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Metrological Traceability of Measurement Results in Chemistry

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Paul De Bièvre
René Dybkaer
Ales Fajgelj
D Brynn Hibbert

Executive Summary

In commerce, society, and science **metrological comparability**[1] of **measured quantity values** and various published values is essential to determine their spatio-temporal differences, ratios, and drifts. Achieving **metrological comparability of measurement results** requires definition of **calibration hierarchies** providing **metrological traceability chains** which enable the establishment of **metrological traceability** of **measured quantity values** to a common **metrological reference**.

Experience has shown that the understanding of the concepts involved, their relation, role, definition, and use is insufficient and varied. Consequently, an attempt is made in this study to arrive at a set of consistent concept systems with associated terminology for **measurement** in chemistry. The systems build on definitions of concepts and associated terms from the new 3rd edition (2007) of the International Vocabulary of Metrology - Basic and General Concepts and Associated Terms – VIM, such as **quantity**, **measurand**, **calibration**, **measurement procedure**, **measurement uncertainty**, **measurement standard**, **calibrator**, **reference material.** Additional concepts such as **metrological equivalence of measurement results**, are also given

Flow charts of generic **calibration hierarchies** are presented as well as a variety of examples. The establishment, assessment, and reporting of **metrological traceability** are discussed, including the needed **metrological institutional hierarchy** and the role of **interlaboratory comparisons**.

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[1] Bold face indicates a concept defined in this report, or in the VIM3.

Recommendations are made about the essential steps in planning and performing a **measurement**, and reporting a **measurement result**.

The precursor of this document was circulated within IUPAC bodies and other chemical fora. in the course of 2007, and amended in response to the comments received.

Preface

This IUPAC study aims at formulating Recommendations concerning the **metrological traceability** of a **measurement result** in chemistry. It is intended to provide the chemical measurement community with a consistent view of the creation, meaning, and role of **metrological traceability** and its underpinning concepts. No distinction is made between **measurement results** obtained in “high metrology” and in the “field”. A description is given of the **calibration hierarchies** needed under different circumstances to arrive at **metrological traceability** along a **metrological traceability chain**.

The concepts needed have essentially been taken from the 2007 3rd edition of the “International Vocabulary of Metrology – Basic and General Concepts and Associated Terms – VIM” (henceforth called VIM3) [1], the 1995 “Guide to the Expression of Uncertainty in Measurement” (GUM)[2], and the International Standards ISO 1087-1:2000 “Terminology Work - Vocabulary - Part 1: Theory and Application”[3], and ISO 704:2000 “Terminology Work – Principles and Methods”[4].

The reader should not expect in this study to see the terms used in daily analytical work because their inconsistency would limit the understanding of **metrological traceability**. Rather an attempt is made to present a consistent set of *concepts* with associated terminology. At the same time, the substitution principle is respected as much as possible, i.e. in a definition or text it should be possible to substitute a term by the definition of the corresponding concept – and still make sense without circularity.

As this document is concerned with **measurement**, only properties that possess a magnitude, i.e. **quantities**, are considered. Nominal properties are therefore not addressed.

A project to formulate the essential characteristics of the “traceability” concept, and related concepts, in chemical measurement was approved by IUPAC on 2001-11-23 (Annexe I). The ensuing Terms of Reference are given in Annexe II. The project team of authors are listed in Annexe III and their schedule of meetings in Annexe IV.

Dissemination

Information about this document was disseminated mainly as follows:

- opening a website, http://www.iupac.org/projects/2001/2001-010-3-500, on 2002-12-04;
- publishing an announcement paper in “Chemistry International” 2003 [5];
- presenting an intermediate version at the IUPAC, Analytical Chemistry Division Committee workshop, Vienna, 2004-02-17/19;
- producing a draft document in the first half of 2005;
- presenting this draft at the Analytical Chemistry Division Committee meeting, General Assembly of IUPAC in Beijing, China, 2005-08-14;
- discussing this draft in an expert meeting at UNIDO in Vienna 2005-12-12/16;
- circulating draft final report to IUPAC bodies and relevant international organizations for comment in 2007-06/07; and
- presenting the draft final version to the IUPAC General Assembly in Torino (IT) on 2007-08-05;
- circulating an updated draft final report to IUPAC bodies for comment in 2007-09/10;
- submitting a final version to IUPAC-ICTNS in 2008;
- publishing the final report in Pure and Applied Chemistry in 2008; and

- making the Recommendations available for publication in other media.

An elementary document, derived from this basic text, but consistent with it, is being prepared in a subsequent IUPAC project.

Conventions

The following conventions are followed:

- bold face indicates the term for a concept defined in this report, or in the VIM3, and is used every time such a term appears;
- following the VIM3, single quotation marks '…' enclose the terms for concepts when not in bold, and double quotation marks "…" enclose terms and quotations from other sources;
- entries in the VIM3 are given verbatim in the case of terms, definitions, and VIM3 conventions, but might not include all its examples and notes; and
- such entries follow the VIM3 conventions of using bold face only the first time a concept appears in an entry.

A number of initialisms, acronyms and abbreviations will be used in the text and are listed in Annexe V.

Acknowledgements

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The authors also acknowledge various institutions which hosted work meetings and provided extensive logistical support for the project team over the years: the University of New South Wales in Sydney, Australia (2001), the Institute for Reference Materials and Measurements of the European Commission in Geel, Belgium (2001), the International Atomic Energy Agency in Vienna, Austria (2002 and 2004), the H:S Frederiksberg Hospital in København, Denmark (2002), IUPAC at its General Assemblies (Ottawa, Canada 2003, Beijing, China 2005, Torino, Italy 2007) and UNIDO, Vienna 2005, private locations such as in Kasterlee, Belgium (2003 to 2007).

Contents

1 Introduction

1.1 Stating the problems

In recent years the concept ‘traceability’ in chemical **measurement** has received an extraordinary amount of attention.

- It has been the theme of numerous workshops and symposia.
- Demonstration of “measurement traceability” is required in the International Standards on accreditation ISO/IEC 17025, ISO 15195, and ISO 15189 [6-8],
- ‘Traceability’ is the subject of ILAC-G2 [9].
- Two standards on assignment of **quantity values** to **calibrators** used in laboratory medicine stipulate and explain **metrological traceability**: ISO 17511 and ISO 18153 [10, 11].
- It is mentioned frequently in CIPM-MRA.
- It is mentioned in ISO Guides 34 and 35 (REMCO) [12, 13].

Still the interpretation of “metrological traceability” varies in the chemical literature and many people concerned with ‘Metrology in Chemistry’ admit that there is no unequivocal, internationally agreed understanding of the concept ‘traceability’. Also, **reference materials** often lack information about **metrological traceability** (and associated **measurement uncertainty**) for assigned **quantity values**. This is an unfortunate state of affairs because lack of clarity about such an important and widely used concept makes it difficult to reach worldwide agreement on its meaning and application. Furthermore, communication about and use of **measurement results** is hampered.

Discussions with analytical chemists have revealed that basic concepts in metrology, including ‘traceability’ are generally not an integral part of university or high school curricula and are not treated in textbooks of analytical chemistry. This might be a cause of many of the problems listed below.

The concept of traceability is defined in the second edition 1993 of the International Vocabulary of Basic and General Terms in Metrology (VIM2) [14] as

> **traceability** (Concept 1.1-1)
>
> property of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken sequence of comparisons all having stated uncertainties
>
> [VIM2-6.10]

which essentially is a rewording of the entry in the first edition of VIM 1984. Still the concept and term “traceability” present the following problems.

- In spite of the definition having traceability as a *property* of a **measurement result**, it is common to refer to the traceability of a
    - document such as a **measurement procedure** (which is a physical object), or
    - sample (which is a physical object), or
    - **measurement** (which is a process).
- It is often claimed that a **measurement result** can be traceable to an institution (e.g. a specified NMI).

- There is a widely held perception that traceability does not apply to **measurement results** in field and routine laboratories.

- It is not generally accepted that traceability to a common stated **metrological reference** is a precondition for **metrological comparability of measurement results**.

- There is the perception that the meaning of the term “comparability” refers to **quantity values** of the same magnitude (size).

- There is a lack of clarity about the relation between **metrological traceability** and **measurement uncertainty** in the 1993 edition of the VIM (VIM2).

- There is the perception that a **measurement unit** from the **International System of Units** (**SI**) is the only possible **metrological reference** in the **metrological traceability** of chemical **measurement results**.

- There is a belief that the use of a **reference material** (**RM**) or a **certified reference material** (**CRM**) for quality control purposes automatically establishes **metrological traceability.**

- Claims are made that participation in an **interlaboratory comparison**, proficiency testing scheme, or external quality assessment scheme automatically provides **metrological traceability** of the participants’ **measurement results**.

- VIM2 does not define concepts such as **metrological reference,** ‘traceability to the SI’, **metrological traceability chain**, and **calibration hierarchy**.

- VIM3 does not define the concept **metrological reference**.

In response to the group of problems identified above under the first solid bullet, **metrological traceability** is only considered to be a characteristic of the concepts of

measured quantity value and **measurement result**. In cases in which the history of physical objects is to be established, it is suggested to designate other concepts by terms such as "document traceability" or "sample traceability".

The VIM3 defines

metrological traceability (Concept 1.1-2)

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**

NOTE 1 For this definition, a 'reference' can be a definition of a **measurement unit** through its practical realization, or a **measurement procedure** including the **measurement unit** for a non-**ordinal quantity,** or a **measurement standard**.

NOTE 2 Metrological traceability requires an established **calibration hierarchy**.

NOTE 3 Specification of the reference must include the time at which this reference was used in establishing the calibration hierarchy, along with any other relevant metrological information about the reference, such as when the first calibration in the calibration hierarchy was performed.

NOTE 4 For **measurements** with more than one **input quantity to the measurement model** each of the input **quantity values** should itself be metrologically traceable and the calibration hierarchy involved may form a branched structure or a network. The effort involved in establishing metrological traceability for each input quantity value should be commensurate with its relative contribution to the measurement result.

NOTE 5 Metrological traceability of a measurement result does not ensure that the measurement uncertainty is adequate for a given purpose or the absence of mistakes.

NOTE 6 A comparison between two measurement standards may be viewed as a calibration if the comparison is used to check and, if necessary, correct the quantity value and measurement uncertainty attributed to one of the measurement standards.

NOTE 7 The ILAC considers the elements for confirming metrological traceability to be an unbroken **metrological traceability chain** to an **international measurement standard** or a **national measurement standard**, a documented measurement uncertainty, a documented measurement procedure, accredited technical competence, metrological traceability to the **SI**, and calibration intervals (see ILAC P 10:2002 [15]).

NOTE 8 The abbreviated term ‘traceability’ is sometimes used to mean “metrological traceability” as well as other concepts, such as “sample traceability” or “document traceability” or “instrument traceability”, or “material traceability”, where the history (“trace”) of an item is meant. Therefore, the full term of “metrological traceability” is preferred if there is any risk of confusion. [VIM3-2.41]

1.2 Importance of metrological traceability

Among the many aspects of **measurement** that affect reliability, **metrological traceability** is essential. It underpins the ability of the analyst to claim that his or her result “is what it purports to be”[16].

A key requirement in many situations, such as in border-crossing trade, in laboratory medicine (clinical laboratory sciences), and in transnational implementation of environmental regulations, is that of **metrological comparability** of **measurement results**. If a given **quantity** is measured in a given material by both buyer and seller, they should be confident that they will obtain **measurement result**s agreeing within their stated **measurement uncertainties**.

The need for **metrological comparability of measurement results** also extends in time. In order to understand temporal changes of a monitored system, such as the carbon dioxide concentration in the atmosphere at a particular location, or the cholesterol concentration in a person’s blood plasma, **measurement results** obtained at one time must be comparable with those obtained at another time, in the same or in another laboratory. This is assured, even if **calibrators** or **measuring systems** are different, when the results are traceable to the *same* **metrological reference**.

‘Comparability’ is introduced in the VIM3 as

> **metrological comparability of measurement results** (Concept 1.2-1)
> **metrological comparability**
>
> comparability of **measurement results**, for **quantities** of a given **kind**, that are metrologically traceable to the same reference
>
> NOTE 1 See Note 1 to 2.41 **metrological traceability**.
>
> NOTE 2 Metrological comparability of measurement results does not necessitate that the **measured quantity values** and associated **measurement uncertainties** compared are of the same order of magnitude.
>
> [VIM3-2.46]

This concept should be distinguished from **metrological compatibility of measurement results** (see 5-6).

2 Concepts related to metrological traceability

Before attempting to describe various aspects and relations of **metrological traceability**, it is necessary to define and comment upon some fundamental concepts used in the description. This is especially true because terminology varies among chemical disciplines. This chapter is based on the concepts and associated terms given in the VIM3 [17], and ISO 17511 [10], interspersed with supplementary proposals.

2.1 General concepts in measurement

This central concept is defined as

measurement (Concept 2.1-1)

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

NOTE 1 Measurement does not apply to **nominal properties**

NOTE 2 Measurement implies comparison of quantities including counting of entities.

[VIM3-2.1]

'Quantity' is defined as

quantity (Concept 2.1-2)

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

[VIM3-1.1]

The concept **quantity** may be divided into the generically subordinate concepts [18, 19], here called types of quantity:

- **ordinal quantity** [VIM3-1.26]
- ‘differential quantity’ (also known as “difference quantity” or “interval quantity”)
- ‘logarithmic differential quantity’
- ‘rational quantity’ (also known as “ratio quantity”)

of which the first cannot be associated with a **measurement unit** whereas the next three all have **measurement units**. When **quantities** of the last three types have the **quantity dimension** [VIM3-1.7] one, the coherent **measurement unit** is one (symbol “1”).

The description of a **quantity** should include information about the system considered, any relevant component(s) and the **kind-of-quantity** [VIM3-1.2]. Each of these three parts may require specifications. The description of the **quantity** intended to be measured, i.e. the **measurand**, may be in the format: System(specification) — Component(specification); **kind-of-quantity**(specification). For identification of a particular system (instantiation), a stated location and calendar time are required. For a component, it may be necessary to specify information such as oxidation state and speciation of an element in a matrix, or isomeric form of a compound. For a **kind-of-quantity**, **calibrator** or **measurement procedure** can be specifications. IUPAC and IFCC have published a number of technical reports using this format under the global title of “Properties and units in the clinical laboratory sciences” [20], but see also [21, 22].

Dedicated **kinds-of-quantity** [21] for each type of **quantity** are given in Table 2.1 – 1.

Table 2.1 – 1 Dedicated **kinds-of-quantity** [21] for each type of **quantity**.

Type of **quantity**	System[*]	Component (Analyte)	**Kind-of-quantity**	**Measurement unit**
ordinal	petroleum fuel	petroleum fuel	*octane number*	not applicable
differential	thermostat	water	Celsius temperature	degree Celsius
logarithmic differential	lake	water	pH	one
rational	butter	sodium chloride	amount-of-substance content substance content	mole per kilogram
	ore	iron	mass fraction	one (= kilogram per kilogram)
	exhaled air	ethanol	mass concentration	kilogram per cubic metre

[*] Location and calendar time are necessary specifications to ‘system’ to convert a dedicated **kind-of-quantity** into a singular quantity (ie an instance).

The allowed mathematical treatment of **quantity values** depends on the type of **quantity**.

The act of **measurement** requires the following set of interacting elements:

- **measurand**, defined by **kind-of-quantity**, any component(s), and instantiated system (**Table 2.1 – 1**);
- **measurement model** or **measurement function**;
- **measurement principle**(s);
- **measurement method**;
- validated **measurement procedure** including a **calibration hierarchy**;
- **measuring system** under quality control; and
- operator(s).

Measurement leads to a

measurement result (Concept 2.1-3)

result of a measurement

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

NOTE 1 A measurement result generally contains “relevant information” about the set of quantity values, such that some may be more representative of the **measurand** than others. This may be expressed in the form of a probability density function (PDF).

NOTE 2 A measurement result is generally expressed as a single **measured quantity value** and a measurement uncertainty. If the measurement uncertainty is considered to be negligible for some purpose, the measurement result may be expressed as a single **measured quantity value**. In many fields this is the common way of expressing a measurement result.

NOTE 3 In the traditional literature and in the previous edition of the VIM, measurement result was defined as a value attributed to a measurand and explained to mean an **indication**, or an uncorrected result, or a corrected result, according to the context.

[VIM3-2.9]

This entry requires three further definitions.

measurand (Concept 2.1-4)

quantity intended to be measured

NOTE 1 The specification of a measurand requires knowledge of the **kind of quantity**, description of the state of the phenomenon, body, or substance carrying the quantity, including any relevant component, and the chemical entities involved.

NOTE 2 In the 2nd edition of the VIM and in IEC 60050-300:2001, the measurand is defined as the 'quantity subject to measurement'.

NOTE 3 The **measurement,** including the **measuring system** and the conditions under which the measurement is carried out, might change the phenomenon, body, or substance such that the quantity being measured may differ from the **measurand** as defined. In this case adequate **correction** is necessary.

EXAMPLE 1 The potential difference between the terminals of a battery may decrease when using a voltmeter with a significant internal conductance to perform the measurement. The open-circuit potential difference can be calculated from the internal resistances of the battery and the voltmeter.

EXAMPLE 2 The length of a steel rod in equilibrium with the ambient Celsius temperature of 23 °C will be different from the length at the specified temperature of 20 °C, which is the measurand. In this case a correction is necessary.

NOTE 4 In chemistry, “analyte”, or the name of a substance or compound, are terms sometimes used for ‘measurand’. This usage is erroneous because these terms do not refer to quantities.

[VIM3-2.3]

The delineation of a system carrying a measurand will influence the type of sampling plan and thereby the sampling measurement uncertainty.

Example 1: in the measurement of amount-of-substance content of total Cd in a given agricultural piece of land, the measurement results will differ depending on whether the chosen system is the whole field, or a single sample; the sampling plan chosen for the field will also influence the measurement result.

Example 2: the amount-of-substance concentration of glucose in fasting human venous blood plasma of a person will depend on whether the system of plasma is thought to come from a group of healthy persons, a given person, or a given sample of a person.

quantity value (Concept 2.1-5)

value of a quantity

value

number and reference together expressing magnitude of a **quantity**

[VIM3-1.19]

measured quantity value (Concept 2.1-6)

measured value of a quantity

measured value

quantity value representing a **measurement result**

NOTE 4 In the GUM, the terms “result of a measurement” and “estimate of the value of the measurand” or just “estimate of the measurand” are used for ‘measured quantity value’.

