (VIM 2.41)

Most chemical analyses involve comparing a laboratory result with values produced at different times and locations, e.g. a value on a certificate, a legal limit, or a result obtained with a different **measurement procedure**.

Metrological traceability (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 reference (see Note 1 of the definition 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 aspartate aminotransferase [18] or the procedures defined in the ISO standard method for the determination of the fat content of dried milk and dried milk products [19].
- A **measurement standard**, e.g. the **certified reference material (CRM)** (VIM 5.14) SRM® 2193a $CaCO_3$ 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 measurement uncertainty** (VIM 2.35) of 0.011 ($k = 2$).

For the majority of **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. In such cases the references are used in combination.

The ‘unbroken chain of calibrations’ is a **traceability chain** (VIM 2.42). 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 [13]. The draft IUPAC document on establishing traceability contains the following seven illustrated examples of **traceability chains** [20]:

- amount of substance concentration of an acid in a material;
- pH of a solution;
- mass concentration of ethanol in breath;
- number ratio of isotopes of an element in a material;
- mass fraction of glyphosate in an agricultural chemical;
- amount of substance concentration of creatininium in blood plasma;
- 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. The kilogram is defined as the mass of the international prototype of the kilogram. The reference mass of the international prototype is that obtained after following a well defined **measurement procedure** [21]. 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 mole is defined as the amount of substance which contains as many elementary entities as there are atoms in 0.012 kilogram of carbon 12. When the mole is used, the elementary entities must be specified and may be atoms, molecules, ions, electrons, other particles, or specified groups of such particles. 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: $n = {}^{m}\!/\!_{M}$. 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. **certified reference materials**.

2.1.3 Route to achieving metrological traceability

Achieving 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 the schematic 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**, 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 can 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 chemist may have a choice.

Fewer standards qualify as **secondary measurement standards**, and there are an even smaller number of **primary measurement 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 transferin in serum performed in medical laboratories are traceable to the **SI** unit g L^{-1} via the **CRM** ERM® DA 470k/IFCC [22]. 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.

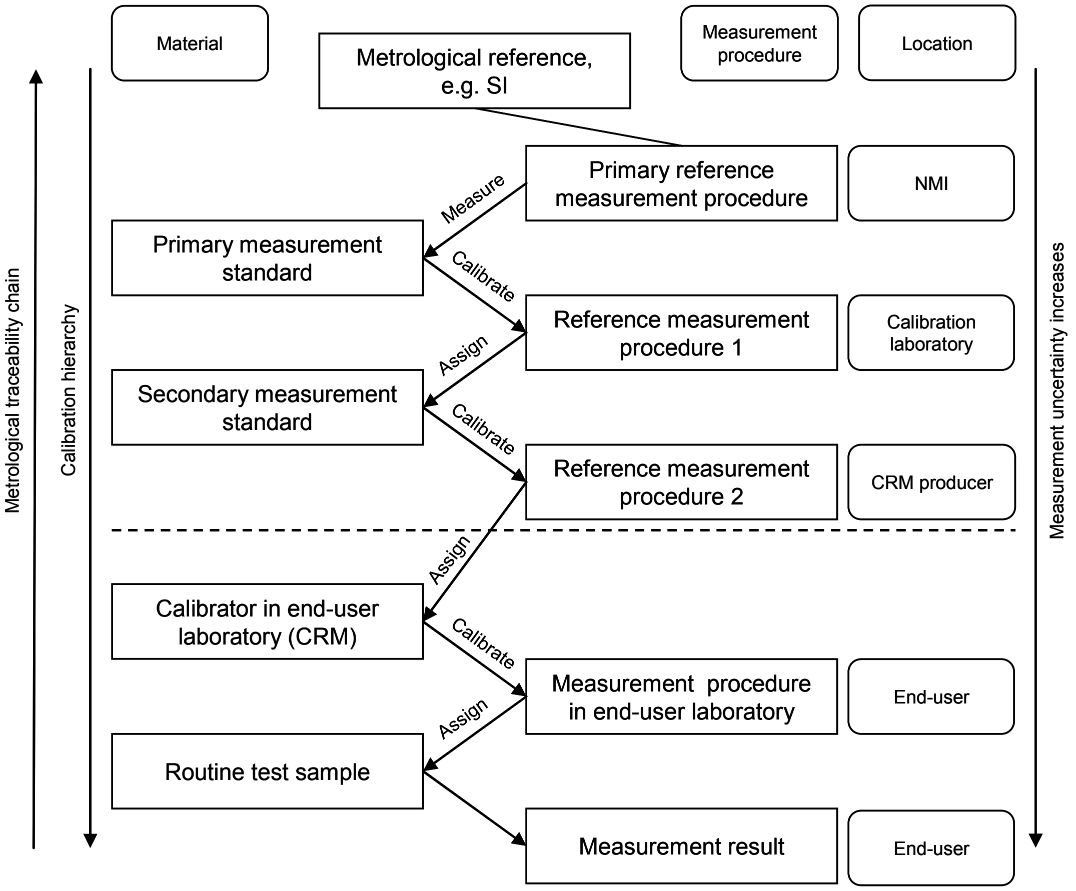

***Figure 2** Example of a generic traceability chain. The traceability chain relates the measurement result for a routine test sample to the reference point (here the SI) via a sequence of calibrations (the arrows). Uncertainties, present in all procedures and calibrators, are propagated to the final 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 [17, 20, 23]. 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 the type of **quantity** (e.g. mass concentration), the analyte (e.g. methyl mercury), and samples (e.g. freshwater, dairy products ...).
- 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 end-point of the **traceability chain**, (e.g. a **measurement unit**, a material with a specified **quantity value** or a **measurement procedure**).
- **Calibration hierarchy** (VIM 2.40): The laboratory can perhaps choose between several working **calibrators**, each one provides its own different, fixed **traceability chain**. Once this choice is made, the **calibration hierarchy** is set out according to the documentation for the **calibrator** of choice.
- Demonstrating **metrological traceability**: 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 chemist can select appropriate equipment and **measurement standards**. It is important to identify the **input** and **influence quantities** 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, two materials are available for preparation of a calibration solution to measure the mass fraction of pesticide *p,p´*-DDE in animal fat [23]:

- a commercial grade chemical with stated purity expressed as a mass fraction >95 %;
- a **CRM** 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 a smaller **measurement uncertainty** associated with the stated purity, may 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**, and thereby the **traceability chain**.

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 accreditations 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 end-user would anticipate.

2.2 Calibration

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

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).

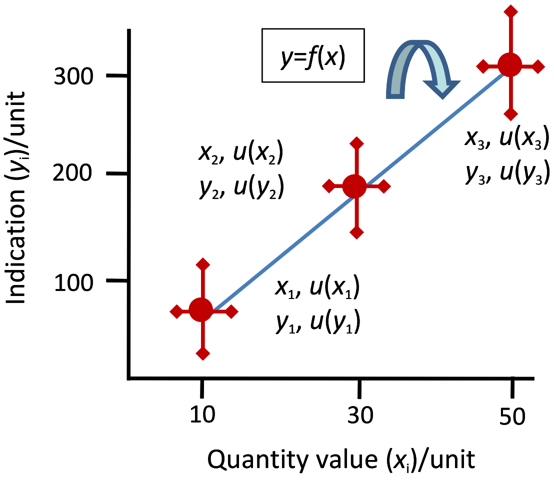

Figure 3 *Schematic of the first clause of the definition of calibration. Indications ('signals'* y_i*) from measurement standards (calibrators) with quantity values* x_i *give the relation (the function)* $y = f(x)$*. The vertical and horizontal arrows indicate the standard uncertainties of the indication and quantity values respectively (these are not to scale).*

In a calibration experiment, the chemist typically prepares a set of calibration solutions (also known as, '**calibrators**', '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 chemist then analyses the unknown sample and uses the **indication** (y_s) to calculate a corresponding **quantity value** (x_s) 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 $y = a + bx$, where b is the gradient of the curve and a is the y-axis intercept when $x = 0$, then $f^{-1}(y)$ is $x = (y - a)/b$.

The **uncertainties** of the **indication**, the **calibration**, and of other **corrections** (VIM 2.53), contribute to the **uncertainty** of the **measurement result**.

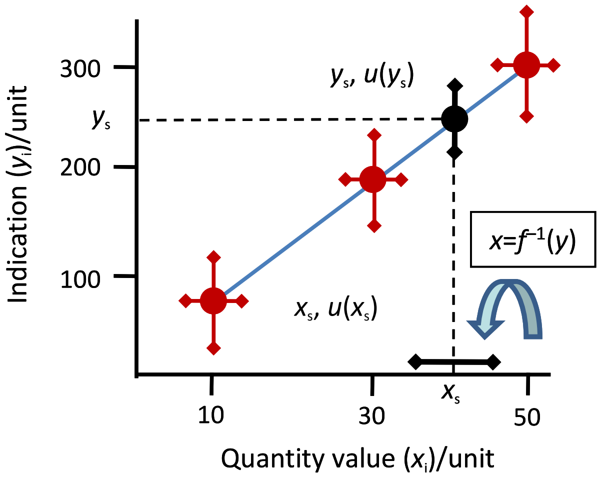

***Figure 4** Schematic calibration diagram illustrating the second clause of the definition of calibration. The indication ('signal' y_s) from a sample corresponds to a quantity value x_s. The vertical and horizontal arrows indicate the standard uncertainty of the indication and of the quantity value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

2.3 Instrumental drift

> continuous incremental change over time in **indication**, due to changes in metrological properties of a **measuring instrument** (VIM 4.21)

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

> realization of the definition of a given **quantity**, with stated **quantity value** and associated **measurement uncertainty**, used as a reference (VIM 5.1)

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 **certified reference material (CRM)** (VIM 5.14) for which, according to the certificate, the value of the mass concentration of cadmium is (1005 ± 3) mg L^{-1}. In this case the **quantity value** is 1005 mg L^{-1} and the value of the **measurement uncertainty** is 3 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 **certified reference materials**, and a **measuring system** 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.

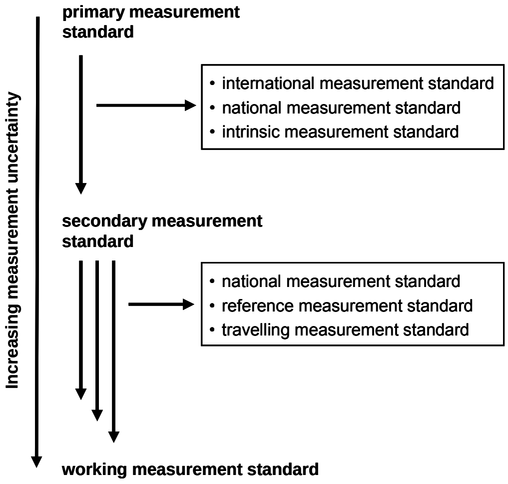

***Figure 5** Illustration of hierarchy of measurement standards.*

The 'Vienna Standard Mean Ocean Water' (VSMOW2) is an **international measurement standard** (VIM 5.2) for differential stable isotope ratio **measurements**. Many metrology institutes have a kilogram prototype serving as a **national measurement standard** (VIM 5.3) for mass. The international prototype of the kilogram is a **primary measurement standard** (VIM 5.4). According to VIM 3, by accurately weighing and dissolving glucose of known purity to a known volume, a chemist can prepare a **primary standard** in the form of a solution of known concentration.