[VIM3-2.10]

A **quantity value** can be expressed as a

- product of a number and a **measurement unit** for a differential, differential logarithmic, or rational **quantity**, e.g. amount-of-substance concentration of Cd^{2+} in a sample of wine = 1.2×10^{-6} mol L^{-1}; or
- number for a differential, logarithmic differential, or rational **quantity** of metrological dimension one, e.g. pH of a blood sample = 7.2, (the **SI unit** “one” is generally not written out), number fractions of lymphocytes among all leukocytes in blood; or

- number and a reference to a **measurement procedure** for an **ordinal quantity**, e.g. Rockwell C hardness (150 kg load) of a steel sample = 43.4 HRC(150 kg); or

- product of a number, a **measurement unit** for a differential or rational **quantity** with **kind-of-quantity** specified by a **measurement procedure,** e.g. a leaching procedure; or

- number, a non-SI **measurement unit** for a differential or rational **quantity** with **kind-of-quantity** specified by convention and carried by a **calibrator**, and some reference to a **measurement procedure**, e.g. arbitrary concentration(WHO second International Standard 91/666; immuno-procedure) of coagulation factor VIII in a plasma sample = 5 000 International Units per litre.

2.1.1 The relation between input and output quantities is described in the most general way by a

measurement model (Concept 2.1-7)
model of measurement
model

mathematical relation among all **quantities** known to be involved in a **measurement**

NOTE 1 A general form of the measurement model is the equation $h(Y, X_1, \ldots, X_n) = 0$, where Y, the **output quantity in the measurement model**, is the **measurand** that is to be inferred from information about **input quantities in the measurement model** $X_1, \ldots, X_n$.

NOTE 2 In more complex cases where there are two or more output quantities, the measurement model consists of more than one equation.

[VIM3-2.48]

A **measurement model** accommodates algorithms as well as explicit functions and will be used later for specific examples of **metrological traceability chains** in Chapters 11 and 12.

In practice, the **output quantity in a measurement model** can often be calculated by using a

measurement function (Concept 2.1-8)

function of **quantities**, the **values** of which, when calculated using known **quantity values**, for the **input quantities in a measurement model**, is a **measured quantity value** of the **output quantity in the measurement model**

NOTE 1 If a **measurement model** $h(Y, X_1, \ldots, X_n) = 0$ can explicitly be written as $Y = f(X_1, \ldots, X_n)$, where Y is the output quantity in the measurement model, the function f is the measurement function. More generally, f may symbolize an algorithm, yielding for input quantity values $x_1, \ldots, x_n$ a corresponding unique output quantity value $y = f(x_1, \ldots, x_n)$.

NOTE 2 The measurement function is used to calculate the **measurement uncertainty** associated with the measured quantity value of Y.

[VIM3-2.49]

Sometimes, the **measurement function** may be written as

$$Y = f(X_1, \ldots, X_j)|(X_k, \ldots, X_n) \qquad \text{(Equation 2.1-1)}$$

where $X_1, \ldots, X_j$ may be

- **input quantities in a measurement model**, measured in the experiment to establish the **quantity value** of Y, that are given by the defining **quantity equation** (VIM3-

1.22) of the **kind-of-quantity** for Y, such as mass concentration = mass of component (i.e. element or compound) divided by volume of system;

- **input quantities in a measurement model,** measured in the experiment to establish the **quantity value** of Y, that are different from those given by the definition of the **kind-of-quantity** for Y;
    - **quantities** taken from literature, such as molar masses or constants;
    - **corrections** (see section 2.10) for **quantities** that are inherent in the measured system or sample such as a **correction** for the effect of haemoglobin concentration when measuring bilirubin concentration in plasma by visible light spectrometry; and
    - **corrections** for external **quantities** that affect the measured system or the **measuring system**, such as ambient temperature, pressure, or humidity;

and X_k, …, X_n may comprise

- **quantities** that influence one or more of the **input quantities** X_1, …, X_j and have given values, such as the specified experimental temperature in **measurement** of catalytic activity; they can be regarded as specifications to the definition of the **measurand**.

All **input quantity values** x_1, …, x_n must be metrologically traceable. They contribute components of the **measurement uncertainty** for the **measurand** Y.

The output is a **measured quantity value**.

The **measured quantity value**, y, calculated by the function $y = f(x_1, …, x_j)$, is an estimate of the location of the distribution of **quantity values** that is attributed to the **measurand**, which belongs to, and describes, an investigated system. A **measurement function** is usually based on the best available theory, which may not be complete. For example, the Bates-Guggenheim **correction** for ionic strength in the **measurement function** for pH determined using a Harned cell is known to be based on an incomplete theory. Known and presumed deficiencies in the definition of the **measurand** and thereby in the **measurement function** or **measurement model** contribute components to the **measurement uncertainty** of the **measured quantity value**. The combination of such components constitutes a

definitional uncertainty (Concept 2.1-9)

component of **measurement uncertainty** resulting from the finite amount of detail in the definition of a **measurand**

NOTE 1 Definitional uncertainty is the practical minimum measurement uncertainty achievable in any **measurement** of a given measurand.

NOTE 2 Any change in the descriptive detail leads to another definitional uncertainty.

NOTE 3 In the GUM:1995, D.3.4, and in IEC 60359 the concept 'definitional uncertainty' is termed "intrinsic uncertainty".

[VIM3-2.27]

Note: Defining the **measurand** is the first step of any **measurement procedure**. The ensuing **definitional uncertainty** can therefore be considered as a part of the **measurement uncertainty**.

For each measured **input quantity** in a **measurement model**, a **measurement principle** has to be chosen and translated into a **measurement method** and **measurement procedure**. A

measuring system is then assembled accordingly, including the indicated measuring equipment, **calibrators**, and any chemical reagents.

measurement principle (Concept 2.1-10)

principle of measurement

phenomenon serving as the basis of a **measurement**

[VIM3-2.4]

Examples of measurement principles are:

- absorption of radiation energy in light spectrometry for the **measurement** of amount-of-substance concentration;
- lowering of the concentration of glucose in blood in a fasting rabbit applied to the **measurement** of insulin concentration in a preparation; and
- conversion of two different kinds of uncharged particles into ions (“ionization”) in a mass spectrometer for the **measurement** of their amount-of-substance ratio.

measurement method (Concept 2.1-11)

method of measurement

generic description of a logical organization of operations used in a **measurement**

[VIM3-2.5]

When a **measurement** requires the sequential or parallel use of several pieces of equipment or reagents or both, the **measurement method** consists of a short presentation of the procedural structure.

The detailed instructions for performing the **measurement** are provided to the operator(s) in a

measurement procedure (Concept 2.1-12)

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**
[VIM3-2.6]

The **measurement procedure** is usually a document including the **measurement model**, **measurement principle**(s), **measurement method**, description of **measuring system**, (including equipment, reagents, and utensils), **calibrators**, **metrological traceability** of obtainable **measurement results**, calculation of **measurement result,** including **measurement uncertainty**, quality control system, and reporting. Any **measurement procedure** must be validated.

Any **measurement procedure** identifies a

measuring system (Concept 2.1-13)

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**

[VIM3-3.2]

2.2 Calibration

Measuring systems in chemistry need to be calibrated in such a way as to ensure **metrological traceability** of the **measurement result**. An unknown **quantity value** embodied in a sample is measured by means of a calibrated **measuring system,** , according to a **measurement procedure.** The calibrated **measuring system** provides an **indication** that is transformed through a **measurement model** into a **measured quantity value** of the **measurand**. The **measurement result** then consists of this **measured quantity value** and its calculated **measurement uncertainty**.

The definition of **calibration** is

calibration (Concept 2.2-1)

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

NOTE 1 A calibration may be expressed by a statement, calibration function, **calibration diagram**, **calibration curve**, or calibration table. In some cases it may consist of an additive or multiplicative **correction** of the indication with associated measurement uncertainty.

NOTE 2 Calibration should not be confused with **adjustment of a measuring system,** often mistakenly called ‘self-calibration’, nor with **verification** of calibration.

NOTE 3 Often, the first step alone in the above definition is perceived as being calibration.

[VIM3-2.39]

Quantity value, y_{cal}, of a **measurement standard**, here chosen to be a **calibrator**, is the independent variable and **indication**, I_{cal} , is the dependent variable in the first step of the definition corresponding to the calibration model $h(I_{\mathrm{cal}}, Y_{\mathrm{cal}}) = 0$. The second step produces the inverse **measurement model** $h(Y_{\mathrm{sample}}, I_{\mathrm{sample}}) = 0$.

The outcome of the **calibration** may be documented in a certification report or **calibration certificate** (see Concept 6-1).

2.3 Calibration hierarchy and metrological traceability chain

Metrological traceability requires an established sequence of **calibrations** and assignments of **quantity values** between a **metrological reference** and a **measurement result**. These operations are performed using **calibrators** and **measuring systems** with **measurement procedures** and constitute a

> **calibration hierarchy** (Concept 2.3-1)
>
> sequence of **calibrations** from a reference to the final **measuring system**, where the outcome of each calibration depends on the outcome of the previous calibration
> [VIM3-2.40]

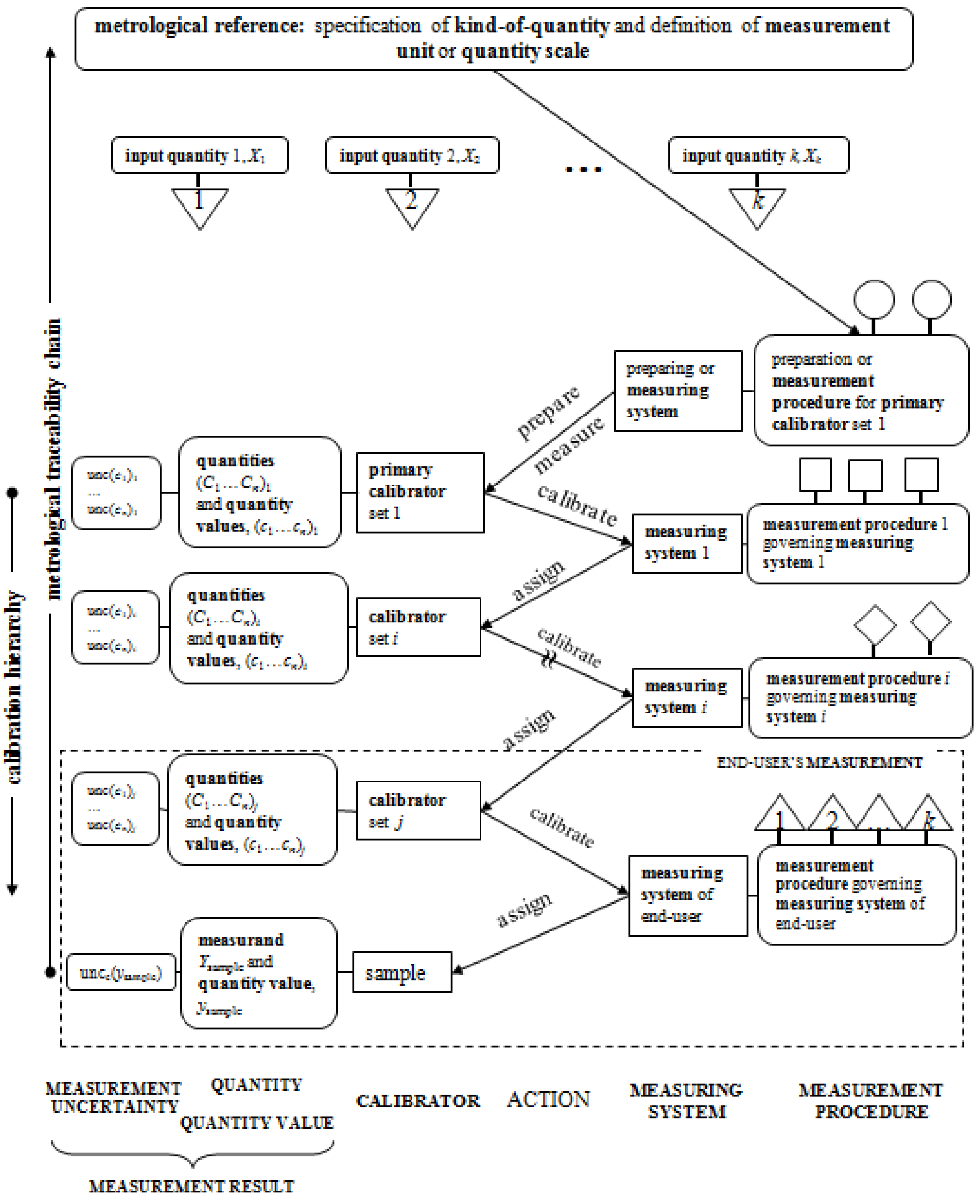
For this definition, a **metrological reference** for a differential, logarithmic differential, or rational **quantity** can be a definition of a **measurement unit** with its embodiment in a **primary calibrator** (material or device), using a **primary measurement procedure** or a production procedure. For an **ordinal quantity**, the **metrological reference** is a definition of an **ordinal quantity-value scale** with its embodiment in a set of **primary calibrators** using a production procedure.

The **calibration hierarchy** extends down from the step following the **metrological reference**, but to describe **metrological traceability** of the **measurement result**, the direction is reversed. The sequence between **measurement result** and **metrological reference** is termed and defined:

> **metrological traceability chain** (Concept 2.3-2)
>
> **traceability chain**
>
> sequence of **measurement standards** and **calibrations** that is used to relate a **measurement result** to a **reference**
> [VIM3-2.42]

A **metrological traceability chain** requires a pre-established **calibration hierarchy** that is chosen before the **measurements** start. As **metrological traceability** characterizes the concept **measurement result**, the **metrological traceability chain** is "attached" to the **measurement result** and links it to the chosen **metrological reference**.

In principle, the elements of a single-stranded **calibration hierarchy** may be coupled as in the generic flow chart shown in Figure 2.3–1.



measurement model $h(Y_{\text{sample}}, C_{1,j}, I_{C1,j}, I_{\text{sample}}, X_1, \ldots, X_k) = 0$

Figure 2.3–1: Generic flow chart of a **calibration hierarchy** providing **metrological traceability** of a **measurement result** for which the **metrological reference** can be

a) “definition of **kind-of-quantity** and **measurement unit**” which is embodied by preparing a set of one or more **primary calibrators**, through **measurement** using a **primary measurement procedure**; or

b) “definition of **kind-of-quantity** and **measurement unit**” which is embodied by preparing a set of one or more **primary calibrators** through a production procedure; or

c) “definition of ordinal **kind-of-quantity** and **ordinal quantity-value scale**” which is embodied in a set of **calibrators** through a production procedure.

unc is an abbreviation signifying a generalized **measurement uncertainty** that is calculated according to GUM in cases a) and b), but not in c). The symbol *u* will be used in specific examples of a) and b).

A rectangle contains a material object, namely a **measuring system**, **calibrator**, or sample. A rounded box contains a documentary object, namely a definition, **measurement procedure**, **measured quantity value**, or **measurement uncertainty**.

Down-pointing triangles contain a number labeling a **metrological reference** for an **input quantity in the measurement model** shown in up-pointing triangles on the end-user’s **measurement procedure**. Each level in the **calibration hierarchy** has its own **measurement model** and set of **input quantities in the measurement model**, depicted by different shapes attached to the right-hand boxes.

A given **calibrator** in a **calibration hierarchy** serves to calibrate a subsequent **measuring system** that, by **measurement** according to a **measurement procedure**, yields the **measured quantity value** and **measurement uncertainty** for the next **calibrator** or, finally, for the end-user’s sample. The **measurement uncertainty** associated with the **quantity value** carried by any **calibrator** is necessarily larger than that of a preceding **calibrator** and smaller than that of a following **calibrator** as well as the expected **measurement uncertainty** of the final **measurement result**.

In physics, **calibration hierarchies** have long been an established part of **measurement** [23, 24]. For complex chemical **measurements**, the formal establishment of **calibration hierarchies** is more recent. A particular concern in chemistry is that when amount-of-substance is reported, i.e. in the **SI unit** mole, the embodiment of the definition of the mole would require a **primary measurement standard** for each of the millions of chemical compounds. CCQM has selected **measurement principles** and **measurement methods** which have the potential for the development of **primary measurement procedures** giving **quantity values** in mole or its derived **measurement units** for the **quantities** carried by **primary calibrators**. This approach is only possible when the chemical entity or entities specified in a **measurand**, can be defined by their atomic or molecular structure, or a suitable part of that. If the elementary entities cannot be thus defined, then amount-of-substance cannot be measured. In this case, and if the component can be otherwise specifically recognized, **kinds-of-quantity** such as mass, which do not need elementary entities to be specified, can be chosen. Provided that the **quantity** for **measurement** is differential or rational, the **metrological reference** may then be the definition of another **measurement unit**, such as the kilogram or a WHO International Unit of a given type of biological activity. For an **ordinal quantity**, no **measurement unit** is involved and the **metrological reference** may be a **measurement procedure** with or without an ensuing **calibrator**.

As mentioned before, the **measurand**, for which the **measurement result** has to be metrologically traceable, must be carefully defined with regard to system, any component(s), and **kind-of-quantity**. In a single-stranded **calibration hierarchy**, the **kind-of-quantity** is the same throughout.

The term "calibration hierarchy" is used in EAL-G12 [25] and ILAC-G2 [9] in the sense of a plurilevel hierarchy of coordinated and interacting bodies responsible for maintaining and disseminating various types and metrological levels of **measurement standards**. To avoid ambiguity, the present text uses the term "**metrological institutional hierarchy**" for such a hierarchy. This is further elaborated in Chapter 8.

2.4 Metrological reference

The concept may be defined as follows:

metrological reference (Concept 2.4-1)

normative document specifying a **kind-of-quantity** and defining one or more conventionally chosen **quantity values** of that **kind-of-quantity**

There are two possible types of normative document providing either

(a) a definition of a **measurement unit**, or

(b) a definition of an **ordinal quantity-value scale** [VIM3-1.28].

The **measurement unit**, whether base or derived, coherent or non-coherent, is embodied in a **primary calibrator**. The embodiment may be achieved by either

- **measurement,** using a **primary measurement procedure** and a **measuring system**, assigning a differential or rational **quantity value** with **measurement uncertainty** (see Figure 2.3–1); or

- production, using a production procedure, the execution of which delivers a differential or rational **quantity value** and its **measurement uncertainty** (see Figure 2.3–1, legend a) and b)), such as by the preparation of a Josephson junction for the volt, an atomic clock for the second, the international prototype of the kilogram for the kilogram, and a batch of high purity copper for the mole per kilogram.

The **ordinal quantity-value scale**, unrelated to any **measurement unit**, is embodied in a set of **primary calibrators** that are made according to a preparation procedure, the execution of which delivers the individual **quantity values** and their **measurement uncertainties** (see Figure 2.3–1, legend c)), such as a set of petroleum fuel **primary calibrators** for **measurement** of octane number. **Measurement uncertainty** for an **ordinal quantity value** cannot be calculated according to GUM, and must be evaluated by another method.

2.5 Measurement standard

A key concept in **measurement** is

measurement standard (Concept 2.5-1)

etalon

realization of the definition of a given **quantity**, with stated **quantity value** and associated **measurement uncertainty**, used as a reference

[VIM3-5.1]

The "realization of the definition of a given **quantity**" can be provided by operating a **measuring system** according to a **measurement procedure**, or by a **material measure**, or by a **reference material (RM)** (**calibrator** or **certified reference material, CRM**). In the case of chemical **measurement standards**, the term "embodiment" is here preferred to "realization" as the latter term carries several non-applicable connotations. In many cases in chemistry, **measurement standards** are embodiments of the definition of a **measurement unit**. Several **quantities** of the same or different **kinds-of-quantity** may be embodied in one **measurement standard**.

Examples of **measurement standards** (partly taken from VIM3) are, a 1 kg mass standard; a standard hydrogen electrode; a set of reference solutions of cortisol in human serum having certified concentrations of cortisol; a **certified reference material** providing certified **quantity values** for the mass concentration of each of ten different proteins; and an ampoule with WHO International Standard 75/589 containing 650 International Units of chorionic gonadotropin. In all cases, a **quantity value** must be accompanied by a **measurement uncertainty** and stated **metrological traceability**.

A series of "descending levels" of **measurement standards** or **calibrators**, i.e. with increasing **measurement uncertainties** of assigned **quantity values** in a given **calibration hierarchy**, is often described by the following concepts.

primary measurement standard (Concept 2.5-2)

primary standard

measurement standard established using a **primary measurement procedure** or created as an artefact, by convention

EXAMPLE a) primary measurement standard of amount-of-substance concentration prepared by dissolving a known amount of substance of a chemical component to a known volume of solution.

[VIM3-5.4]

A **primary measurement standard** of a differential or rational **quantity** embodies its **measurement unit**. **Ordinal quantities** have no **measurement units** and the established **quantity value** and **measurement uncertainty** rely on the **metrological reference** and on the means of embodiment described in Section 2.4.

The first **measurement standard** (or **calibrator**) of a **calibration hierarchy** for a differential or rational **quantity** is always a **primary measurement standard** (or **primary calibrator)**. The assignment of **quantity value** with the associated **measurement uncertainty** to a **primary measurement standard** is done by means of a **primary measurement procedure**.

A **primary measurement standard** can be used to calibrate a **measuring system** by which a **quantity value** with associated **measurement uncertainty** is assigned to a

secondary measurement standard (Concept 2.5-3)

secondary standard

measurement standard established through **calibration** with respect to a **primary measurement standard** for a **quantity** of the same **kind**

[VIM3-5.5]

The following concept is much used:

reference measurement standard (Concept 2.5-4)

reference standard

measurement standard designated for the **calibration** of other measurement standards for **quantities** of a given **kind** in a given organization or at a given location

[VIM3-5.6]

The metrologically lowest **measurement standard** defined by VIM3 is

working measurement standard (Concept 2.5-5)

working standard

measurement standard that is used routinely to calibrate or verify **measuring instruments** or **measuring systems**

[VIM3-5.7]

Note – A **measurement standard** should only be used for one function (either as a calibrator or as a verification material) in a **measurement**.

The **quantity value** and **measurement uncertainty** of a **working measurement standard** is established using the **measurement procedure** located just above the end-user's **measurement procedure** in the **calibration hierarchy**.

In independent terminological dimensions, modifiers such as “international” [VIM3-5.2], “national“ [VIM3-5.3], “regional”, “travelling” [VIM3-5.8], “intrinsic” [VIM3-5.10] or “reference” [VIM3-5.6] are sometimes used as prefaces to “measurement standard”.

2.6 Calibrator

When a **measurement standard** is used specifically for the purposes of **calibration** rather than for quality control, it becomes a

calibrator (Concept 2.6-1)

measurement standard used in **calibration**
[VIM3-5.12]

In addition to the assigned **quantity value** and **measurement uncertainty**, a **calibrator** must be accompanied by information about: the origin (material traceability), production, definition of **quantity**, any matrix, and homogeneity, stability, procedure used in the assignment of **quantity value** and **measurement uncertainty**, statement of **metrological traceability**, expiry date, intended use of the **calibrator** [26, 27], and instructions for use. In addition to these essential properties, its use in a **calibration hierarchy** requires that it be commutable (see Concept 3.1-3).

In other words, the relative behaviour of a **calibrator** vis-à-vis a preceding **measurement procedure** assigning a **quantity value** and the subsequent **measurement procedure** in a **calibration hierarchy** must be the same as that of relevant routine materials.

2.7 Measurement uncertainty

This concept is defined as

measurement uncertainty (Concept 2.7-1)

uncertainty of measurement

uncertainty

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

[VIM3-2.26]

The dispersion is due to **definitional uncertainty** of the **measurand**, random effects from various sources, and the **measurement uncertainty** associated with corrections for systematic effects in the **measurement**.

The **measurement uncertainty** may be expressed as a standard deviation called **standard measurement uncertainty** or a given multiple of it, or the half-width of an interval, having a stated **coverage probability**.

Measurement uncertainty comprises, in general, many components [2]. Some of these components may be evaluated by **Type A evaluation of measurement uncertainty,** based on the statistical distribution of the **quantity values** from replicated **measurements,** and can be described by standard deviations. The other components, which may be evaluated by **Type B evaluation of measurement uncertainty**, can also be described by standard deviations, evaluated from assumed probability density functions based on experience or other information.

It is understood that the **measured quantity value** of a **measurement result** is the best estimate of the **quantity value** of the **measurand**.

All components of **measurement uncertainty** contribute to the dispersion, including those arising from a correction for each systematic effect, such as components associated with **recovery**, bias corrections, and the assigned **quantity values** of **measurement standards** including **calibrators**.

The **degree of metrological equivalence of measurement results** for the same **quantity** in the same material is evaluated by statistical procedures based on the absolute difference between the two **measured quantity values** and their respective **measurement uncertainties**.

The **quantity value** of each **calibrator**, except the first one, in a **calibration hierarchy**, has a **combined standard uncertainty** that incorporates the **combined standard uncertainty** of the **quantity value** of the previous **calibrator**, and it must be evaluated and stated. Therefore, in the **calibration hierarchy** of, for example, Figure 2.3–1, each relative **measurement uncertainty** $u(y_{i+1})/y_{i+1}$ is perforce greater than the previous relative **measurement uncertainty** $u(y_i)/y_i$ because $u(y_{i+1})/y_{i+1}$ combines $u(y_i)/y_i$ and the new components of **measurement uncertainty** incurred at step i+1.

Obviously the **quantity value** of a **primary calibrator** is established to a smaller **measurement uncertainty** than the **quantity value** of a **secondary calibrator** and so on. Also, the **measurement uncertainty** of the **quantity value** of a **calibrator** will be smaller than that of the following **measurement result**.

How **measurement uncertainties** are evaluated and combined is beyond the scope of this document. Reference is made to GUM [2] and QUAM[28].

Although the **quantity values** of **input quantities in a measurement model** should be metrologically traceable, quantifying the **measurement uncertainty** of a **measurement result** does not of itself establish **metrological traceability**, which is either established or not. Neither is it a useful analogy to say that **measurement uncertainty** demonstrates the “strength” of the **metrological traceability chain**.

2.8 Target measurement uncertainty

The acceptability of a **measurement uncertainty** is determined by the requirements for the intended use of the **measurement result**. That requirement can be formulated as

target measurement uncertainty (Concept 2.8-1)
target uncertainty

measurement uncertainty specified as an upper limit and decided on the basis of the intended use of **measurement results**
[VIM3-2.34]

A **measurement uncertainty** is calculated after a **measurement** has been performed or is assumed to apply to a **measurement result** due to validation of the **measurement procedure** and an accepted outcome of concomitant internal quality control. As the **traceability chain** of the **measurement result** to a **metrological reference** has been decided in the planning stage of the **measurement**, the types of component of the **measurement uncertainty** are fixed by that choice. Its actual value can only be calculated after the initial **measurement** or adopted for later measured quantity values obtained by a process under statistical control. The achieved **measurement uncertainty** can be appropriate for the intended use, or it can be too large, or it can be too small. Thus, the *a priori* fixing of a **target measurement uncertainty** requires a study of the use of the expected **measurement result**. **Target measurement uncertainty** may guide an *a priori* selection of a **calibration hierarchy**, using available knowledge and skill, and is influenced by available equipment and measurement procedures. If the minimum **measurement uncertainty** obtainable in current practice is too large, that may lead to the conclusion that one has to accept a larger

measurement uncertainty than originally desired, or that better **measurement procedures, measuring systems**, and **measurement standards** must be developed to comply with a given requirement.

2.9 Multiple metrological traceability chains

The **measured quantity value** of each **quantity in a measurement model** must be metrologically traceable. In most chemical **measurements** there are several such **input quantities**, each requiring a specified **metrological traceability chain**. If the specification of the **measurand** includes **quantities** with given **quantity values** they too must have demonstrated **metrological traceability chains**. For example, the temperature at which a measurement is made is often specified.

Where the **input quantity in a measurement model** is a conversion factor such as molar mass or a fundamental constant, there is no change in the requirement for **metrological traceability** of its **quantity value**, but it is likely that its **metrological traceability** will have been established elsewhere at an earlier time with a sufficiently small relative **measurement uncertainty**; a short statement to this effect is all that is required when documenting the **metrological traceability**, for example, quoting the use of the latest IUPAC molar masses (or atomic weights), and published CODATA fundamental constants, with their **measurement uncertainties**, is sufficient, and no further documentation of **metrological traceability** of these **quantity values** is needed.

2.10 Correction for systematic effects

When a **quantity value** pertaining to a system is estimated by **measurement** according to a **measurement procedure**, there are cases in which the “initially estimated **quantity**”, must be corrected for systematic effects, caused *inter alia* by:

- sampling from an inhomogeneous system;

- inadequate presentation of the system carrying the **measurand** to the **measuring system**;
- **instrumental bias** [VIM3-4.20];
- **measurement bias** inherent in other elements of a **measurement procedure** , for example using an indicator in an acid-base titration that changes colour at a value of pH other than the equivalence point; and
- influence factors, for example use of volumetric glassware at a temperature different from that of its calibration.

Correction is defined as

correction (Concept 2.10-1)

compensation for an estimated systematic effect

[VIM3-2.53]

It is a general requirement of GUM [2] that **corrections** should be applied for all recognized and significant systematic effects. Correction factors or correction addends for systematic effects may be estimated by replicate **measurements** of an appropriate **certified reference material** using the **measurement procedure**, or by comparison between the **measurement results** obtained with the **measurement procedure** and those obtained using a **reference measurement procedure**. When systematic effects are found to be significant, the **quantity value** of the **measurement result** is the initially estimated **quantity value** corrected for the systematic effects; the **measurement uncertainty** in the **measurement result** is the combination of the **measurement uncertainty** of the initially estimated **quantity value** and the **measurement uncertainties** of the **corrections** for the systematic effects. Clearly, the **metrological traceability** of the **measurement result** requires that both the initially estimated **quantity value** and the **corrections** for the systematic effects be **metrologically traceable**. Therefore, in the estimation of **corrections** for systematic effects, the use of **measurement procedures** that give metrologically traceable **measurement results** and **reference materials** with metrologically traceable **quantity values** are necessary.

In some types of measurement method, “recovery” is related to a form of systematic effect. The concept ‘recovery’ is currently defined by IUPAC in several ways, but it is possible to define a set of concepts with more explicit terms as follows [29].

actual quantity (Concept 2.10-2)

quantity related to a system, including any specified component(s), having an inherent or intentionally increased and known **quantity value**

Note 1: The **quantity** is rational, i.e. it can be divided by other **quantities** of the same **kind**. It is usually *either* a type of amount, i.e. an extensive **quantity** (having a **quantity value** dependent on size of system), such as mass, number of entities, amount-of-substance; *or* a type of concentration or content, i.e. an intensive **quantity** (having a value independent of size of system), such as mass concentration, number concentration, amount-of-substance concentration, amount-of-substance content, mass fraction. Which one is relevant must be specified.

Note 2: A **measured quantity value** is usually obtained by applying a **reference measurement procedure**, which must be specified.

[29]

initially estimated quantity (Concept 2.10-3)

quantity related to a system, including any component(s), having a **quantity value** that is found by **measurement** before **correction** for any loss

Note 1: See Note 1 of ‘actual quantity’

Note 2: The **measurement procedure** must be specified.

Note 3: “Yield” and “recovery” are not recommended synonyms.

[29]

recovered quantity ratio (Concept 2.10-4)

initially estimated quantity related to a system divided by **actual quantity** related to the same system

Note 1: The **quantities** involved are rational and of the same **kind**.

Note 2: See Note 1 of ‘actual quantity’

Note 3: The respective **measurement procedures** must be specified.

Note 4: “Yield”, “recovery”, “recovery factor”, “apparent recovery” and “relative bias” are not recommended synonyms.

Note 5: This concept is a ratio rather than a fraction or relative **kind-of-quantity** because the numerator and denominator relate to the same system.

[29]

2.11 Traceability vs “tracing” and vs “establishing traceability”

The PTB in Germany prefers to stress the *operation* of “establishing the trace” of a **measurement result**, which in German is called “Rückführen”, rather than viewing “traceability” as a property of a **measurement result**. “Traceability” is translated into German as “Rückführbarkeit” by PTB and in Swiss German as “Rückverfolgbarkeit” by

METAS. As of today, there is still no agreement between the two institutes for the German-speaking measurement community on this concept and associated term.

3 Calibration of measuring systems in a calibration hierarchy

3.1 Function of reference materials in a calibration hierarchy

In any given **measurement**, a **reference material** as defined below can function as *either* a **calibrator** *or* a control material in a given **measurement**, not as both. In a **calibration hierarchy**, the first is the obvious role. The term **reference material** is being used with different meanings thus giving rise to ambiguity. Terminologically, **reference material** is generically superordinate to the concept **certified reference material**; yet in a metrological hierarchy, **certified reference material** has a higher status, as it carries a certified **quantity value** with associated **measurement uncertainty**. The definition of **reference material** in the VIM3 is naturally broad in order to cover a variety of meanings, used in practice:

reference material (Concept 3.1-1)

RM

material, sufficiently homogeneous and stable with reference to specified properties, which has been established to be fit for its intended use in **measurement** or in examination of **nominal properties**

NOTE 2 Reference materials with or without assigned quantity values can be used for **measurement precision** control whereas only reference materials with assigned quantity values can be used for **calibration** or **measurement trueness** control.

NOTE 3 'Reference materials' comprises materials embodying **quantities** as well as **nominal properties**.

EXAMPLES OF REFERENCE MATERIALS EMBODYING QUANTITIES

a) water of stated purity, the dynamic viscosity of which is used to calibrate viscometers

b) human serum without an assigned quantity value for the amount-of-substance concentration of the inherent cholesterol, used only as a measurement precision control material

c) fish tissue containing a stated mass fraction of a dioxin, used as a **calibrator**

EXAMPLES OF REFERENCE MATERIALS EMBODYING NOMINAL PROPERTIES

d) colour chart indicating one or more specified colours

e) DNA compound containing a specified nucleic acid sequence

f) urine containing 19-androstenedione

NOTE 4 A reference material is sometimes incorporated into a specially fabricated device.

EXAMPLES

a) substance of known triple-point in a triple-point cell

b) glass of known optical density in a transmission filter holder

c) spheres of uniform particle size mounted on a microscope slide

NOTE 5 Some reference materials have assigned quantity values that are metrologically traceable to a **measurement unit** outside a **system of units**. Such materials include vaccines to which International Units (IU) have been assigned by the World Health Organization.

NOTE 6 In a given **measurement**, a reference material can only be used for either calibration or quality assurance.

NOTE 7 The specifications of a reference material should include its material traceability, indicating its origin and processing.

[VIM3-5.13]

A special type of **reference material** is

certified reference material (Concept 3.1-2)

CRM

reference material, accompanied by documentation issued by an authoritative body and providing one or more specified property values with associated uncertainties and traceabilities, using valid procedures

EXAMPLE

human serum containing cholesterol with assigned **quantity value** and associated **measurement uncertainty** stated in an accompanying certificate, used as **calibrator** or **measurement trueness** control material

NOTE 1 'Documentation' is given in the form of a 'certificate', see ISO Guide 31:2000. [30]

NOTE 2 Valid procedures for the production and certification of certified reference materials are given, e.g., in ISO Guides 34 and 35.[12, 31]

NOTE 3 In this definition, "uncertainty" covers both 'measurement uncertainty' and 'uncertainty associated with the value of a **nominal property**', such as for identity and sequence, expressed as probabilities. "Traceability" covers both '**metrological traceability** of a quantity value' and 'traceability of a nominal property value'.

NOTE 5 Specified quantity values in certified reference materials require metrological traceability with associated measurement uncertainty.

[VIM3-5.14]

commutability of a reference material (Concept 3.1-3)

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

NOTE 1 The reference material in question is usually a **calibrator** and the other specified materials are usually routine samples.

NOTE 2 The measurement procedures referred to in the definition are the one preceding and the one following the reference material (calibrator) in question in a **calibration hierarchy**, see ISO 17511 [10].

NOTE 3 The stability of commutable reference materials is monitored regularly.

[VIM3-5.15]

A **primary calibrator** is often assumed to embody a **quantity** and its **quantity value** with the smallest achievable **measurement uncertainty**, but the size of the relative **measurement uncertainty** is not a criterion for being called “primary”.

The concept may be defined as

primary calibrator (Concept 3.1-2)

calibrator established without reference to another **calibrator** for the same **kind-of-quantity**

Note: The **quantity value** and **measurement uncertainty** of a **primary calibrator** are obtained by a direct **primary measurement procedure** or by production.

Such a **calibrator** is usually accompanied by a certification report [26] or a **calibration certificate** issued by an International or National Metrology Institute.

The next **calibrator** in the **calibration hierarchy** is a

secondary calibrator (Concept 3.1-3)

calibrator established by **measurement** according to a **secondary measurement procedure**

In case no **primary calibrator** is available, it is recommended by ISO 17511 [10] to produce an

international conventional calibrator (Concept 3.1-4)

calibrator established by international agreement

The **kind-of-quantity** must be specified in the **measurement procedure**. It is noted that the **quantity values** of some **international conventional calibrators** are expressed in **SI measurement units** or in non-**SI measurement units** with **measurement procedures** specified.

The ISO 17511 [10] identifies the following two consecutive levels of material.

manufacturer's working calibrator (Concept 3.1-5)

calibrator established by **measurement** according to the manufacturer's selected **measurement procedure** or a higher **measurement procedure** calibrated by a **primary calibrator** or **secondary calibrator** or an **international conventional calibrator**

[adapted from ISO 17511 [10]]

manufacturer's product calibrator (Concept 3.1-6)

calibrator established according to the manufacturer's standing **measurement procedure** calibrated by the **manufacturer's working calibrator**

[adapted from ISO 17511 [10]]

The **manufacturer's product calibrator** may serve as the end-user's working calibrator. It is the obligation of any producer of a **calibrator** to document the **metrological traceability** of a **quantity value** and its **measurement uncertainty**.

Typical disseminations of **calibrators** are shown in Figure 3.1–1, and Figure 3.1–2.