The standards mentioned above and **secondary measurement standards** (VIM 5.5) as well as other **reference measurement standards** (VIM 5.6) are needed by producers of **reference materials** (VIM 5.13), instrument manufacturers and reference laboratories. In addition, for routine applications laboratories may use **working standards** (VIM 5.7) to check **measuring systems**.

Two other types of **measurement standard** are shown in Figure 5. An **intrinsic measurement standard** (VIM 5.10) is a **measurement standard** based on an inherent physical constant or inherent physical property. For example, the triple point of water cell is an **intrinsic standard** of thermodynamic temperature. A **travelling measurement standard** (VIM 5.8) is simply a **measurement standard** intended for transport between locations.

2.5 Calibrator

measurement standard used in **calibration** (VIM 5.12)

Analytical chemists frequently use the term calibrant, **calibrator** or standard when referring to **measurement standards** used in **calibration**. Many **measurements** are made using **measuring instruments** and **systems** that require regular **calibration**. An inherent part of the daily work for the chemist is, therefore, preparation and/or maintenance of this type of **measurement standard**.

Measurement standards are produced and used for different purposes. There are a number of documents which provide guidelines on choosing appropriate **measurement standards**, for example reference 24. Not all materials described by suppliers and producers as **measurement standards** can be used for **calibration**. The user needs to exercise caution when purchasing 'standards' as the producer may not interpret the requirements in the same way as in VIM 3.

Many routine **measuring systems** are designed to handle samples, without isolation or pre-concentration of the analyte. In such cases it is also necessary to demonstrate that the **calibrator** behaves in the same way as the routine samples. This is done when the manufacturer or the user investigates the **commutability of a reference material** (see section 2.6).

Below are some examples of materials frequently used by chemists when carrying out **calibration**.

- Materials produced by manufacturers and intended to be used for **calibration** or **verification** of a commercial **measuring system**, e.g. a **working measurement standard** (VIM 5.7) with assigned **quantity value** and **measurement uncertainty** for amount of substance concentration of glucose in human serum, supplied as part of an *in vitro* diagnostic medical device.
- **Reference materials** (VIM 5.13) and **certified reference materials (CRM)** (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** should have a statement of **measurement uncertainty** and **metrological traceability**.

2.5.1. Check the 'intended use'!

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

A description of the 'intended use' is an essential part of the certificate for a **CRM** [25]. The primary purpose for which a **CRM** is issued by the producer should be stated. Many materials are not described as **certified reference materials** but still qualify as **calibrators**. Check the documentation and your own needs, e.g. in the case of medical laboratories the *In Vitro* Diagnostics Directive 98/79/EC applies [14].

Some materials could very well qualify as **calibrators** but the intention of the manufacturer of the material and/or measuring system is different, e.g. due to legislative restrictions. For instance, the manufacturer of a **measuring system** will only take responsibility if the prescribed **calibrator** is used. The laboratory may, however, wish to check the results by using other **measurement standards**, and 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

> property of a **reference material,** demonstrated by the closeness of agreement between the relation among the **measurement results** for a stated **quantity** in this material, obtained according to two given **measurement procedures**, and the relation obtained among the measurement results for other specified materials (VIM 5.15)

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 **reference material** (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. In such cases **calibration** with closely matching materials is essential for accurate **measurement results**. **Commutability of reference materials** is also of concern where the **measurement procedure** cannot be modified by the analyst but the **reference materials** available do not simulate the sample matrix. Medical laboratories may encounter this problem when using analysers with **calibrators** supplied by the manufacturer.

The ‘other specified materials’ mentioned in the definition are usually samples analysed routinely in a laboratory.

The concept of commutability is best described diagrammatically as shown in Figure 6. Figure 6(a) illustrates a case where the **reference material** M1 is commutable whereas in Figure 6(b) the **reference material** M2 is not commutable. M1, M2 and S1 represent the **indication** for the **reference materials** M1 and M2 and the sample S1, respectively. The **indication** may be an instrument signal or a particular **quantity value**.

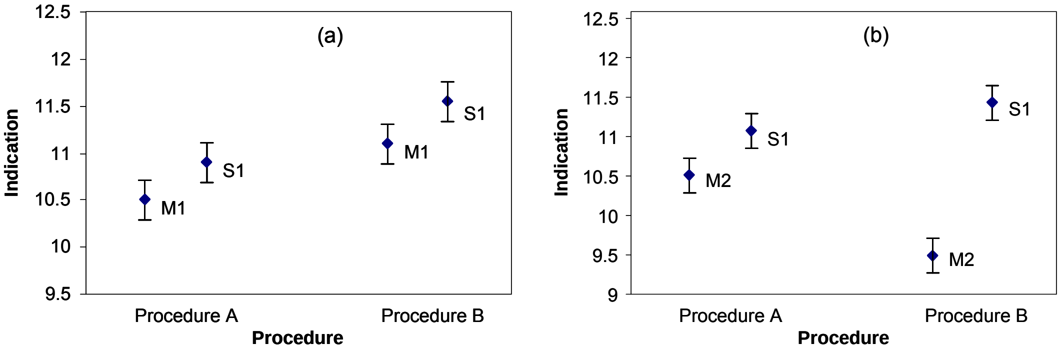

Figure 6 *Schematic to illustrate the commutability of a reference material, showing the measurement results and their associated confidence intervals. In case (a) the reference material is considered to be commutable – the relation between the indication obtained for the reference material (M1) and 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.*

3.0. Measurement Uncertainty

This chapter describes the terminology relating to measurement uncertainty. ISO/IEC Guide 98-3, Guide to the expression of uncertainty in measurement (GUM), describes the principles of uncertainty evaluation [26]. Further information on how to evaluate measurement uncertainty can also be found in the Eurachem/CITAC Guide on quantifying uncertainty in analytical measurement [27].