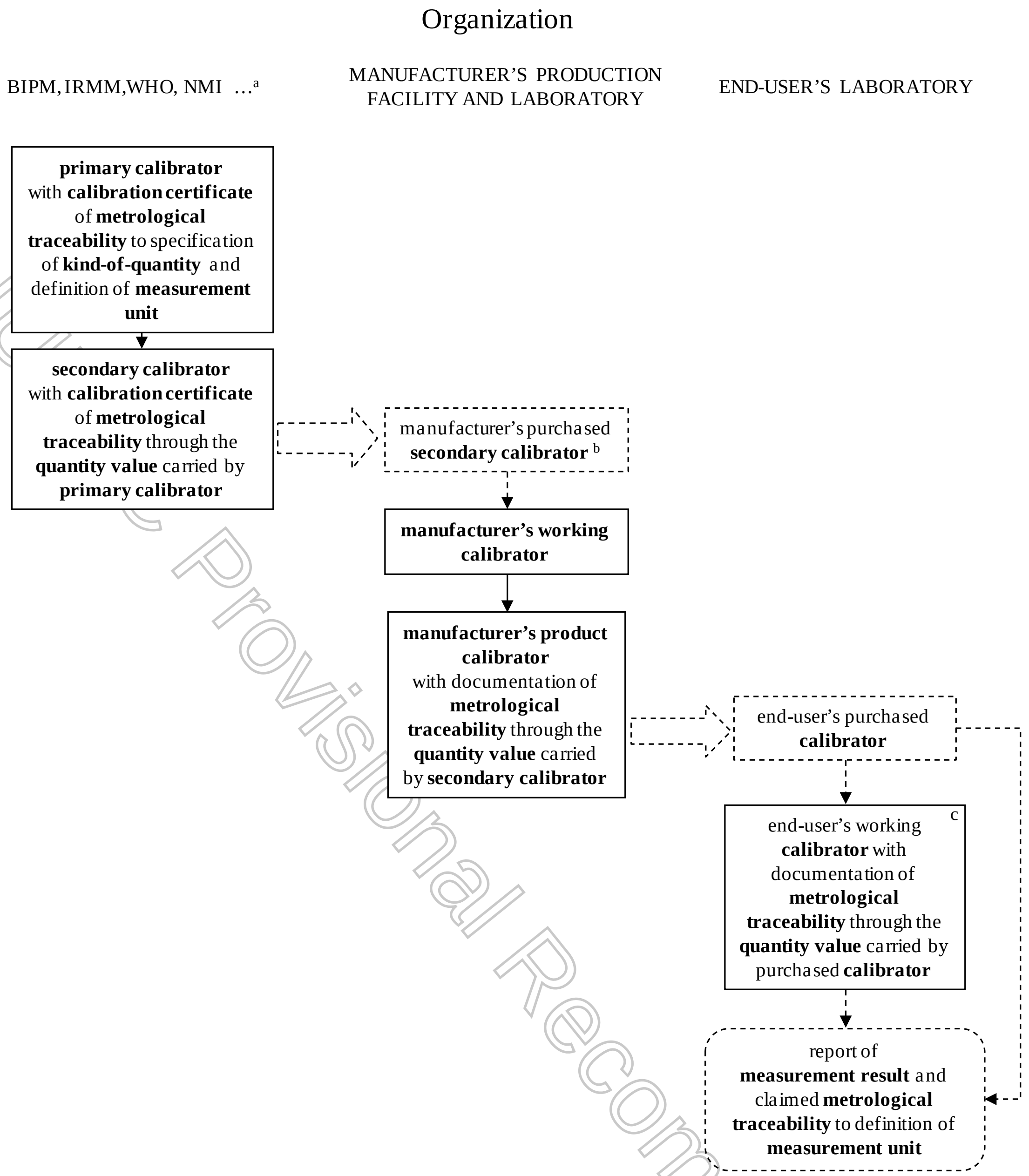


Figure 3.1–1: A hierarchy of calibrators starting with a "**primary calibrator** with **calibration certificate** of **metrological traceability** to specification of **kind-of-quantity** and definition of **measurement unit**".

Boxes connected by a vertical line with an arrow indicates that the **quantity value** and **measurement uncertainty** of the **quantity** of the material described in the lower box are established by **measurement** using the **calibrator** in the upper box as reference. A horizontal block arrow indicates that the **calibrator** in the left hand box is delivered with its **calibration certificate** to become the **calibrator** described in the right hand box.

[a] The **quantity value** and the **measurement uncertainty** of the **quantity** of the **calibrator** may be assigned by a reference measurement laboratory under contract with BIPM or an NMI.

[b] The VIM3 definition of **reference measurement standard** [VIM3-5.6] covers this hierarchical level of **calibrator**.

[c] An end-user may use the purchased **calibrator** directly for routine **measurements** or to assign the **quantity value** and **measurement uncertainty** to the **quantity** of the end-user's working **calibrator** produced in-house to be used for **calibration** in the **measurement** of routine samples (not depicted here).

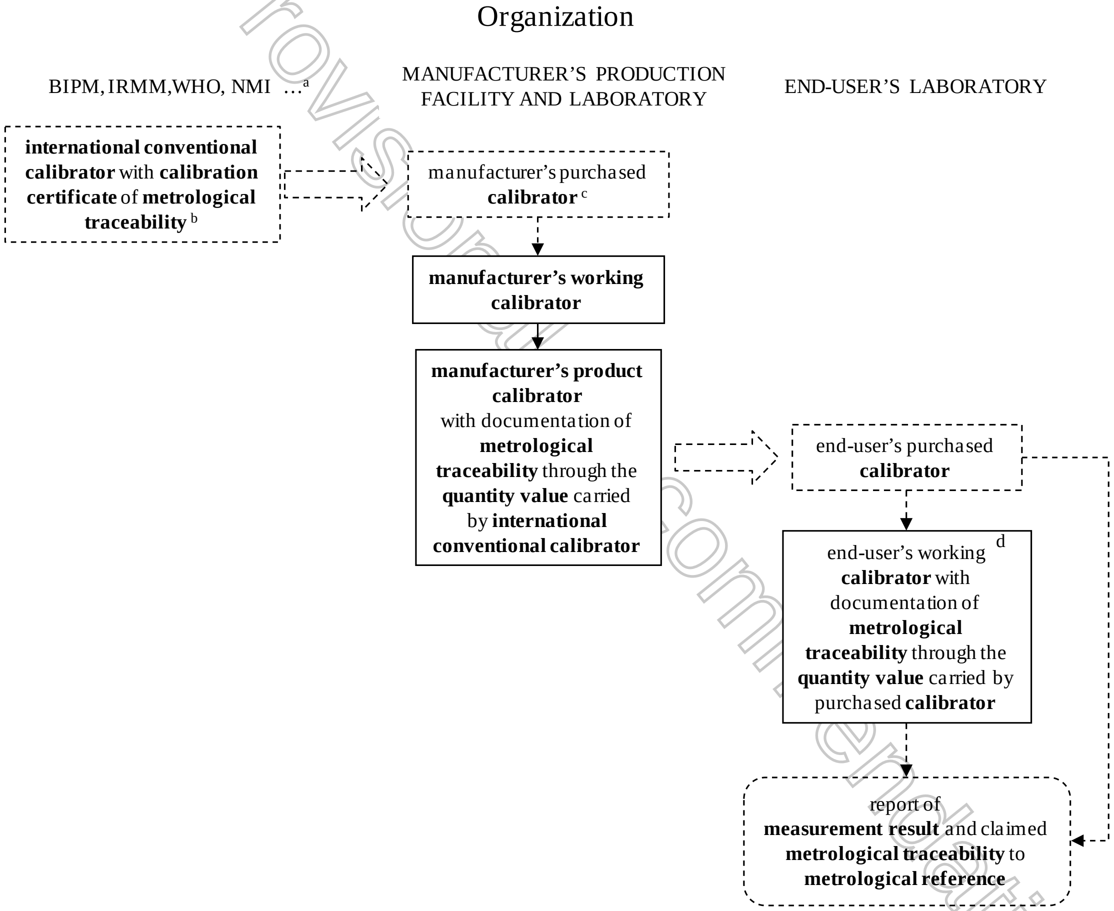


Figure 3.1–2: A hierarchy of calibrators starting with "**international conventional calibrator** with certificate of **metrological traceability**". Boxes connected by a vertical line with an arrow indicates that the **quantity value** and **measurement uncertainty** of the

quantity of the material described in the lower box are established by **measurement** using the **calibrator** in the upper box as reference. A horizontal block arrow indicates that the **calibrator** in the left hand box is delivered with its certificate to become the **calibrator** described in the right hand box.

[a] The **quantity value** and the **measurement uncertainty** of the **quantity** of the **calibrator** may be assigned by a reference measurement laboratory under contract with BIPM or an NMI.

[b] The **international conventional calibrator** is called “International Standard” by WHO. The **quantity value** and **measurement uncertainty** of the **quantity** of such a **calibrator** may be assigned by one or more reference measurement laboratories under contract with WHO.

[c] The VIM3 definition of **reference measurement standard** [VIM3-5.6] covers this hierarchical level of **calibrator**.

[d] An end-user may use the purchased **calibrator** directly for routine **measurements** or to assign the **quantity value** and **measurement uncertainty** to the **quantity** of the end-user’s working **calibrator** produced in-house to be used for **calibration** in the **measurement** of routine samples (not depicted here).

3.2 Function of reference measurement procedures in a calibration hierarchy

Measurement procedures and **calibrators** are essential in most **calibration hierarchies** and the ensuing **metrological traceability chain,** which ends in a definition of a **measurement unit**. The **metrological reference** may further require stipulating a **measurement procedure**. When one **measurement procedure** is commonly agreed, ie stated to be a part of the **metrological reference**, it is called a

reference measurement procedure (Concept 3.2-1)

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**, **calibration**, or in characterizing **reference materials**

[VIM3-2.7]

Especially in case an **SI unit** or another **measurement unit** is not (yet) available, **metrological comparability** of measurement results can be claimed if a **reference measurement procedure** is agreed *a priori* and preferably *internationally*, and if this **reference measurement procedure** is used as the sole **metrological reference** [26].

There is much debate of and ambiguity in the use of the adjective “primary” in relation to **measurement procedure**. Hence it is useful to define

primary reference measurement procedure (Concept 3.2-2)

primary reference procedure

reference measurement procedure used to obtain a **measurement result** without relation to a **measurement standard** for a **quantity** of the same **kind**

NOTE 2 Definitions of two subordinate concepts, which could be termed “direct primary reference measurement procedure” and “ratio primary reference measurement procedure”, are given by CCQM (5th Meeting, 1999).

[VIM3-2.8]

The term “method” in the CCQM text is here replaced by the term “procedure”.

It is also useful to define

secondary reference measurement procedure (Concept 3.2-3)

secondary reference procedure

measurement procedure that has been calibrated by a **primary measurement standard**

4 Establishing metrological traceability of a measurement result

The following checklist presupposes that the **measurement** will be made in a laboratory which is operating under an accreditation scheme (ISO/IEC 17025 [6], ISO 15189 [8], ISO 15195 [7] or GLP [32]), or at least has validated **measurement procedures** and well defined quality assurance procedures in place. **Metrological traceability** may be established as follows.

- Definition of **measurand**, intended use of **measurement results,** and **target measurement uncertainty**

  This will include a clear statement of the type of **quantity** to be measured, including system, relevant components, and **kind-of-quantity** with a statement of the **measurement model** or **measurement function** and description of the **measuring system**, **measurement procedure** including whether any **correction** is to be made for **recovered quantity ratio**[29]. The **target measurement uncertainty** will influence the choice of **metrological traceability chain**; the **measurement uncertainty** will be larger than that associated with the **calibrator(s)** used to establish **metrological traceability.**

- Selection of **metrological reference(s)**

  Establishment of **metrological traceability** can only be achieved to an existing and documented **metrological reference**. In many cases the only reference will be the definition of the **measurement unit** of the **measurement result**, but other situations may apply (see 2.3) and must be stated.

- Selection of **calibration hierarchy**

  By making the selection of the end-user's working **calibrator** on available documentary evidence, its **calibration hierarchy** is fixed. Attention should also be paid to the **calibration** and **metrological traceability** of **measurement results** for **input quantities in a measurement model** and **influence quantities,** including those measured by accessory equipment such as balances, thermometers, and volumetric ware.

- Selection of suitably validated **measurement procedure**

  The analyst should undertake appropriate **verification** that a previously validated "standard" **measurement procedure** may be implemented in the analyst's laboratory.

- Acquisition and **verification** of **manufacturer's product calibrator**

  Such a product **calibrator** should be verified for integrity, validated for **commutability of a reference material**, have documented **metrological traceability** of its stated **quantity value** with associated **measurement uncertainty**.

- End-user's **measurement** on system or sample to obtain **measurement result**, including **measurement uncertainty**, based on an **uncertainty budget** [VIM3-2.33].

- Documentation of **metrological traceability**

  This requires readily available evidence, e.g. certificates, statements etc, of **metrological traceability** for all **calibrators** used, and **calibration certificates** for equipment.

- Reporting of **metrological traceability**

  The amount of detail to be reported should be appropriate to the use of the **measurement result** (see chapter 6).

5 Verification, validation, and equivalence

The VIM3 has changed the definitions of **validation** and **verification** to make the former subordinate to the latter.

verification (Concept 5-1)

provision of objective evidence that a given item fulfils specified requirements

[VIM3-2.44]

validation (Concept 5-2)

verification, where the specified requirements are adequate for a stated use

[VIM3-2.45]

A valid **measurement result** requires a 'validated measurement procedure'. Application of this generic definition to the **validation** of a **measurement procedure** leads to a definition of a

measurement procedure validation (Concept 5-3)
validation of a measurement procedure

confirmation, through provision of objective evidence, that the application of a **measurement procedure** fulfils the requirements for its stated intended use

An analyst is interested in a valid **measurement result**. A statement of 'validity' of a **measurement result** for a specified intended use requires an evaluation of its **metrological traceability** and **measurement uncertainty** against specification fixed *a priori*, including a **target measurement uncertainty**.

This leads to a definition of

validation of a measurement result (Concept 5-4)

confirmation through provision of objective evidence that a **measurement result** with specified **metrological traceability** has a **measurement uncertainty** not exceeding the **target measurement uncertainty**

A validated **measurement result** can be compared to another validated **measurement result** for the same **measurand** in order to establish their

metrological equivalence of measurement results (Concept 5-5)

equivalence of measurement results

property of two or more **measurement results** for a given **measurand** whereby they are each acceptable for a specified intended use

Since **metrological equivalence** usually is not a matter of a yes or no decision, it is useful to define a quantity that characterizes the metrological equivalence of measurement results. VIM3 has defined

metrological compatibility of measurement results (Concept 5-6)

metrological compatibility

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

NOTE 1 Metrological compatibility of measurement results replaces the traditional concept of “staying within the error”, as it represents the criterion for deciding whether two measurement results refer to the same measurand or not. If in a set of **measurements** of a measurand, thought to be constant, a measurement result is not compatible with the others, either the measurement was not correct (e.g. its **measurement uncertainty** was assessed as being too small) or the measured **quantity** changed between measurements.

NOTE 2 Correlation between the measurements influences metrological compatibility of measurement results. If the measurements are completely uncorrelated, the standard measurement uncertainty of their difference is equal to the root mean square sum of their standard measurement uncertainties, while it is lower for positive covariance or higher for negative covariance.

[VIM3-2.47]

This definition implies another quantity, which could be termed

degree of metrological equivalence of measurement results **(Concept 5-7)**

The absolute value of the difference of any pair of **measured quantity values** from two different **measurement results** for a specified **measurand** divided by the **standard measurement uncertainty** of that difference

Note – If the measurements are completely uncorrelated, the standard measurement uncertainty of their difference is equal to the root mean square sum of their standard measurement uncertainties, while it is lower for positive covariance or higher for negative covariance.

6 Reporting of metrological traceability

The purpose of performing a **measurement** is to provide information, in the form of a **measurement result**, on the magnitude of a **measurand**, embodied in a specified system. The communication can be made orally or in writing. The latter can take the form of a **calibration certificate** or more extensively a **certification** report [30]. In addition to the **quantity value** with associated **measurement uncertainty**, the **metrological traceability** of the **measurement result** is an essential component of such a report because it

- underpins the authority of the **measurement result** by demonstrating how the result has been arrived at through the use of **calibrators** and **measurement procedures**;
- identifies the **metrological reference** needed to achieve **metrological comparability of measurement results** for **quantities** of the same **kind**; and
- shows the elements in the **uncertainty budget** of the **quantity value** that are necessary for the calculation of the final **measurement uncertainty**.

It is useful to define

calibration certificate (Concept 6-1)

document, authenticated with respect to its origin, carrying one or more **quantity values** with their associated **measurement uncertainties** and **metrological traceabilities** attributed to a **reference material** or **measurement standard**

A **calibration certificate** is usually accompanied by, or referenced to, a **certification** report (see [26], 4.3), which specifies all necessary details to understand the production, properties, and use of the **certified reference material** or **measurement standard**, its **quantity value** and **measurement uncertainty.**

7 Bodies concerned with metrological traceability

The system of bodies constituting a framework for providing elements of **calibration hierarchies** may be defined and termed as follows:

metrological institutional hierarchy (Concept 7-1)
metrological institutional structure

hierarchical system of international, regional, national, and local bodies, both public and private, responsible for providing **metrological references**, the metrological higher elements of **calibration hierarchies**, and general dissemination of **metrological traceability**

The CIPM has the responsibility for the maintenance of the **SI** under the authority of CGPM. The BIPM is the executive office with laboratories which maintain some **primary measurement standards** and **primary measurement procedures**. In principle, the Directors of NMIs are members of the Consultative Committee on Amount of Substance: Metrology in Chemistry (CCQM) to CIPM on chemical **measurement**. Some of the scientists responsible for Metrology in Chemistry at the NMIs also attend the annual meetings. NMIs operate under the authority of their governments. They produce, conserve, disseminate, or supervise the required **measurement standards** and **measurement procedures** of the highest order in their respective countries. Any **measurement** laboratory in a given country should have direct or indirect access to these references for **metrological traceability** of its **measurement results**. Thus a worldwide **measurement system** can operate satisfactorily and be available to everybody. This should result in global **metrological comparability of measurement results**.

Other laboratories than NMIs can act as Reference Laboratories under contract with NMIs or with a regional or international body and provide **measurement standards** for a variety of types of **quantity**. A **metrological institutional hierarchy** can look as shown in Figure 7–1

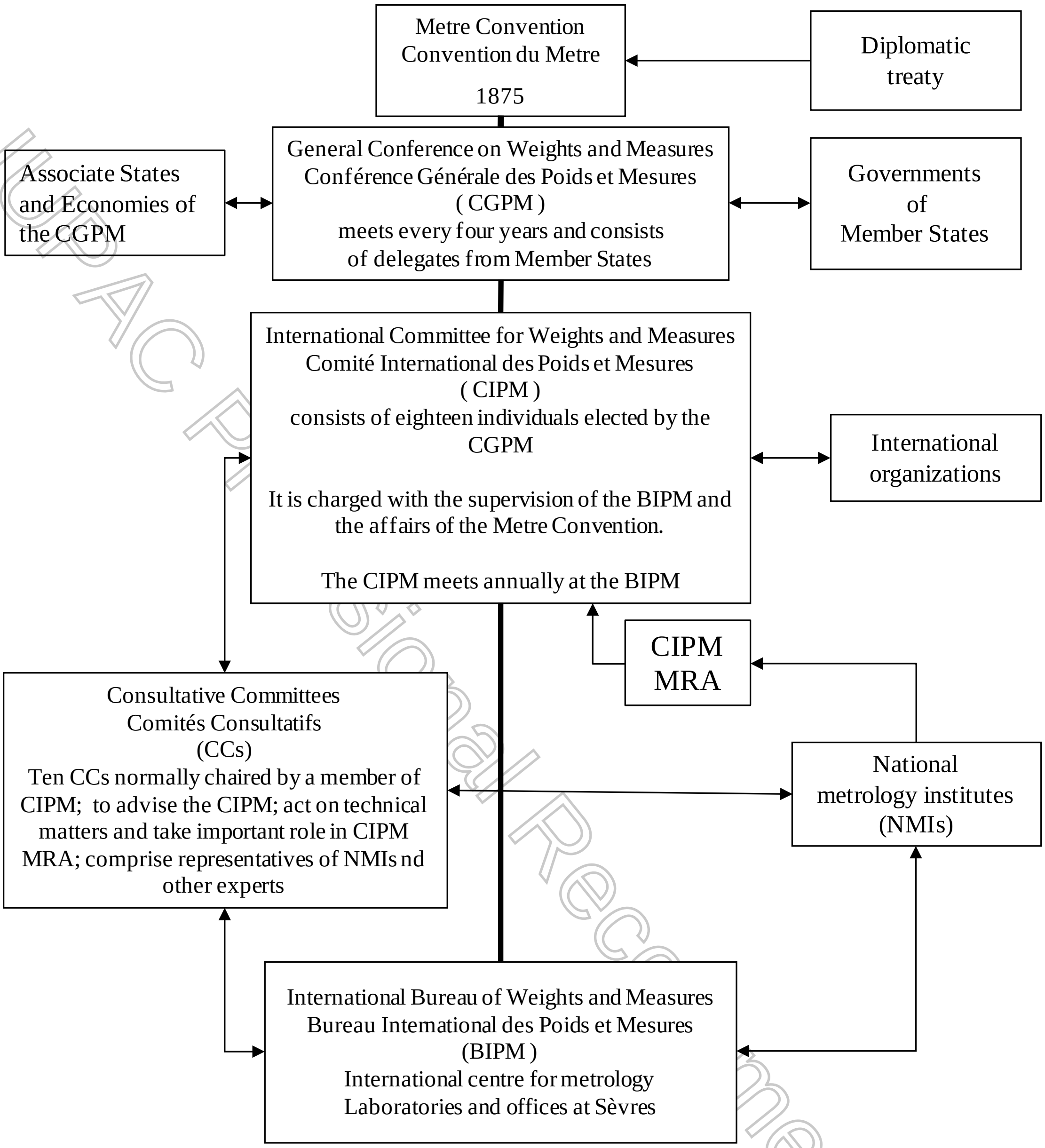


Figure 7–1: **Metrological institutional hierarchy** of bodies having a metrological duty in the global **measurement** structure

8 Interlaboratory comparison (ILC), including proficiency testing scheme (PTS), CCQM Key Comparison (KC) and external quality assessment scheme (EQAS)

Interlaboratory comparisons are organized in the measurement community for a variety of purposes, including a complementary role in establishing **metrological traceability**.

8.1 What is an ILC?

Interlaboratory comparison (ILC) is a generic concept for endeavours to obtain and compare **measurement results** obtained by two or more measurement laboratories for the same **measurand** in the same material. An **ILC** usually involves an organization or body responsible for the organizational aspects of the **ILC**.

Interlaboratory comparisons are organized by the Association of Official Agricultural Chemists, today called the Association of Official Analytical Chemists (AOAC International), with the aim to study analytical measurement procedures. Harmonization of such studies has been aided by the IUPAC/ISO/AOAC Interdivisional Working Party on Harmonization of Quality Assurance Schemes for Analytical Laboratories [33, 34]. The scope of an **interlaboratory comparison** evolved from being a **measurement procedure validation** study to performing proficiency testing and further to assessing a **degree of equivalence** of pairs of **measurement results**. Infrastructural requirements were described [35] and used in ISO Guide 43 (parts 1 and 2), updated recently [36]. A special category of **interlaboratory comparisons** is a study aiming at characterizing **quantity values** carried by materials [31].

Interlaboratory comparison is defined in ISO Guide 43-1 [37] as 'organization, performance and evaluation of tests on the same or similar test items by two or more laboratories in accordance with predetermined conditions'. In some circumstances, one of the laboratories involved in the intercomparison may be the laboratory that provides the assigned **quantity value** for the material. An improved definition of an **ILC** may be:

> **interlaboratory comparison** (Concept 8-1)
>
> **ILC**
>
> operation of having two or more laboratories carry out **measurements** and compare **measurement results** for the same **quantity** embodied in samples of the same material

The operation enables the determination of the **degree of equivalence** of pairs of **measurement results** of the participants.

8.2 Purposes of an ILC

Interlaboratory comparisons are organized in the measurement community for the following main purposes:

- assessment of laboratory performance (proficiency testing),
- assessment of **degree of metrological equivalence of measurement results** obtained by any pair of participating laboratories,
- **measurement procedure validation** studies, and
- material characterization (assigning **quantity values** to **measurands** embodied in materials).

All of these are tools in quality assurance, including the assessment of measurement performance of participating laboratories for a specific type of **measurement** (see Table 8.2 – 1). Assessment is based on the agreement of the participants" **measurement results** with those assigned to the **interlaboratory comparison** material . **ILC**s are announced by the organizers, participation is open to any interested laboratory, and participation of laboratories is voluntary, independent of their quality. According to the ISO/IEC 17025 [6] and ISO

15189 [8] International Standards, regular laboratory participation in **ILC**s is a requirement for accredited laboratories. But participation in **ILC**s is also an integral part of a laboratory's quality assurance. It is complementary to the laboratory internal quality control, but is not replacing it.

Key Comparisons are organized in a similar fashion in the frame of the CIPM-MRA between National Metrology Institutes or NMI-designated institutions, strictly following established protocols. The main aim of a Key Comparison is the assessment of the **degree of metrological equivalence of measurement results** obtained by any pair of participating laboratories. A Pilot Study enables the participants to familiarize themselves, prior to a Key Comparison, with any problems arising in the **measurement** of a particular **quantity** in a particular material. After a Key Comparison is performed, a Key Comparison Reference Value (KCRV) is established from participants' **measurement results**. However, approaches for calculating the KCRV and associated **measurement uncertainty** are still subject of discussion. Due to the fact that NMIs or NMI-designated institutes are participants, their **measurement results** are sometimes used for characterization of a candidate **reference material**. Such arrangements are made by NMIs separately and outside the frame of a Pilot Study or Key Comparison. Further use of such data is the responsibility of the reference material producer.

Measurement procedure validation studies (usually called "method validation studies") require the use of the same **measurement procedure** by all laboratories. In such validation studies, at least one well characterized **reference material** needs to be available before the start.

In material characterization studies aiming at measuring **quantity values** embodied in candidate **reference materials**, the organizing body, e.g. a reference material producer, invites participating laboratories on the basis of their demonstrated **measurement capability**. Material characterization studies are carried out by using prescribed and well established, often different, quality assured **measurement procedures** yielding **quantity values** with established **metrological traceability** and associated **measurement uncertainty**. See also [12, 31].

Table 8.2 – 1 : Types of **interlaboratory comparison** and their purposes

Category	Usual Name	Purpose	Comments
assessment of laboratory's measurement performance	proficiency testing; intercomparison study; intercomparison run; external quality assurance scheme; laboratory measurement evaluation programme	to test the ability of a laboratory to obtain **measurement results** similar to those of peer laboratories or to document measurement performance	often required as part of an accreditation (e.g. to ISO/IEC 17025) or when taking regulatory or legal action; sometimes external **reference measurement procedure quantity values** obtained from elsewhere rather than the average of participants' **measurement results** to assess performance
	interlaboratory **measurement bias** study International Measurement Evaluation Programme (IMEP)	to determine **measurement bias** of a **measurement procedure**, assessment of **measurement capability**	based on a **reference quantity value** with demonstrated **metrological traceability** and associated **measurement uncertainty**
	cooperative trial	one-off comparison of laboratory performance	may be for contractual purposes

Continued

Continued

Category	Usual Name	Purpose	Comments
assessment of **degree of equivalence of measurement results**	CIPM key comparison, CIPM pilot study,	assessment of **degree of equivalence** of any pair of **measurement results** of participating institutions; assessment of **measurement capability**	organised in the frame of the CIPM MRA to support claims of NMIs related to their measurement and calibration capabilities
measurement procedure validation study	collaborative trial	to provide data for the **validation** of a **measurement procedure**	determines the **measurement reproducibility** of **measurement results** obtained using a given **measurement procedure** and, if a **CRM** is used, the **measurement bias** of each laboratory may be calculated
	improvement scheme	**validation** of new or improved **measurement procedures** by comparison with an established, fully validated **measurement procedure**	less costly programme than full **validation**

Continued

Continued

Category	Usual Name	Purpose	Comments
material characterization	multi-laboratory or multi-**measurement method** approach to assign **quantity values** to materials	to provide **measurement results** to be used in assigning **quantity value** and **measurement uncertainty** to an **RM** or **CRM**	a **measured quantity value** from each laboratory must have a stated **metrological traceability** and associated **measurement uncertainty**; assignment of the **quantity value** and **measurement uncertainty** – and possible certification of the material – is the responsibility of the reference material producer Note: All participants' **measurement results** should be metrologically traceable to the same **metrological reference**

8.3 Assigning a reference value to a quantity embodied in an ILC material

A **reference quantity value** [VIM3-5.18] assigned to an **ILC** material can be obtained in one of the following ways:

- **measurement** by a reference laboratory,

- use of materials carrying one or more pre-established **quantity values**, e.g. a **CRM**,
- using a preparation procedure such as spiking, or use of portions of materials with known content,
- using a consensus **quantity value** decided by selected or expert laboratories, or
- using a consensus **quantity value** based on some form of averaging **measurement results** from participants.

The **measurement uncertainty** of the **quantity value** assigned to an **ILC** material must be taken into account when evaluating **ILC** participants' results.

8.4 Measurement capability

This concept may be defined as follows

> **measurement capability** (Concept 8.4-1)
>
> demonstrated competence of a laboratory to measure a specified **quantity** of a given **kind** in a specified interval of **quantity values**, embodied in a specified material, expressed by a **measurement uncertainty**

A comparison of the **measurement uncertainty** in the **measurement result** obtained by one participant to that of the **measurement result** obtained by another laboratory for the same **quantity** in the same material, compares their respective **measurement capabilities**. Many **national measurement standards** are compared to each other for their certified **quantity values** and **measurement uncertainties** in order to determine the **degree of metrological equivalence** of two **measurement results** for the same **measurand** and thereby the extent to which **measurement standards** can be substituted for each other for a specified intended use.

8.5 ILC and metrological traceability

Each laboratory participating in an **ILC** must establish the **metrological traceability chain** of its **measurement results**. That chain should preferably end in the same **metrological reference**, as that of the other participants, usually (the definition of) a **measurement unit**, with or without a specified **measurement procedure** as prescribed by the **ILC** organizer. In contrast to **measurement procedure validation** studies, a **measurement procedure** is not prescribed in proficiency testing, intercomparison studies, external quality assurance schemes and laboratory measurement evaluation programs. In addition to the **measurement uncertai**nty associated with the **quantity valu**e assigned to a **working calibrator** selected for the **metrological traceability chain**, different **influence quantities** will contribute to the **measurement uncertainty** of each participant's **measurement result** even if **measurement results** have an established **metrological traceability**, that in itself does not guarantee that they are "correct".

8.6 ILC and laboratory performance

An assessment of the **ILC** participants' **measurement results** can be performed by evaluating parameters associated with these results. Which laboratory performance properties might be assessed in a specific **ILC** depend on a decision taken prior to the execution of an **ILC** and how the **ILC reference quantity value** was established. Evaluation of participants' **measurement results** will enable the assessment of the **compatibility of measurement results**, independently of whether the results are "correct" or not. Such evaluation may or may not take into account the **quantity value** and associated **measurement uncertainty** of the **ILC** material used.

The **measurement accuracy** or **measurement trueness** of participants' **measurement results**, however, can only be evaluated if the ILC quantity value has an established **measurement accuracy** or **measurement trueness**.

Use of so-called 'consensus quantity values' obtained from a number of selected expert laboratories or as consensus quantity value from all participants in an **ILC**, is not appropriate for assessing **measurement accuracy** or **measurement trueness**. It would be a circular approach as the participants' **measurement results**, which will influence the ILC quantity value, will at the same time be evaluated using this ILC quantity value. Such evaluation might not detect a **measurement bias**. Also, it would be perfectly possible that a laboratory identified as submitting an outlier, may actually be reporting the most correct **measurement result**.

Nevertheless, in certain types of **ILC**, a consensus quantity value is the only **quantity value** possible, e.g. in an **ILC** assessing laboratory performance for the **measurement** of operationally defined measurands, and the **ILC** can only establish the **degree of equivalence** of participants' results, and not their **measurement trueness**.

8.7 ILC and quality assurance

ILCs are important quality assurance tools, providing evidence of a laboratory's performance and establishing the **degree of metrological equivalence** of any pair of participants' **measurement results**. Laboratories may take action if their results do not agree sufficiently well with the **measurement results** from other participants or with the pre-established **ILC quantity value**. For a given laboratory the outcome of an **ILC** should be considered together with internal quality control results and other quality assurance measures.

9 Metrological traceability in field laboratories

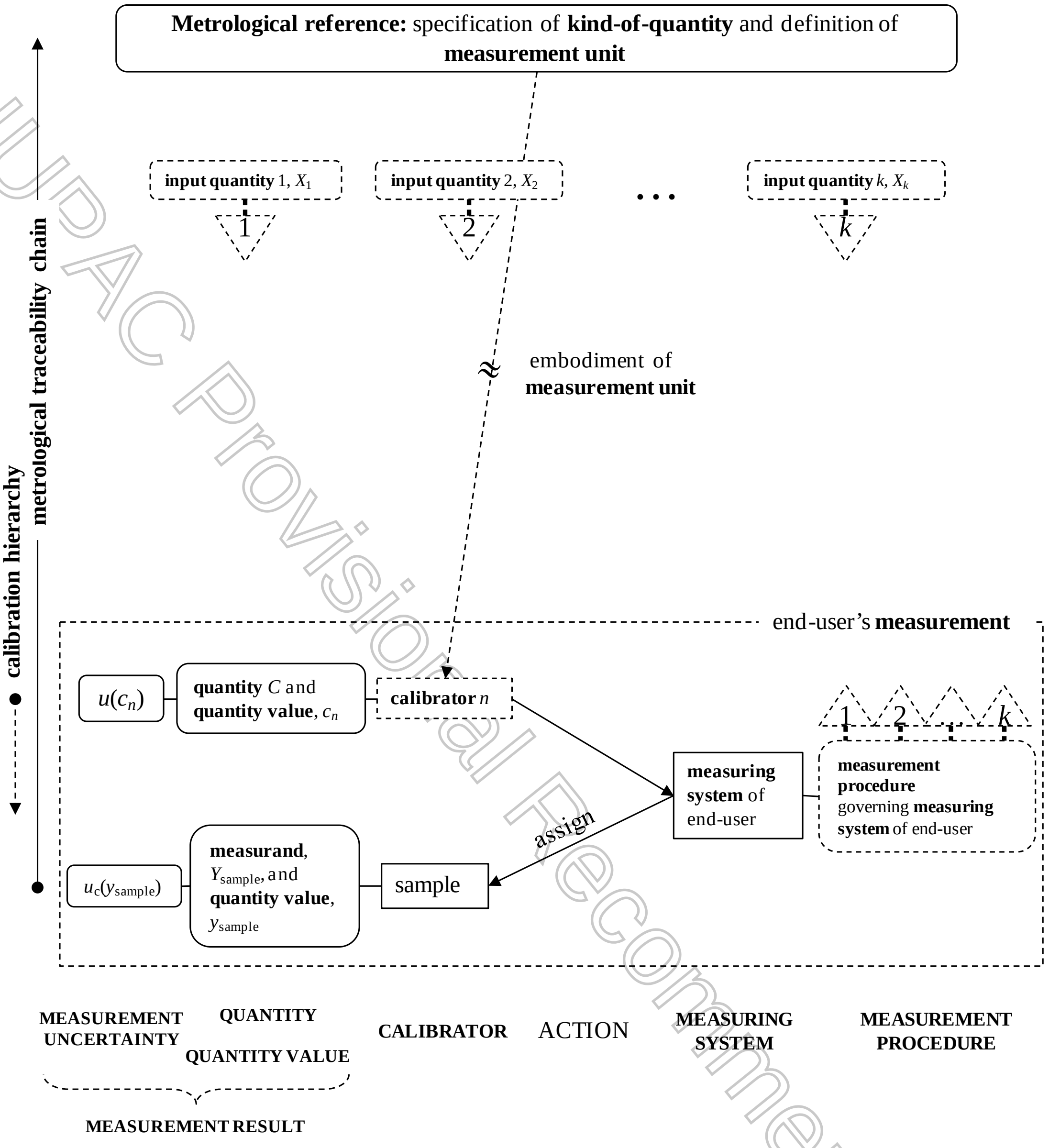
9.1 Function of metrological traceability in quality assurance

Understanding of, and appropriate dealing with, **metrological traceability** and **measurement uncertainty** should be a prime concern of any analytical laboratory because these concepts are vital to the establishment of a proper quality system. Both require consideration by the analyst and a suitable understanding of the analytical problem. Before any measurement request is accepted from a customer, the analyst in the receiving laboratory must know how to solve the chemical measurement problem including a statement of the **measurand**, choice of a **calibration hierarchy**, and defining a **target measurement uncertainty**.

9.2 Demonstration of metrological traceability by field laboratories

Applying the basic concepts in chemical **measurement** renders the establishment by the field analyst of the **metrological traceability** of his **measurement results** simple as is illustrated in Figure 9.2–1. The lower levels in any calibration hierarchy are the end user's **calibrator**, the end-user's **measuring system** calibrated by means of the **calibrator**, and the sample which carries the **measurand**. Usually the **calibrator** is purchased from a producer of **RMs** or **CRMs,** or from a National or International Metrology Institute.