3.1 Measurement uncertainty

non-negative parameter characterizing the dispersion of the **quantity values** being attributed to a **measurand**, based on the information used (VIM 2.26)

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 used to describe the dispersion of distributions, e.g. standard deviations, are usually positive. The statement, 'based on the information used', explains why it is necessary to declare what is included in the estimate of **measurement uncertainty**. This does not mean we can choose what to include and what to leave out. There are many approaches to evaluating **measurement uncertainty** and these are described in the literature [27, 28, 29].

Measurements consist of many steps and require various items of equipment. For example, calculating the **measurement result** may involve reagent concentrations and values from **measuring instruments**, **calibrators** and **reference materials** (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 the manual operations carried out, also contribute to **measurement uncertainty**. This means that, for a specific calculated result, there is not one but a whole range of **true quantity values** (VIM 2.11) that could reasonably have given rise to the **measured quantity value**. **Measurement uncertainty**, as defined by VIM 3, is a parameter, such as a standard deviation or confidence interval that describes the dispersion of these possible values.

The **result of a measurement** consists of two quantitative parts: i) the **measured quantity value**, often an average or median of individual measurements, and ii) the **measurement uncertainty**. If when the result is reported the **uncertainty** is included, it can be presented in the format (value ± uncertainty) and units. 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).

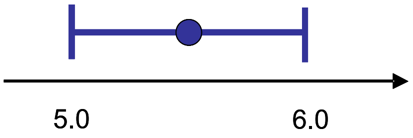

Figure 7 *Illustration of the result (5.5 ± 0.5) mL.*

3.1.1 Expression of uncertainty

Estimates of **measurement uncertainty** can be expressed in a number of different ways, e.g. as a standard deviation or a confidence interval. However, to be able to combine uncertainty estimates they must be expressed in the same form, so some conversion may be necessary. Following ISO guidelines, uncertainty estimates should be expressed as **standard measurement uncertainties** (VIM 2.30) (see below) before they are combined [26].

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

- $u(x_i)$ – the **standard measurement uncertainty** (VIM 2.30) for quantity x_i is an **uncertainty** expressed as a standard deviation;
- $u_c(y)$ – the **combined standard measurement uncertainty** (VIM 2.31) for the **measurand**, is a mathematical combination of several individual **standard measurement uncertainties**;
- U – the **expanded measurement 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 measurement uncertainty** $u_c(y)$ 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 $u(x_i) < u_c(y) < U$. These **uncertainties** are often expressed in relation to the value, e.g. as a **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 water status 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 relevant environmental quality standards' [30]. 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} [31].

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 evaluated as variances. In many cases combining these two **uncertainty** components using the law of propagation of uncertainty is a reasonable estimate of the **standard measurement uncertainty** of the results obtained when using the **measurement procedure**. 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 end-user 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

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, e.g. show if an **uncertainty** contribution is based on statistical analysis of **quantity values** obtained under defined conditions, i.e. **Type A evaluation** (VIM 2.28) or by any other means, i.e. **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 a **reference material** (VIM 5.13) certificate is an example of a **Type B evaluation**. The **uncertainty budget** should also include the applied probability density function and degrees of freedom for each **uncertainty** contribution, and the **coverage factor** (VIM 2.38) used to calculate the **expanded measurement 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 [27]. The mass concentration of cadmium, ρ_{Cd} (mg L^{-1}) is given by:

$\rho_{Cd} = (1000 \cdot m \cdot P)/V$

where m is the mass in mg of the cadmium, P its purity, and 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 the balance manufacturer and their recommendations on **uncertainty** estimation. The purity of the metal is obtained from the certificate of the **certified reference material** (VIM 5.14) and converted to a **standard measurement uncertainty** (VIM 2.30) assuming a rectangular distribution. The **uncertainty** in the volume of the flask consists of three components – **calibration** (u_{cal}), **repeatability** (VIM 2.21) of filling the flask (u_{rep}), and the difference between the temperature at which the calibration was made and the temperature when the flask is used (u_{temp}).

Table 2 *Uncertainty budget for mass concentration of a cadmium calibration standard; values taken from the Eurachem/CITAC Guide [27]. The standard uncertainty in* ρ_{Cd} was calculated by combining the relative standard uncertainties and then multiplying by the value for ρ_{Cd}.

Quantity	**Value**	**Standard uncertainty**	**Units**	**Relative standard uncertainty $u(x)/x$**	**Degrees of freedom**	**Type of evaluation**	**Distribution**
m	100.28	0.050	mg	0.00050	50	B	normal
P	0.9999	5.8×10^{-5}	mass fraction	5.8×10^{-5}	∞	B	rectangular
V	100.00	0.066	mL	0.00066	1100	Contributions below*	
$\boldsymbol{\rho_{Cd}}$	**1002.70**	**0.84**	**mg $\mathbf{L^{-1}}$**	0.00083	340		
Expanded uncertainty k = 2		**1.7**	**mg $\mathbf{L^{-1}}$**				
***Volume contributions**		**Standard uncertainty**	**Units**		**Degrees of freedom**	**Type of evaluation**	**Distribution**
	u_{cal}	0.041	mL		∞	B	triangular
	u_{temp}	0.049	mL		∞	B	rectangular
	u_{rep}	0.020	mL		9	A	normal
Volume, combined standard uncertainty		0.066	mL		1100		

4.0. Validation and Method Performance

This chapter describes the terminology relating to validation and method performance. Further information on method validation can be found in the Eurachem guide on the fitness for purpose of analytical methods [32].

4.1 Verification

provision of objective evidence that a given item fulfils specified requirements (VIM 2.44)

Verification is closely related to the concept **validation**.