Figure 9.2–1 implies that the **calibrator** seller should provide the end-user with an established **metrological traceability chain** for the assigned **quantity value** with associated (GUM) **measurement uncertainty**, possibly a **measurement budget**. The end user will have to combine this **measurement uncertainty** with that caused by using the **measuring system** in order to calculate a **combined standard measurement uncertainty**. Knowing the **measurement uncertainty** of any **RM quantity value** embodied in an **RM**, also enables the end-user to evaluate, prior to the **measurement,** whether it will be possible to attain a **target measurement uncertainty**.



measurement model for the end-user $\underline{h}(Y_{sample}, C_n, I_{Cn}, I_{sample}, X_1, \ldots, X_k) = 0$

Figure 9.2–1: **Metrological traceability chain** available to an end-user.

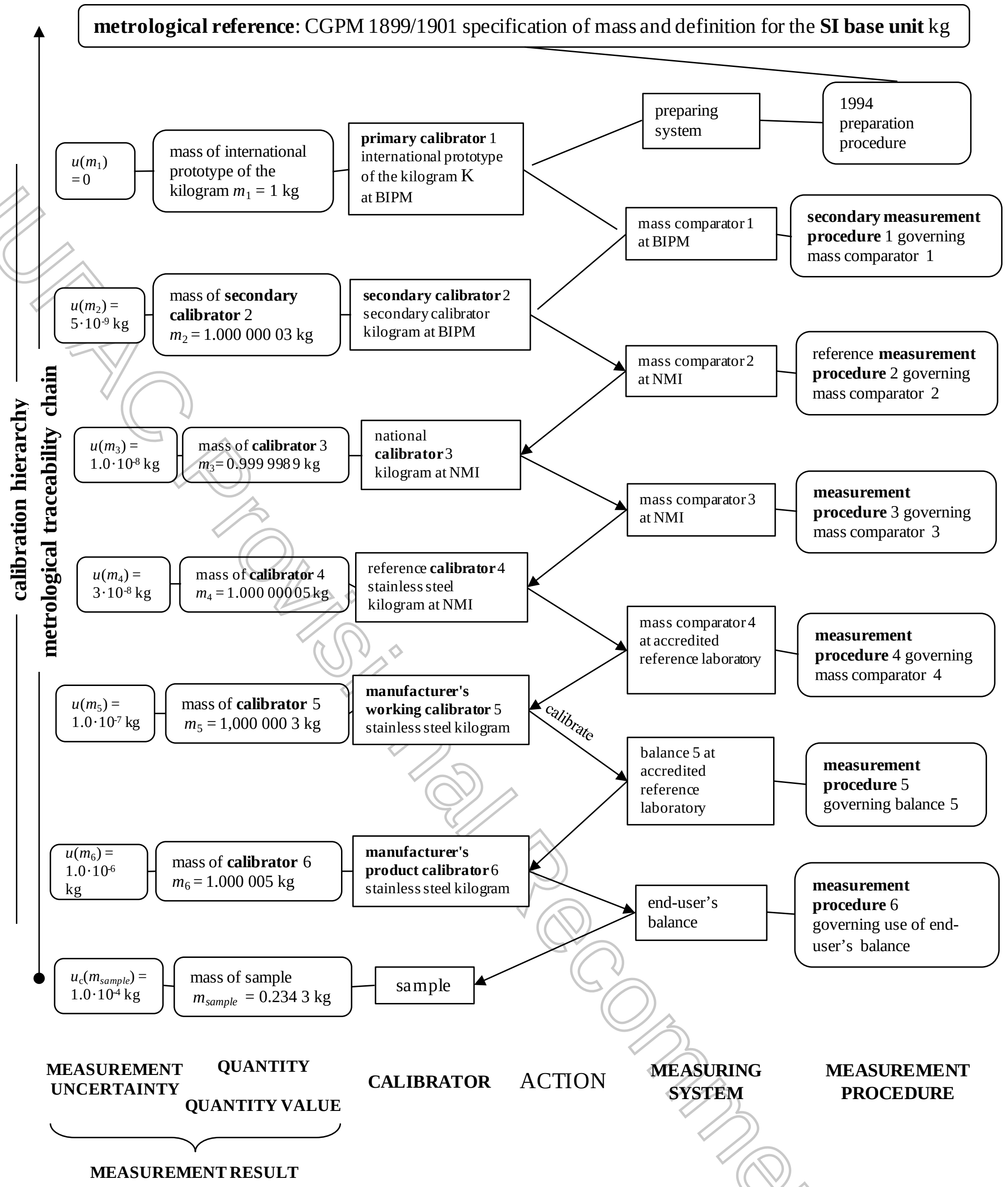
Note. The scheme does not apply in the case of an **ordinal quantity**.

10 Examples of metrological traceability chains for measurement results in physics

Chemical **measurements** often involve physical properties such as mass, molar mass, volume, and temperature. Thus, in the **metrological traceability chain** of a chemical **measurement result**, a **metrological traceability** of one or more physical **measurement results** will add further **metrological traceability chains** (see section 2.9). It is stressed that both chemical and physical **measurements** follow the same rules of **measurement**, and any distinction made here is for didactic purposes only. It is likely that such **metrological traceability chains** will be grafted onto the "fundamental" **metrological traceability chain** of a chemical **measurement result**. A graft is here designated by a symbol such as △ , attached to the **measurement procedure** box. In the following examples of **metrological traceability chains** for some **measurement results** of a physical nature, are presented. A chemist in a field laboratory will probably establish **metrological traceability** of **quantities** of such **kinds** by purchasing and maintaining suitably calibrated equipment such as balances, thermometers, voltmeters, and pressure **measuring instruments**.

10.1 Mass

In almost every chemical **measurement,** material is weighed at some stage. An amount-of-substance is then calculated by dividing the mass of the component by its molar mass. A **metrological traceability chain** for a mass **measurement result** is given in Figure 10.1–1. At each stage, a **measurement** is carried out by comparing a known mass and an unknown mass using a balance. Some **measurements** in the **metrological traceability chain** require buoyancy **corrections**, which themselves have **input quantities in a measurement model** such as the mass density of the material being weighed, the volumic mass (mass density) of air and its temperature. These are not shown in the figure.



measurement model for end-user $h(m_{\text{sample}}, m_{\text{calibrator 6}}, p, □, I_{\text{sample}}) = 0$

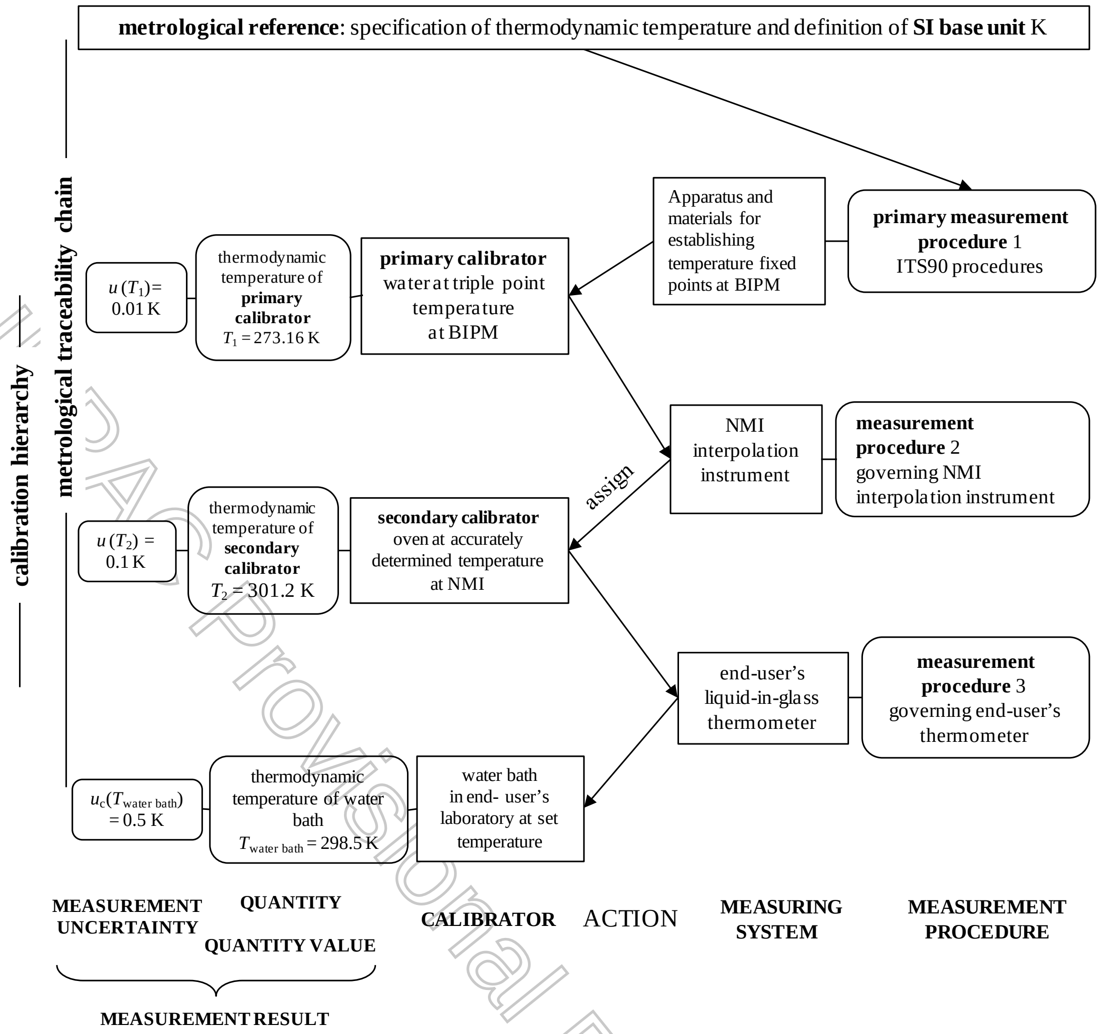
Figure 10.1–1: **Metrological traceability** of a mass **measurement result**, according to the generic flow chart of Figure 2.3–1. Subsidiary **metrological traceability chains** for **influence quantity values** such as temperature, air volumic mass, and pressure are not shown.

10.2 Temperature

Measurements of temperature are made by instruments based on several different physical principles, such as for liquid-in-glass thermometers, platinum resistance thermometers, thermocouples, and radiation thermometers. Temperature is either the thermodynamic temperature (T) with **SI base unit** kelvin (symbol K) or the Celsius temperature (symbol t or θ) with **SI unit** degree Celsius (ºC), where $\theta = T - T_0$ and $T_0 = 273.15$ K.

The International Temperature Scale of 1990 (ITS 90) lists 17 fixed points to be used to establish a temperature scale. A fixed point is the temperature of a phase transition of a pure material. For example pure zinc freezes at a thermodynamic temperature of 692.677 K. National Metrology Institutes maintain many of the ITS90 fixed points which are used to calibrate the NMI’s interpolating instruments, by methods specified in ITS90. These are then used to calibrate **measuring instruments** that can be disseminated to industry and the **measurement** community. The **measurement uncertainty** incurred at each stage in the **calibration hierarchy** depends on the techniques employed.

A **metrological traceability chain** is shown in Figure 10.2–1



measurement model for end-user $h(T_{\text{water bath}}, T_{\text{cal 2}}, I_{\text{liquid-in-glass therm}}) = 0$

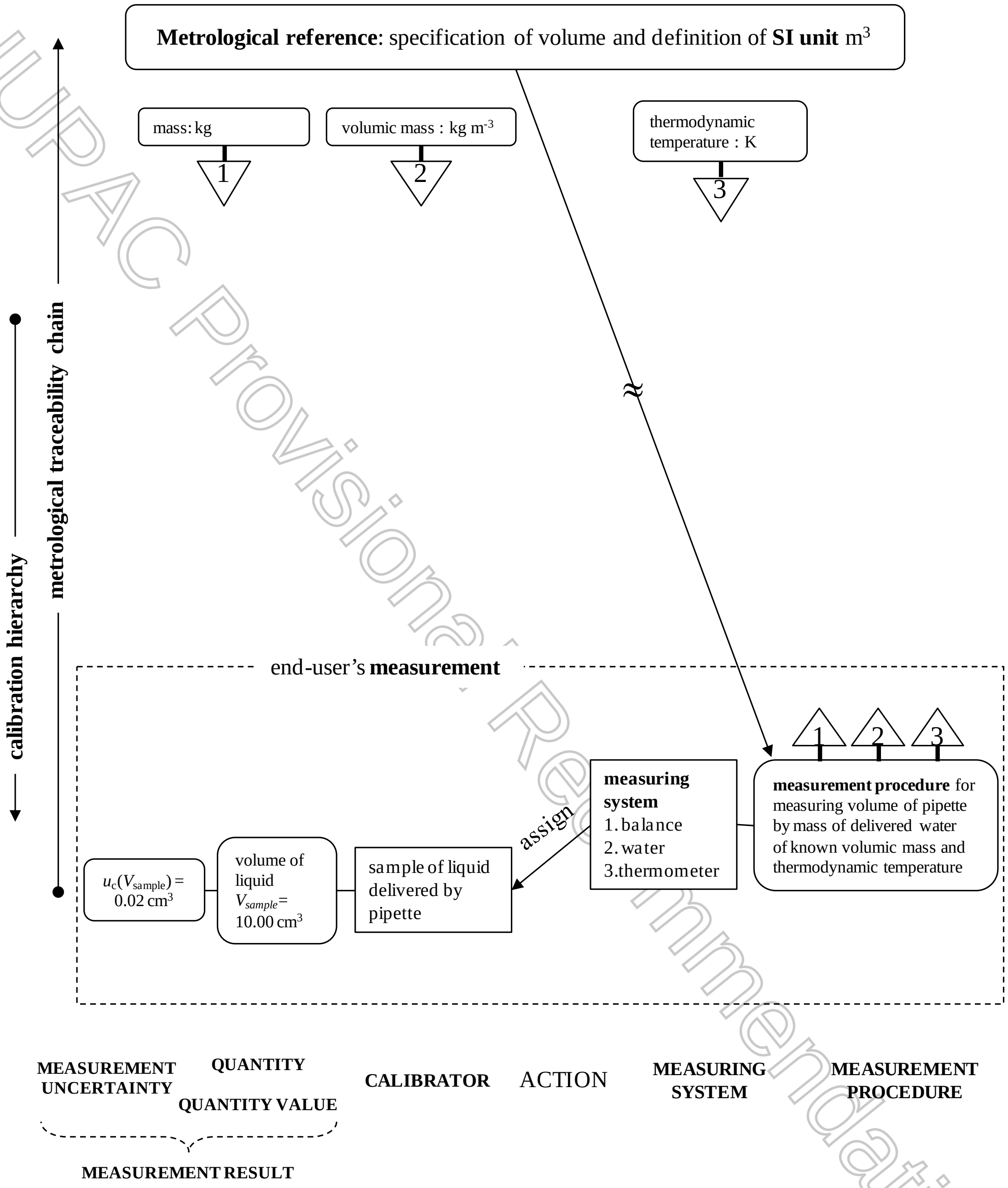
Figure 10.2–1: **Metrological traceability chain** for the temperature of a water bath in an analytical laboratory

10.3 Volume

Volumes of liquids delivered in an analytical **measurement procedure** are measured so that the volume dispensed is a function of the manufactured dimensions of the container (pipette, burette, measuring cylinder, syringe). At a given temperature (T) the volume of the container (giving V_{sample}) is calibrated in the manufacturing plant by weighing the volume of a dispensed liquid (m) of known volumic mass (mass density) (ρ_T) using the **quantity equation**

$$V = m / \rho_T \text{ where } \rho_T = m / V \qquad \text{(Equation 10.3-1)}$$

Metrological traceability is then established through the respective **metrological traceability chains** of the mass value, the volumic mass value and the temperature value, Figure 10.3–1.



measurement model of end-user $h(V_{\text{sample}}, m_{\text{sample}}, T_{\text{sample}}, \square) = 0$

Each of the three **input quantities** in the **measurement model** has a **measurement model**, 1, 2 and 3.

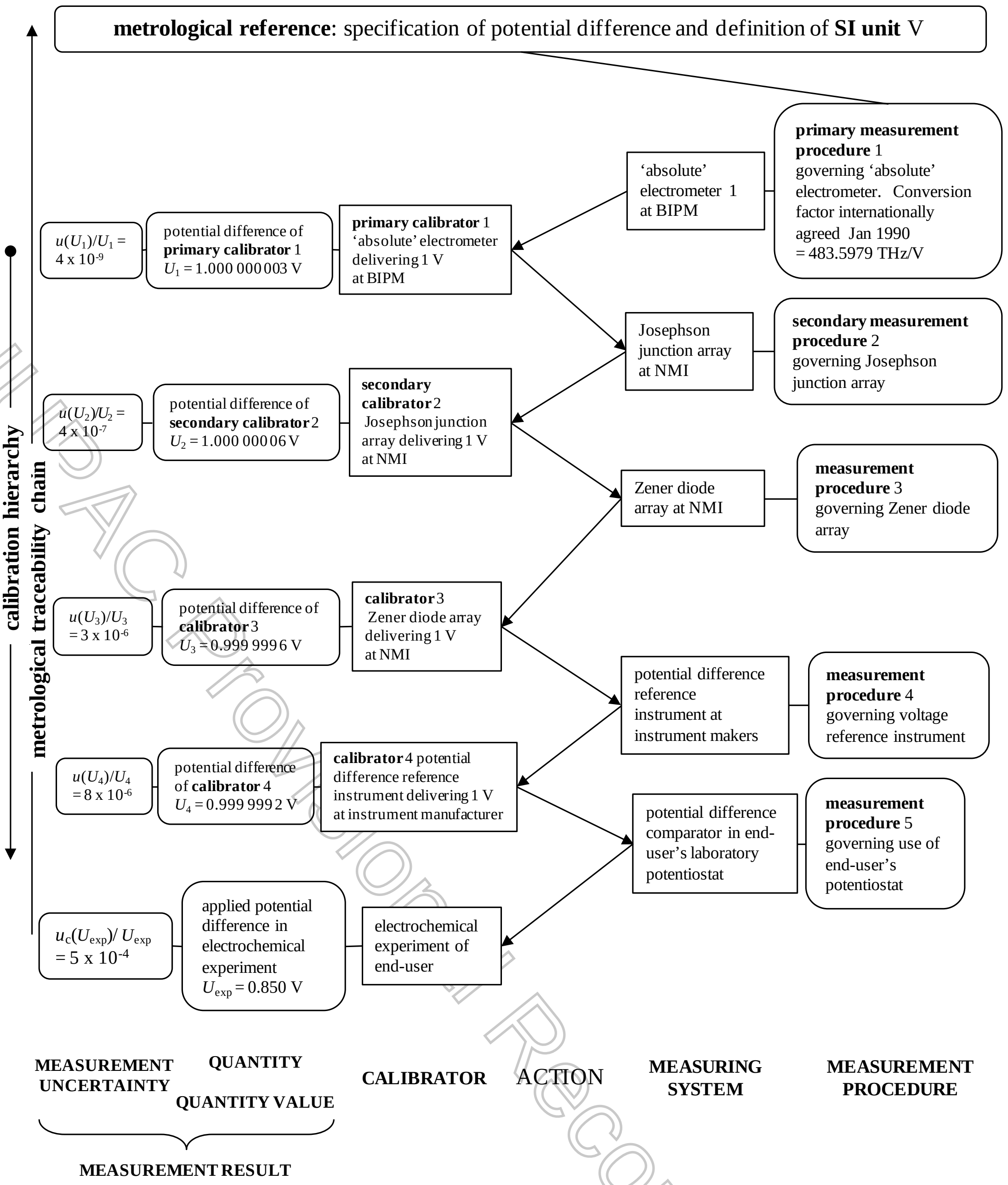
Figure 10.3–1: **Metrological traceability chain** for a measured value of the volume of a 10-mL pipette. Concerning the **metrological traceability chain** for the mass value of the water delivered by a pipette, see Figure 10.1–1.

10.4 Potential difference (Voltage)

The **SI coherent derived unit** of potential difference , the volt, is embodied at the highest metrological level in terms of a microwave frequency and the Josephson effect [38]. The frequency (f) and potential difference (V) across a superconducting junction enters into the **quantity equation**

$$V = \frac{nhf}{2e} \qquad \text{(Equation 10.4-1)}$$

where n is an integer (1, 2 …) h is the Planck constant and e the charge on the electron. The value of $2e/h$, known as the Josephson constant K_{J} was agreed to be 483.5979 THz/V by the Metre Convention on 1990-01-01. Thus the volt can be embodied in an apparatus in which microwaves of known frequency are applied to a junction. In principle, the microwave frequency f can be stable to $10^{-11}f$ although the resulting potential difference may limit the stability of the **primary measurement standard** potential difference to about $10^{-9}f$,. because of small thermal effects and other interferences. Arrays of Josephson junctions are used by NMIs to assign potential differences to **secondary measurement standards**, Zener diodes. These, in turn, are used to calibrate reference **measuring instruments** that calibrate working voltmeters, Figure 10.4–1, where **influence quantities** are not shown.

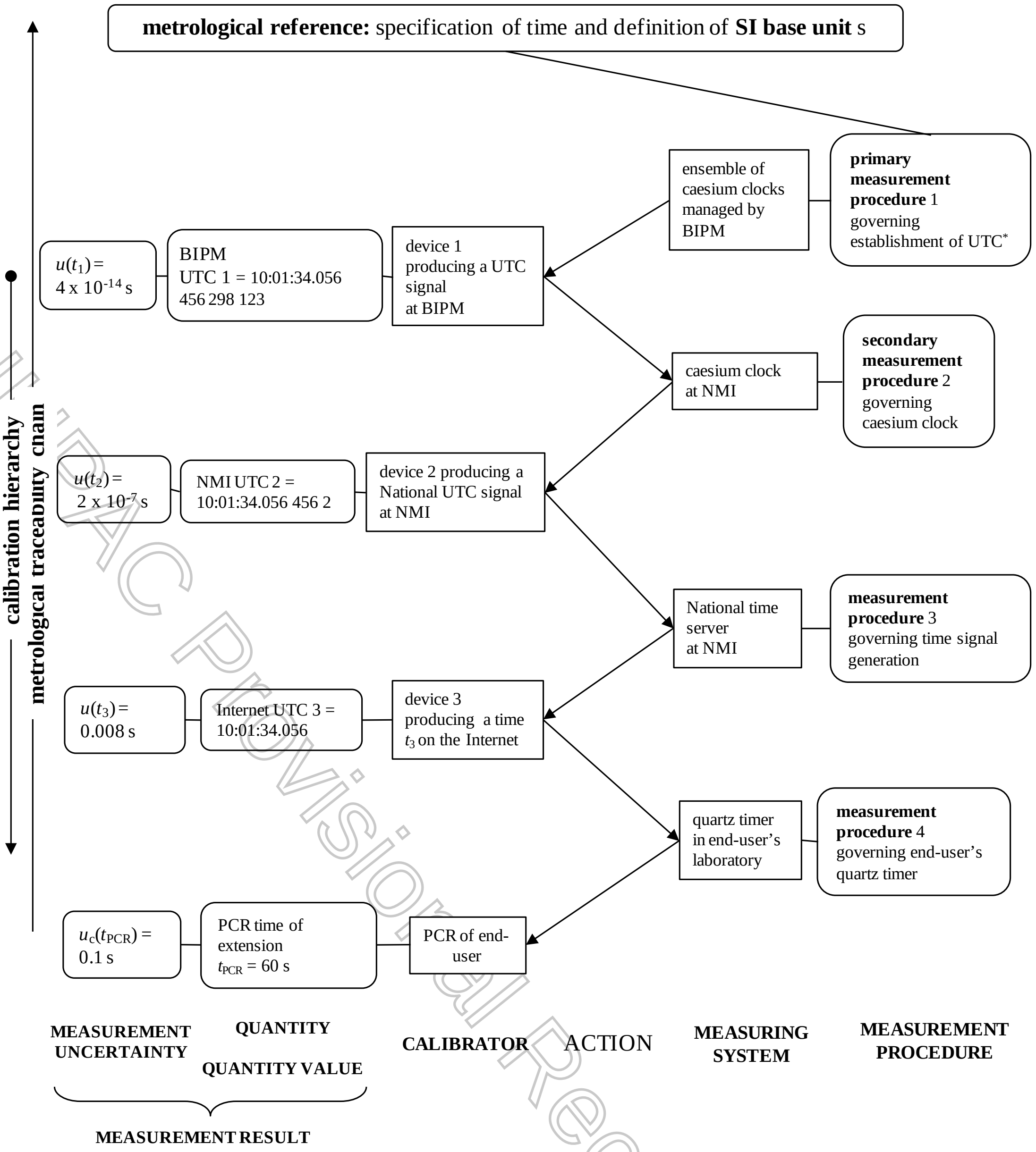


measurement model for end-user $h(U_{exp}, U_{cal\ 4}, I_{cal\ 4}, I_{exp}) = 0$

Figure 10.4–1: **Metrological traceability chain** of the potential difference value (voltage value) for a laboratory potentiostat in an electrochemical experiment. **Measurement uncertainty** is given as a relative **standard measurement uncertainty**.

10.5 Time

The **SI base unit** of time (second) is the duration of 9 192 631 770 periods of the radiation corresponding to the transition between two hyperfine levels of the ground state of the caesium-133 atom. In a caesium clock, an atomic beam apparatus is used to calibrate the oscillations of a 5 MHz quartz crystal. There are many of these clocks in NMIs around the world, and the BIPM is tasked with coordinating their output via Global Positioning Satellites. The result of this intercomparison is known as UTC, or Coordinated Universal Time and is the world's reference for time of day. Each NMI then uses its own clocks to create a 'national time' that is disseminated via computer networks. A manufacturer of timers, which are usually based on quartz crystal oscillators, will use the national UTC to calibrate these timers. National **measurements** of time agree with UTC with an **expanded measurement uncertainty** (for $k = 2$) of less than 50 ns. Dissemination of the national time is by Global Positioning Satellites or networked computers. The former is more accurate than the latter. Figure 10.5–1 shows a **metrological traceability chain** for the **measured quantity value** of the duration in a **measurement procedure** in an analytical laboratory.



measurement model for end-user: $h(t_{\mathrm{PCR}}, \mathrm{UTC}_3, I_{\mathrm{quartz\ timer}}) = 0$

Figure 10.5–1: **Metrological traceability chain** of a **measurement result** for the duration of the extension phase of a polymerase chain reaction (PCR)

* UTC = Coordinated Universal Time

11 Examples of metrological traceability chains of chemical measurement results

11.1 pH

pH is one of the most fundamental and important concepts of chemistry. It is the chemical **kind-of-quantity** most frequently measured.

The thermodynamic definition of pH is given by the **quantity equation** [39]

$$\mathrm{pH} = -\log_{10}\left(a_{\mathrm{H}^+}\right) = -\log_{10}\left(\frac{b_{\mathrm{H}^+}\gamma_{\mathrm{H}^+}}{b^{\circ}}\right) \qquad \text{(Equation 11.1-1)}$$

where a_{H^+} is the activity, b_{H^+} is the molality, γ_{H^+} the activity coefficient of protons, and b° is the standard molality in a solution (1 mol kg^{-1}). It has long been recognised that this definition cannot be realised because of the impossibility of creating a solution containing a stated activity of protons, and the determination of a single ion activity without non-thermodynamic assumptions being made [40]. The 1985 IUPAC definition of pH scales [41] left the subject in some confusion, recommending two different approaches that led to different pH values (different by up to 0.02) being assigned to the same buffer solution. The recommendation also did not address the **metrological traceability** of the **measurement results**. **Measurements** that follow the 1985 IUPAC recommendations appear to be traceable only to the **measurement procedure** specified (and the **SI measurement unit** one). There has been no attempt to establish **metrological traceability** to a higher authority, which leaves the possibility of the assignment of different pH values to the same solution, and therefore the lack of **metrological comparability** of pH **measurement results**.

In 2002 IUPAC issued a recommendation for revision of the pH scale based on the concept of a **primary measurement procedure** for pH [42]. It is asserted that the use of the Harned cell fulfils the criteria for a **primary measurement procedure** and that a pH value so obtained is unequivocally metrologically traceable to the **International System of Units**, here the **SI measurement unit** one. If this assertion is valid, then a buffer solution whose pH is measured by such a cell at the highest metrological level may be classified as a **primary measurement standard**. The use of the Harned cell, but not at the highest metrological level, or the use of other procedures that compare the pH of a solution to that of a **primary measurement standard**, give buffers that are classed as **secondary measurement standards**.

11.1.1 Primary measurement procedure – the Harned cell

The Harned cell [43] is a cell without transference comprising a hydrogen electrode and a silver, silver chloride electrode:

Pt|H_2 | solution, Cl^- | AgCl| Ag (Cell 1)

the use of which leads to the following **quantity equation** for pH (corrected to a pressure of 101.325 kPa)

$$\mathrm{pH} = \lim_{b_{\mathrm{Cl^-}} \to 0} \left\{ \frac{\left(E_1 - E^0\right)F}{RT \ln 10} + \log_{10}\left(\frac{b_{\mathrm{Cl^-}}}{b^\circ}\right) \right\} - \frac{AI^{1/2}}{1 + 1.5\left(I/b^\circ\right)^{1/2}} \qquad \text{(Equation 11.1.1-1)}$$

where A is the Debye-Hückel constant which is given in tables for the temperature of the experiment, I is the ionic strength of the solution, E_1 is the cell potential difference, E^0 is the standard electrode potential of the cell, F is the Faraday constant, b° the standard molality (1 mol kg^{-1}), and b_{Cl^-} the molality of chloride ions in the solution. It is suggested that the **measurement** be made on at least three solutions of different molality of chloride ion and a linear extrapolation be made.

An **uncertainty budget** has been prepared, and buffer solutions that fulfil requirements for **calibration** of a pH **measuring system** have been identified as candidates for **primary measurement standards**.

11.1.2 Secondary measurements

Operating the Harned cell at the highest metrological level is possible for NMIs but would not be contemplated for routine **measurements**.

There are a number of cells having liquid junctions, which may be used for comparisons of **primary measurement standards** (PMS_1, PMS_2) or the determination of the pH of a **secondary measurement standard** (SMS) by comparison with a **primary measurement standard**. These cells are:

Pt| H_2 | SMS ¦¦ PMS_1 | H_2 | Pt (Cell 2)

Pt| H_2 | PMS_2 ¦ KCl (≥ 3.5 mol dm^{-3}) ¦ PMS_1 | H_2 | Pt (Cell 3)

Ag| AgCl | KCl (≥ 3.5 mol dm^{-3}) ¦ buffer S | H_2 | Pt (Cell 4)

Ag| AgCl | KCl (≥ 3.5 mol dm^{-3}) ¦ buffer S | Glass electrode (Cell 5)

Issues concerning the minimization and estimation of residual liquid junction potentials are discussed in detail in reference [42] and remain problems.

11.1.3 Metrological traceability of pH measurement results

It is argued [42] that the **measurement procedure** using a Harned cell to measure the pH of a solution meets the criteria of a **primary measurement procedure**, because:

(a) the pH value is obtained by a well-defined **measurement model** in which all the variables can be determined experimentally in terms of **SI measurement units**, and

(b) all sources of **measurement uncertainty** are identified and effects quantified, including that associated with the use of the Bates-Guggenheim convention.

Unfortunately, the **measurement uncertainty** imparted to the pH value, arising from the use of the Bates-Guggenheim convention to establish $-\log_{10}(\gamma_{\mathrm{Cl}^-})$ (the value 1.5 in the term $-\frac{AI^{1/2}}{1+1.5(I/b^\circ)^{1/2}}$ in Equation 11.1.1-1), is estimated to be 0.01 (**expanded measurement uncertainty**, $k = 2$, corresponding to a level of confidence of approximately 95 %). The experimental **expanded measurement uncertainty** ($k = 2$) for a typical primary **measurement** is, however, only 0.004. If the **measurement uncertainty** of the use of the Bates-Guggenheim convention is not included then the **measurement results** are still traceable to the **SI measurement unit** one, but the pH is no longer defined by Equation 11.1-1 but by Equation 11.1.1-1. By not including the full **measurement uncertainty**, if in the future an improved **quantity value** for the trace activity coefficient of chloride ion were used (γ^0_{Cl}), then **measurement results** obtained with the new equation would no longer be metrologically comparable with earlier **measurement results**.

A **metrological traceability chain** of a routine laboratory **measured quantity value** of pH is depicted in Figure 11.1.3–1.

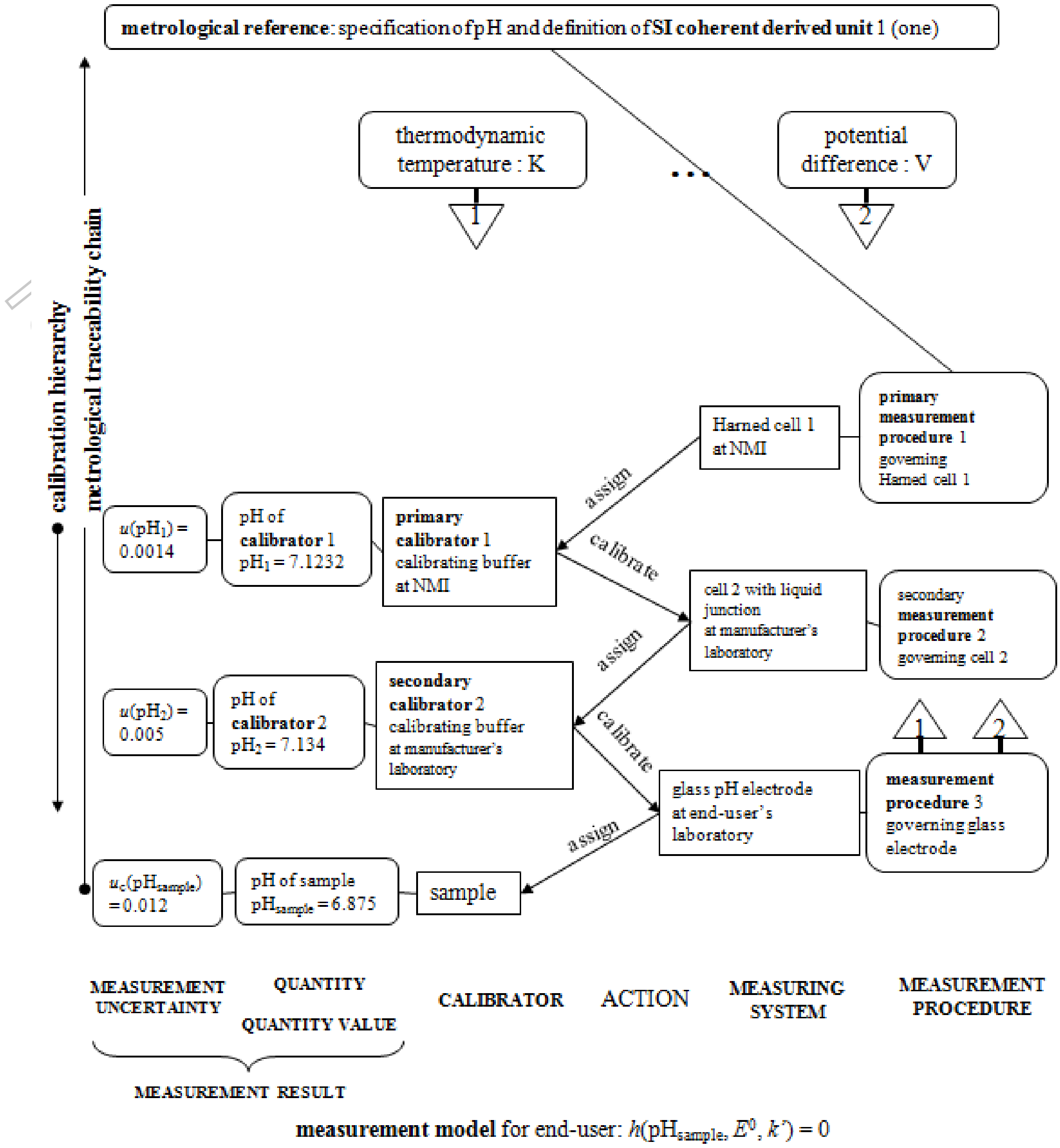


Figure 11.1.3–1: **Metrological traceability** of a pH **measurement result** using a **primary measurement procedure** (Harned cell). The **input quantities in the measurement model**, standard electrode potential E^0 and constant *k*’ are obtained from calibration using the **secondary calibrator** 2.

Note that cell 2 in Figure 11.1.3–1 could be Cell 2 described in the text above.

There is, therefore, an interesting, but unfortunate dilemma; if we wish to have **metrological traceability** to the **SI** without specification, rather than involving a conventional **measurement procedure**, then we must accept a **measurement uncertainty** 2 ½ times greater, even though the **measurement procedure** is exactly the same.

11.1.4 Metrological traceability of pH values of buffer solutions

The direct assignment of a pH value and associated **measurement uncertainty** of a particular solution can only be done by the **primary measurement procedure** described above. Once the pH value is established by the **primary measurement procedure**, and published, for a solution of given composition, then a solution of identical composition prepared elsewhere will have the reported pH with associated **measurement uncertainty**.

Aqueous buffer solutions are usually made up from pH **reference materials** dissolved in a prescribed mass of water. However, in general, the preparation of a buffer solution from compounds according to a recipe can not be recommended. Not only is the purity of the material but also the stoichiometry very important. The solids for making primary buffer solutions are certified not for purity but only for pH. A detailed instruction is given how to prepare the solution e.g. for NIST SRM and for commercial solids appropriate for preparation of pH buffers according to DIN 19266. Only these buffer solutions may get the attribute primary buffer solutions, and can be considered directly metrologically traceable. If it is necessary for any reason to prepare buffers similar in composition to the primary ones from solids of different kind it is recommended to use cell 2 for comparison.