4.2 Validation

verification, where the specified requirements are adequate for an intended use (VIM 2.45)

In order to illustrate these two concepts, consider an example where a laboratory purchases an instrument. After the instrument has been installed in the laboratory, an analyst plans a series of experiments to check that the instrument's performance meets that specified by the manufacturer. This process is called **verification** – the analyst will obtain objective evidence (experimental data) which demonstrates that the instrument meets the manufacturer's specification. Once it has been confirmed that the instrument performance is satisfactory it will be used as part of a particular **measurement procedure**. The performance criteria for the procedure have been set by the laboratory and agreed with the customer as being fit for the intended purpose. The analyst plans another set of experiments to establish that the performance of the **measurement procedure** meets the customer's requirements. This process is called **validation** – the analyst will obtain data to demonstrate that the performance of the **measurement procedure** is adequate for the purpose specified by the customer.

In VIM 3, **validation** is the **verification** or check that the 'given item', e.g. a **measurement procedure** or a **measuring instrument** is fit for the intended purpose. This is assessed by determining whether the 'specified requirements' – performance criteria such as the **measuring interval**, **selectivity**, **trueness**, **precision** and **measurement uncertainty** – are fulfilled.

The **verification** involves designing a set of experiments which produce values for the performance parameters; this is the 'objective evidence'. The values obtained must meet the requirements set for the analytical results.

Note that these definitions are in essence what is meant by the definition for **validation** used in ISO/IEC 17025 [4]. The term 'verification' was previously used for a less detailed study whereby a laboratory would demonstrate that it could achieve the published performance of an already validated procedure, e.g. an ISO standard procedure. This could be regarded as being in line with the current VIM 3 definition of **verification**. For a given item (an ISO standard procedure) evidence is obtained to show that at a laboratory the staff using the procedure are able to achieve the stated performance criteria for the procedure.

The following sections describe the performance parameters which are commonly studied during **verification/validation**.

4.3 Measuring interval

set of **values** of **quantities** of the same **kind** that can be measured by a given **measuring instrument** or **measuring system** with specified **instrumental measurement uncertainty**, under defined conditions (VIM 4.7)

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', 'measurement range' and 'range' (ISO/IEC 17025). 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 mg L^{-1} to 0.9 mg L^{-1}, written as [0.3, 0.9], and the range is 0.6 mg L^{-1}.

The lower limit of the **measuring interval** is often considered to be the limit of quantitation (LOQ) (a concept not defined in VIM 3). The upper limit is usually determined by the unacceptable change in **measurement uncertainty** or in the **sensitivity** (VIM 4.12). Figure 8 illustrates the relationship between some of the key terms related to '**measuring interval**'. The **limit of detection** (LOD) is below the limit of quantitation. The **sensitivity of a measuring system** is, in the case of linear dependence, given by the slope of the **calibration curve** (VIM 4.31).

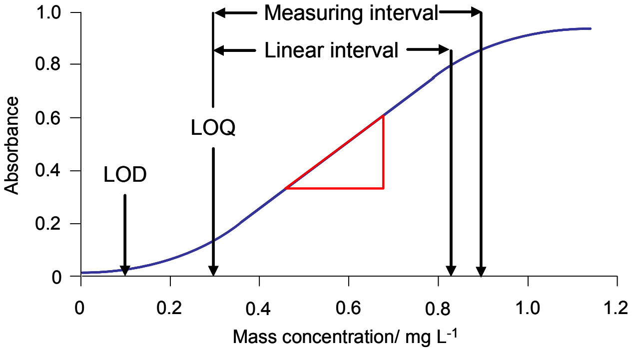

Figure 8 *A calibration diagram showing absorbance versus mass concentration where the measuring interval, linear interval, LOQ and LOD are identified. The triangle illustrates the calculation of the sensitivity or the slope of the calibration curve (Δindication/Δquantity = Δabsorbance/Δmass conc.).*

4.4 Detection limit

VIM defines the limit of detection (LOD) in terms of a **measured quantity value**.

> **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)

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 yet 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 [33].

Many analysts will be familiar with calculating the **limit of detection** 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 concentration 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 3.3.

This section 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 α, 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 α = 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, α = 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 declared positive.

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 is intended to represent the true concentration for which the false negative rate is acceptable given the critical value. The false negative error, β, is usually set equal to the false positive error, this is largely for historical reasons (IUPAC recommends default values of $\alpha = \beta = 0.05$). Using $\alpha = \beta = 0.05$, the LOD needs to be 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. This is based on several approximations which are described in the literature [33].

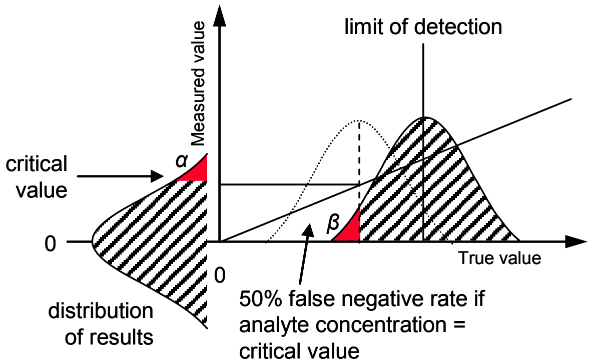

Figure 9 *Illustration of statistical basis of detection limit calculations.*

4.5 Selectivity of a measuring system

property of a **measuring system,** used with a specified **measurement procedure,** whereby it provides measured **quantity values** for one or more **measurands** such that the values of each measurand are independent of other measurands or other **quantities** in the phenomenon, body, or substance being investigated (VIM 4.13)

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.'[34] 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 it has not been defined in VIM 3.

4.6 Measurement trueness

closeness of agreement between the average of an infinite number of replicate **measured quantity values** and a **reference quantity value** (VIM 2.14)

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 **certified reference material (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**.

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**.

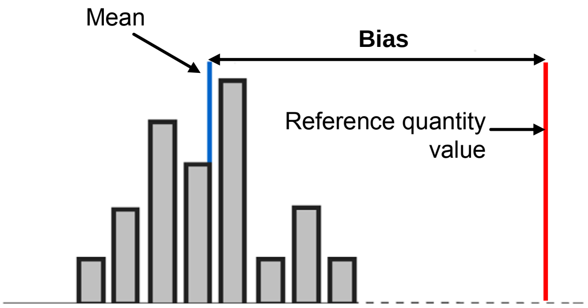

Figure 10 *Schematic illustration of the estimation of measurement bias. The mean of several measurement results is compared with a reference quantity value (note that the uncertainty in the reference value is not shown).*

A **measurement bias** may be due e.g. to inappropriate **calibration** or to lack of **selectivity** (see section 4.5).

An estimate of the **bias** in **measurement results** produced by a laboratory can be obtained by measuring the **quantity value** of one or more **reference materials** (VIM 5.13) several times under **repeatability conditions** (VIM 2.20) or under **intermediate precision conditions** (VIM 2.22), and calculating the mean value. The estimate of **bias** is then the difference between the mean value obtained and the **reference quantity value**. Note that there will be a **measurement uncertainty** associated with the bias value due to the uncertainties in the mean value and in the **reference quantity value**.

Example: The mean value of the mass fraction of CaO in a cement **CRM** calculated from 10 **measurement results** obtained over a six month period using XRF is 63.53% with a standard deviation of the mean of 0.1%. The certified **quantity value** is 63.23% with an **expanded measurement uncertainty** (VIM 2.35) of 0.21% (k=2). The **measurement bias** determined under **intermediate precision conditions** using this **CRM** is therefore estimated as 63.53–63.23 = 0.3%. The **bias** can also be expressed as a relative value, i.e. 100 x 0.3/63.23 = 0.47%.

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)

In everyday language precision is a synonym of **accuracy** but in measurement science it is restricted to describing random variability.

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 material under specified conditions. VIM 3 defines three measurement conditions: **repeatability condition** (VIM 2.20), **intermediate precision condition** (VIM 2.22) and **reproducibility condition** (VIM 2.24).

Estimates of **measurement repeatability** (VIM 2.21) and **intermediate measurement precision** (VIM 2.23) are obtained in a single laboratory. **Repeatability condition of measurement** refers to **measurements** being made on portions of the same material by a single analyst, using the same procedure, under the same operating conditions over a short time period. **Measurement repeatability** is often used to provide an estimate of within-batch variability in results. Under **intermediate measurement conditions**, **measurements** are made on portions of the same material using the same procedure, but over an extended time period and possibly by different analysts who may be using different pieces of equipment. **Intermediate measurement precision** is often used to provide an estimate of between-batch variability. **Intermediate measurement conditions** are user-defined and the conditions used should always be recorded (note that some laboratories use the term within-laboratory reproducibility for **intermediate precision**).

Since **measurement repeatability** only reflects the variation in results over a short time period it is likely to underestimate the variability in results obtained when the **measurement procedure** is used routinely. Assuming appropriate **intermediate measurement conditions** have been used during the **validation** study, the **intermediate measurement precision** provides a more realistic estimate of the long-term variability of **measurement results** in the laboratory.

Estimates of **measurement reproducibility** (VIM 2.25) are obtained from **measurement results** produced at different laboratories. **Reproducibility condition of measurement** refers to **measurements** being made on portions of the same material by different analysts working in different locations. In 'collaborative' validation studies the same **measurement procedure** is used at all the participating laboratories. However, the term 'reproducibility condition' also applies to interlaboratory comparisons where different **measurement procedures** may be used for the same **measurand** (VIM 2.24, Note 1), for example in a proficiency testing scheme. Therefore it is essential that the conditions under which **reproducibility** is evaluated are specified.

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-batch replicates' represents replication of the whole **measurement procedure** under **repeatability conditions**.

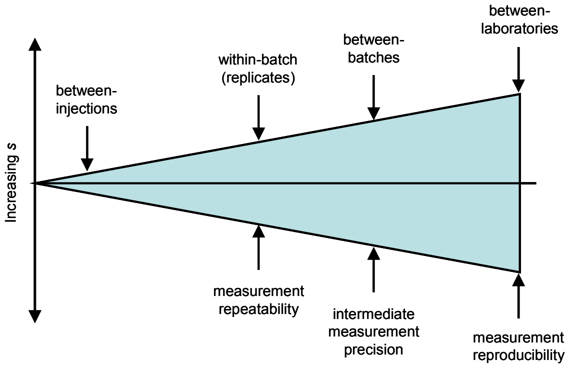

Figure 11 *Schematic diagram illustrating the expected relationship between precision estimates obtained under different measurement conditions, shown in terms of the magnitude of the observed imprecision. As the conditions of measurement become more variable (e.g. moving from replicating only part of the measurement procedure ('between-injections') to replicating the entire measurement procedure under repeatability or intermediate precision conditions) the standard deviation of measurement results generally increases.*

4.8 Measurement accuracy

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

In common usage outside the field of **metrology**, accuracy is a synonym of precision and in note 3 of VIM 2.13 it is stated that **measurement accuracy** is sometimes understood as 'closeness of agreement between **measured quantity values**'. This usage is unacceptable in analytical chemistry.

Measurement accuracy describes how close a *single* **measurement result** is to the **true quantity value** (VIM 2.11). **Accuracy** therefore includes the effect of both **precision** and **trueness**. **Accuracy** cannot be given a numerical value but **measurement results** are said to be 'more accurate' when the **measurement errors**, and therefore the **measurement uncertainty**, are reduced as illustrated in Figure 12.

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).

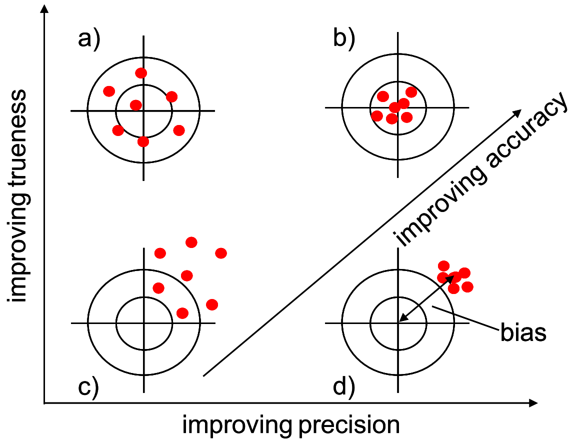

Figure 12 *The 'shots' on the target represent individual measurement results; the reference quantity value is the centre of the target. The best accuracy (lowest measurement uncertainty) is achieved in case b) where the individual results are all close to the reference value. In cases a) and b) there is no significant bias as the results are all clustered in the centre of the target. However, the precision is poorer in case a) as the results are more widely scattered. The precision in case d) is similar to that in case b). However, there is a significant bias in case d) as all the results are off-set from the centre in the same area of the target. The accuracy is poorest in case c) as the results are widely scattered and are off-set to the right of the target.*

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.*

Concept	**Synonym**	**VIM 3 Reference**
base quantity		*1.4*
base unit		*1.10*
blank indication	background indication	*4.2*
calibration		**2.39**
calibration curve		*4.31*
calibration diagram		*4.30*
calibration hierarchy		*2.40*
calibrator		**5.12**
certified reference material	CRM	*5.14*
combined standard measurement uncertainty	combined standard uncertainty	*2.31*
commutability of a reference material		**5.15**
correction		*2.53*
coverage factor		*2.38*
definitional uncertainty		*2.27*
derived quantity		*1.5*
derived unit		*1.11*
detection limit	limit of detection	**4.18**
displaying measuring instrument		*3.4*
expanded measurement uncertainty	expanded uncertainty	*2.35*
indicating measuring instrument		*3.3*
indication		**4.1**
influence quantity		*2.52*
input quantity in a measurement model	input quantity	*2.50*
instrumental drift		**4.21**
intermediate measurement precision	intermediate precision	*2.23*
intermediate precision condition of measurement	intermediate precision condition	*2.22*
international measurement standard		*5.2*
International System of Quantities	ISQ	**1.6**
International System of Units	SI	*1.16*
intrinsic measurement standard	intrinsic standard	*5.10*
kind of quantity	kind	*1.2*

Concept	**Synonym**	**VIM 3 Reference**
material measure		*3.6*
measurand		**2.3**
measured quantity value	value of a measured quantity, measured value	**2.10**
measurement		**2.1**
measurement accuracy	accuracy of measurement, accuracy	**2.13**
measurement bias	bias	*2.18*
measurement error	error of measurement, error	**2.16**
measurement method	method of measurement	*2.5*
measurement model	model of measurement, model	*2.48*
measurement precision	precision	**2.15**
measurement principle	principle of measurement	*2.4*
measurement procedure		**2.6**
measurement repeatability	repeatability	*2.21*
measurement reproducibility	reproducibility	*2.25*
measurement result	result of measurement	**2.9**
measurement standard	etalon	**5.1**
measurement trueness	trueness of measurement, trueness	**2.14**
measurement uncertainty	uncertainty of measurement, uncertainty	**2.26**
measurement unit	unit of measurement, unit	**1.9**
measuring instrument		**3.1**
measuring interval	working interval	**4.7**
measuring system		**3.2**
metrological comparability of measurement results	metrological comparability	**2.46**
metrological compatibility of measurement results	metrological compatibility	**2.47**
metrological traceability		**2.41**
metrological traceability chain	traceability chain	*2.42*
metrological traceability to a measurement unit	metrological traceability to a unit	*2.43*
metrology		**2.2**
national measurement standard	national standard	*5.3*
nominal property		**1.30**
nominal quantity value	nominal value	**4.6**
primary reference measurement procedure	primary reference procedure	**2.8**
primary measurement standard	primary standard	*5.4*
quantity		**1.1**
quantity value	value of a quantity, value	**1.19**

Concept	**Synonym**	**VIM 3 Reference**
random measurement error	random error of measurement, random error	*2.19*
reference material	RM	*5.13*
reference measurement procedure		**2.7**
reference measurement standard	reference standard	*5.6*
reference quantity value	reference value	**5.18**
relative standard measurement uncertainty		*2.32*
repeatability condition of measurement	repeatability condition	*2.20*
reproducibility condition of measurement	reproducibility condition	*2.24*
secondary measurement standard	secondary standard	*5.5*
selectivity of a measuring system	selectivity	**4.13**
sensitivity of a measuring system	sensitivity	*4.12*
standard measurement uncertainty	standard uncertainty of measurement, standard uncertainty	*2.30*
system of quantities		**1.3**
system of units		*1.13*
systematic measurement error	systematic error of measurement, systematic error	*2.17*
target measurement uncertainty	target uncertainty	*2.34*
travelling measurement standard	travelling standard	*5.8*
true quantity value	true value of a quantity, true value	*2.11*
type A evaluation of measurement uncertainty	type A evaluation	*2.28*
type B evaluation of measurement uncertainty	type B evaluation	*2.29*
uncertainty budget		**2.33**
validation		**2.45**
verification		**2.44**
working measurement standard	working standard	*5.7*

References

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1. International vocabulary of metrology – Basic and general concepts and associated terms (VIM), ISO/IEC Guide 99:2007, International Organization for Standardization (ISO)/International Electrotechnical Commission (IEC), Geneva, 2007
2. International vocabulary of metrology – Basic and general concepts and associated terms (VIM), JCGM 200:2008, Joint Committee for Guides in Metrology (JCGM), 2008, www.bipm.org
3. International vocabulary of metrology – Basic and general concepts and associated terms (VIM), JCGM 200:2008 Corrigendum, Joint Committee for Guides in Metrology (JCGM), 2010, www.bipm.org
4. General requirements for the competence of testing and calibration laboratories, ISO/IEC 17025:2005, International Organization for Standardization (ISO)/International Electrotechnical Commission (IEC), Geneva, 2005
5. Conformity assessment – General requirements for proficiency testing, ISO/IEC 17043:2010, International Organization for Standardization (ISO)/International Electrotechnical Commission (IEC), Geneva, 2010
6. General requirements for the competence of reference material producers, ISO Guide 34:2009, International Organization for Standardization (ISO), Geneva, 2009
7. Reference materials – General and statistical principles for certification, ISO Guide 35:2006, International Organization for Standardization (ISO), Geneva, 2006
8. International vocabulary of basic and general terms in metrology, 2nd Edition, ISBN 92-67-10175, International Organization for Standardization (ISO), Geneva, 1993
9. Medical laboratories – Particular requirements for quality and competence, ISO 15189:2007, International Organization for Standardization (ISO), Geneva, 2007
10. Use of litre (L) with the International System of Units, Bureau International des Poids et Mesures, The International System of Units (SI), 8th edition, section 4.1, Table 6, 2006, www.bipm.org
11. Bureau International des Poids et Mesures, The International System of Units (SI), 8th edition, 2006, www.bipm.org
12. Council Directive 80/181/EEC of 20 December 1979 on the approximation of the laws of the Member States relating to units of measurement and on the repeal of Directive 71/354/EEC, Official Journal L 039, 15/02/1980, p40-50
13. In vitro diagnostic medical devices – Measurement of quantities in biological samples – Metrological traceability of values assigned to calibrators and control materials, ISO 17511:2003, International Organization for Standardization (ISO), Geneva, 2003
14. Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on *in vitro* diagnostic medical devices, Official Journal L 331, 07/12/1998, p1-37
15. JCTLM Database of higher-order reference materials, measurement methods/procedures and services, www.bipm.org/jctlm/
16. S. S-C. Tai and M. J. Welch, Development and evaluation of a candidate reference method for the determination of total cortisol in human serum using ID-LC/MS and LC/MS/MS, Anal. Chem., **76**, 1008-1014, 2004
17. S. L. R. Ellison, B. King, M. Rösslein, M. Salit, A. Williams, Eurachem/CITAC Guide: Traceability in chemical measurement – A guide to achieving comparable results in chemical measurement, 2003, www.eurachem.org
18. G. Schumann et al., International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37 degrees C. Part 5. Reference procedure for the measurement of catalytic concentration of aspartate aminotransferase, Clin. Chem. Lab. Med. **40**, 725-733, 2002
19. Dried milk and dried milk products – Determination of fat content – Gravimetric method (Reference method), ISO 1736:2008, International Organization for Standardization (ISO), Geneva, 2008

20. P. De Bièvre, R. Dybkaer, A. Fajgelj, D. B. Hibbert, Metrological traceability of measurement results in chemistry: Concepts and implementation, (IUPAC Provisional Recommendations 2009), www.iupac.org
21. R. Davis, The SI unit of mass, Metrologia, **40**, 299-305, 2003
22. Certificate of analysis, ERM®- DA470k/IFCC, 2009, http://irmm.jrc.ec.europa.eu
23. V. Barwick and S. Wood, Meeting the traceability requirements of ISO 17025, 3rd ed., ISBN 0-948926-23-6, LGC, Teddington, 2005, www.nmschembio.org.uk
24. Guidelines for the selection and use of reference materials, 2005, ILAC-G9:2005, www.ilac.org
25. Reference materials – Contents of certificates and labels, ISO Guide 31, International Organization for Standardization (ISO), Geneva, 2000
26. Uncertainty of measurement – Part 3: Guide to the expression of uncertainty in measurement (GUM:1995), ISO/IEC Guide 98-3, International Organization for Standardization (ISO), Geneva, 2008
27. S. L. R. Ellison, M. Rösslein, A. Williams (Eds), Eurachem/CITAC Guide: Quantifying uncertainty in analytical measurement, 2nd ed., 2000, ISBN 0 948926 15 5, www.eurachem.org
28. Measurement uncertainty revisited: Alternative approaches to uncertainty evaluation, Eurolab 2007/1, 2007, www.eurolab.org
29. Guidance for the use of repeatability, reproducibility and trueness estimates in measurement uncertainty estimation, ISO 21748:2010, International Organization for Standardization (ISO), Geneva, 2010
30. Commission Directive 2009/90/EC of 31 July 2009 laying down, pursuant to Directive 2000/60/EC of the European Parliament and of the Council, technical specifications for chemical analysis and monitoring of water status, Official Journal L 201, 07/08/2009, p36-38
31. Directive 2008/105/EE of the European Parliament and of the Council of 16 December 2008 on environmental quality standards in the field of water policy, amending and subsequently repealing Council Directives 82/176/EEC, 83/513/EEC, 84/156/EEC, 84/491/EEC, 86/280/EEC and amending Directive 2000/60/EC of the European Parliament and of the Council, Official Journal L 348, 24/12/08, p84-97
32. Eurachem Guide: The fitness for purpose of analytical methods: A laboratory guide to method validation and related topics, 1998, ISBN 0 948926 12 0, www.eurachem.org
33. L. A. Currie, Nomenclature in evaluation of analytical methods including detection and quantification capabilities (IUPAC Recommendations 1995), Pure Appl. Chem., **67**, 1699 – 1723, 1995
34. J. Vessman, R. I. Stefan, J. F. van Staden, K. Danzer, W. Lindner, D. Thorburn Burns, A. Fajgelj, and H. Müller, Selectivity in analytical chemistry, (IUPAC Recommendations 2001), Pure Appl. Chem., **73**, 1381–1386, 2001

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