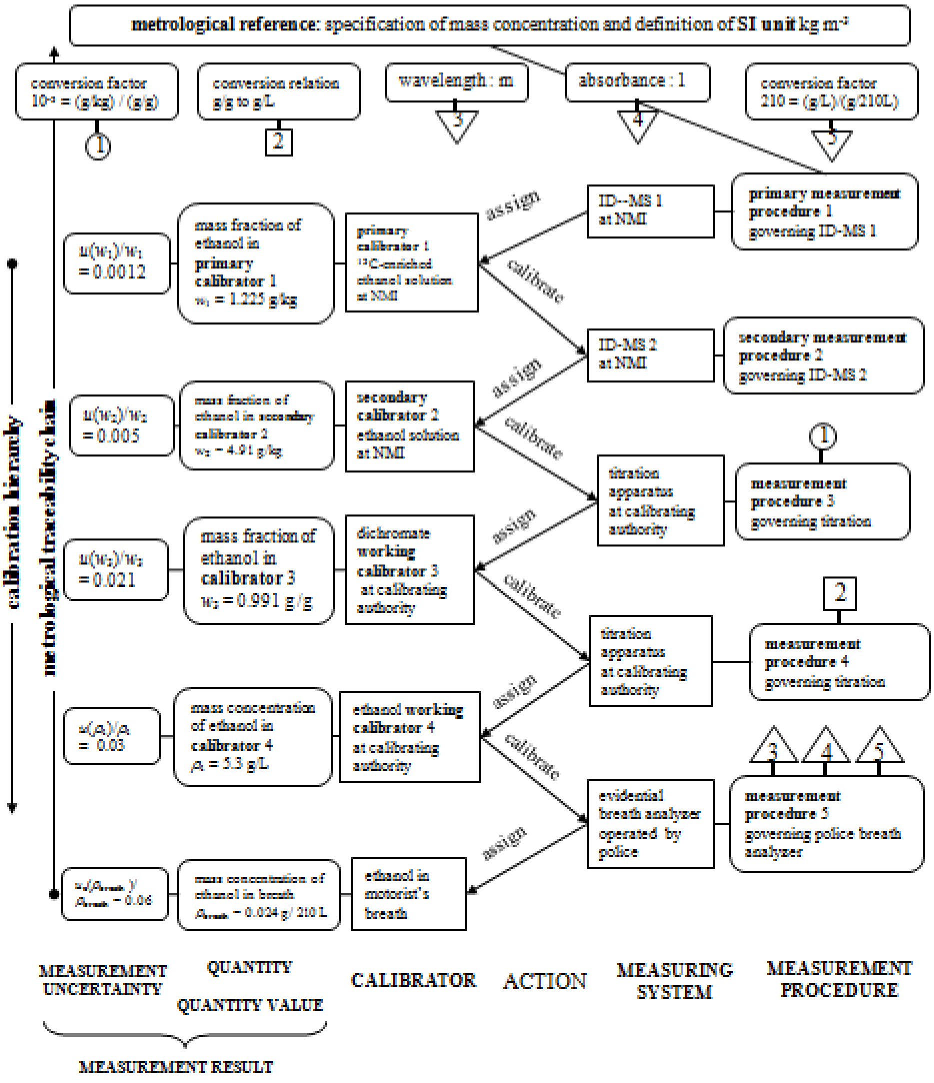
If the published pH value of some material has been determined by **interlaboratory comparisons** between NMIs on many samples of buffer solution made from different sources of solids, then that pH may be deemed to include batch-to-batch variation. If not (ie if the pH was established on a single sample) then the batch-to-batch variation must be included separately in the final **uncertainty budget**. For comparisons, NMIs normally use solutions of compositions different from those of the composition of the primary **measurement standards**.

If the pH value of a particular solution is established by the **primary measurement procedure**, the purity of the compound making up the solution is not required. If, however, the buffer is described as, for example, a solution of potassium dihydrogen citrate with a molality of 0.05 mol kg^{-1}, and this information is to be used to make up similar solutions that will be assigned the pH value of the **primary measurement standard**, then the **measurement uncertainty** of the molality (including the contribution from the purity of the component used) and its effect on the pH value must be known and quoted. Here lies a problem as it is not usually possible to know how different impurities will affect the pH of a solution. Indeed citrate is not used to make primary buffer solutions for the reason of lack of source material of sufficient quality [44].

11.2 Mass concentration of ethanol in breath

Breath analysis, for testing compliance with drink-driving laws, was developed in the USA in the 1950s and is used in many countries. Initially, breath analysis was based on the colour change when ethanol reacts with potassium dichromate. This was replaced in the early 1990s with electronic breath analysis, based on the absorption of infra-red light (at selected wavelengths) by ethanol in a sample of air. The **measurement result** was expressed as mass of ethanol per volume of blood, multiplied by a factor which represented the partition coefficient of ethanol between blood and breath. The use of this conventional factor made **metrological traceability** of a blood ethanol **measurement** impossible because the factor was biased and did not have a **measurement uncertainty**. The decision has been made, in some jurisdictions, to intend to amend the legislation to make it an offence to drive with greater than a given mass of ethanol (0.05 g) in a defined volume (210 L) of exhaled breath. This definition is adopted in order to retain the same nominal **numerical quantity value** for the legal limits, which has strong public recognition (for example 0.05 or 0.08).

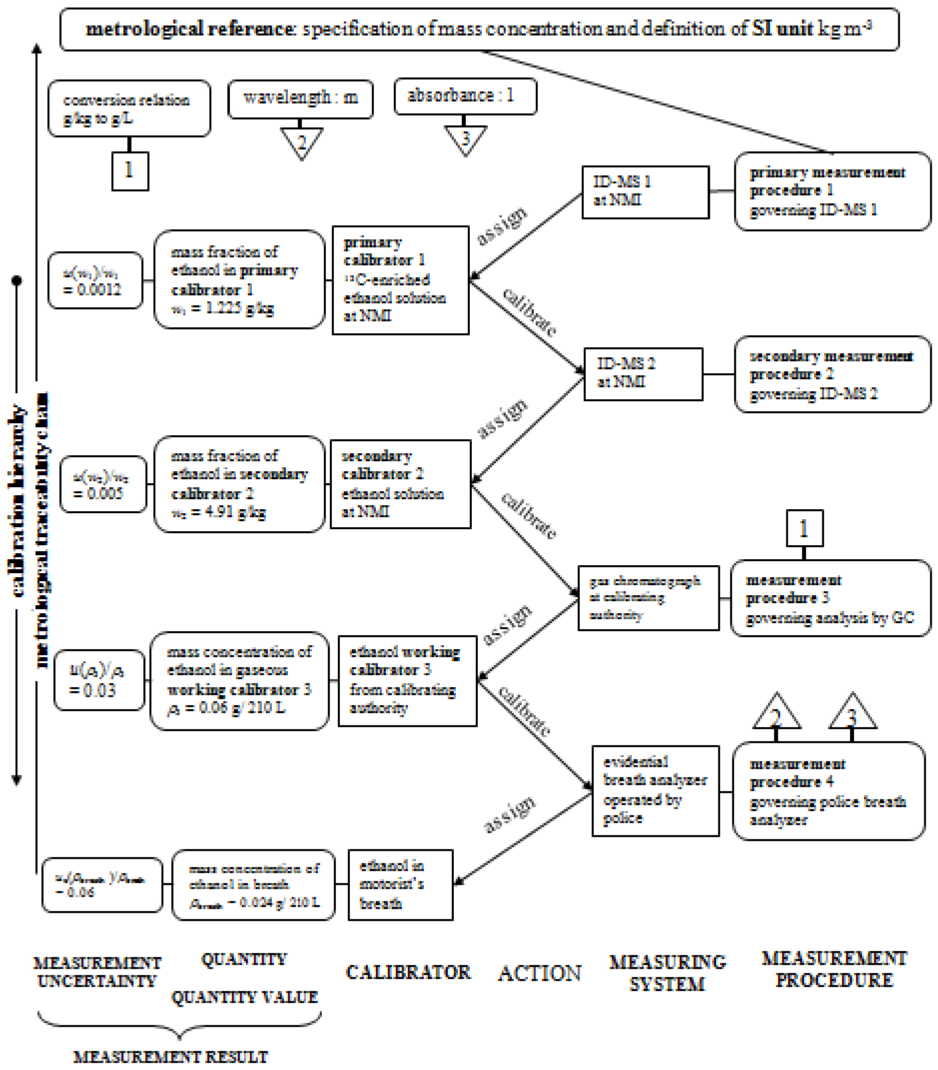
Evidential breath analysers are verified and calibrated using aqueous ethanol solutions. In former times these have been made by gravimetric dilution of absolute ethanol with water, but the hygroscopic nature of ethanol makes the **measurement uncertainties** of final solutions used for **calibration** too great for use in the field. It is therefore necessary to measure the ethanol mass fraction in the calibration solution. This is done by titration with dichromate, or by gas chromatography. A metrologically traceable **quantity value** for an ethanol **measurement standard** has been made in Australia by the **measurement** of the ethanol mass fraction of a solution by ID-MS at the Australian NMI. This “National ethanol calibrator” (**secondary calibrator** 2 in Figure 11.2–1) is used to calibrate either a dichromate **measurement standard** for titration, or a gas chromatograph. These in turn are used to assign **quantity values** to **working calibrator** ethanol solutions that are supplied to the police to calibrate field breathalyzer **measuring systems**. M**etrological traceability chains** are illustrated in Figure 11.2–1 and Figure 11.2–2.



measurement model for end-user : $h(\rho_{\text{ethanol in breath}}, \rho_{\text{ethanol calib 4}}, \alpha_{\lambda,\text{breath}}, \alpha_{\lambda,\text{calib 4}}, \mathrm{CF}_{\rho}) = 0$

Wavelength and absorbance have their respective **measurement models**, 3 and 4.

Figure 11.2–1: **Metrological traceability chain** of **measurement result** obtained with a breathalyzer calibrated via dichromate titration. **Measurement uncertainties** are given as relative standard measurement uncertainties.



measurement model for end-user : $h(\rho_{\text{ethanol in breath}}; \rho_{\text{ethanol cal 3}}; \alpha_{\lambda,\text{breath}}; \alpha_{\lambda,\text{cal 3}}; \mathrm{CF}_{\rho}) = 0$

Wavelength and absorbance have their respective **measurement models**, 2 and 3.

Figure 11.2–2: **Metrological traceability chain** of **measurement result** obtained with an evidential breath analyzer calibrated via gas chromatography. **Measurement uncertainties** are given as relative standard measurement uncertainties.

11.3 Amount-of-substance ratio of isotopes in an element

Measurements of the **quantity** 'amount-of-substance ratio *R* between isotopes in an element E of a sample', are of key importance in the determination of the molar mass *M*(E) (or relative atomic mass, atomic weight) of an element E because, nowadays, any molar mass value is computed from such measured ratios.

11.3.1 The measurement model

Measurements of the **measurand** ‘amount-of-substance ratio between isotopes $^{i}\mathrm{E}$ and $^{j}\mathrm{E}$ in an element E of a sample’

$$R_{i/j} = n(^{i}\mathrm{E})/n(^{j}\mathrm{E}) \qquad \text{(Equation 11.3.1-1)}$$

are carried out by means of a mass spectrometer in which the neutral atoms of the isotopes are converted to singly charged ions forming an ion current which is separated in a magnetic field into as many composing ion currents as there are isotopes. The pairwise ratios of the resulting isotopic ion currents are measured as electric current $I(^{i}\mathrm{E}^{+})/I(^{j}\mathrm{E}^{+})$.

$R_{\mathrm{i/j}}$ meets the definition of a **kind-of-quantity** in VIM3.

The electric current ratio **measurements** must be calibrated in order to yield the corresponding isotope amount-of-substance ratios.

That requires a **measurement model** which is

$$h[R_{i/j}, K_{i/j}, I(^{i}\mathrm{E}^{+})/I(^{j}\mathrm{E}^{+})] = 0 \qquad \text{(Equation 11.3.1-2)}$$

where $K_{i/j}$ is the calibration factor (sometimes called the conversion factor).

From this measurement model, the **measurement function** can be derived:

$$R_{i/j} = K_{i/j} \cdot I(^{i}\mathrm{E}^{+})/I(^{j}\mathrm{E}^{+}) \qquad \text{(Equation 11.3.1-3)}$$

But other **measurement functions** can be derived from this **measurement model** also, such as

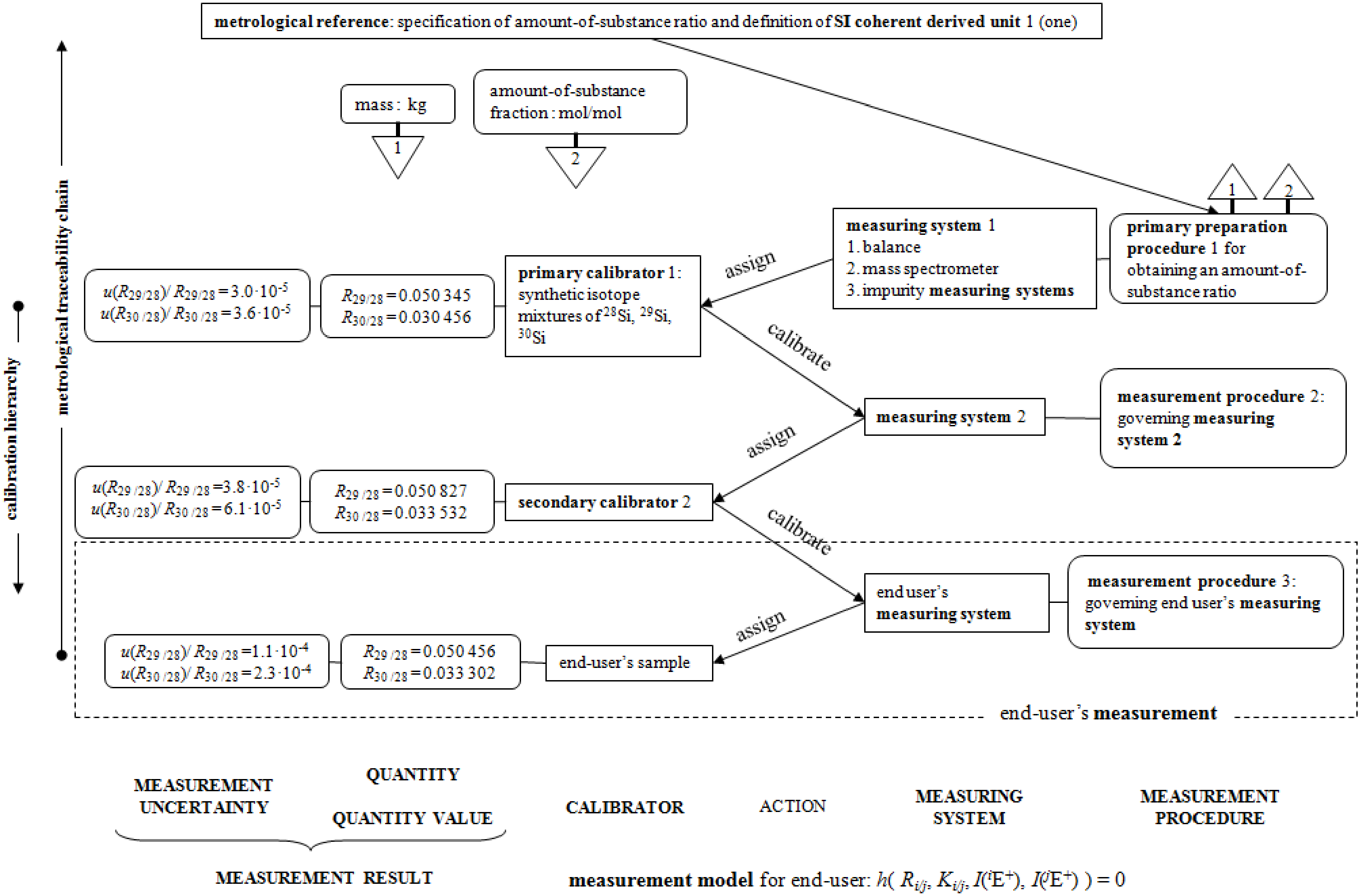
$$K_{i/j} = (R_{i/j})_{\mathrm{cal}} / [I(^{i}\mathrm{E}^{+})/I(^{j}\mathrm{E}^{+})]_{\mathrm{cal}} \qquad \text{(Equation 11.3.1-4)}$$

where ($R_{i/j}$) and [$I(^{i}\mathrm{E}^{+})/I(^{j}\mathrm{E}^{+})$] are the amount-of-substance ratios and their corresponding measured electric current ratios, of the chosen isotopes in the element E in a **calibrator**, which is an isotope **measurement standard**, usually called and marketed as a “certified isotope reference material”. Such a **calibrator** enables to determine the calibration factor used in the **measurement function** described in equation 11.3.1-3.

A description of the related calibration hierarchy is given in the following subsections.

11.3.2 The definition of the measurement unit

Examining the measurement model, the **SI measurement unit** for amout-of-substance the **derived measurement unit** mol/mol equal to one (1). The embodiment of the **measurement unit** requires a **primary measurement procedure** or a **primary preparation procedure**. So far, there is no **measurement procedure** meeting the VIM3 definition of a **primary measurement procedure**, hence a primary preparation procedure is used to embody the **measurement unit**.



measurement model for end-user: $h(R_{i/j}, K_{i/j}, I({}^{i}\mathrm{E}^{+}), I({}^{j}\mathrm{E}^{+})) = 0$

Figure 11.3.3–1: Metrological traceability of a **measurement result** for an isotope amount-of-substance ratio.

11.3.3 The primary preparation procedure governing the preparation system 1 (see Figure 11.3.3–1)

A primary preparation procedure can be achieved by using (highly) enriched or pure isotopes which are built into stoichiometrically well-known molecular compounds (or even as pure elements, if possible). These are weighed and mixed to achieve homogeneity of the isotope atoms on the atomic level. The mass ratios of the compounds can be converted to amount-of-substance ratios for the isotopes concerned by measuring the molar mass of the element E in the enriched isotopes $^{i}\mathrm{E}$ as well as determining the deviation from theoretical stoichiometry of the compounds used. The closer the degree of isotope enrichment comes to 100 % in each compound, the closer the **measurement uncertainties** of the molar mass values of the enriched isotopes approach the **measurement uncertainties** of the atomic mass values of 100 % pure isotopes, typically $10^{-7}M(^{i}\mathrm{E})$ or better.

11.3.4 The measuring system 2

The **measuring system** 2, governed by **measurement procedure** 2, can be used to assign calibrated **measured quantity values** of an amount-of-substance ratio to a **secondary calibrator** 2. See Figure 11.3.3–1.

11.3.5 The end-user's measuring system

The **secondary measurement standard** or **secondary calibrator** 2 can be made available to end-users for measuring unknown isotope amount ratios in, e.g., geological, nuclear, or other samples. It is the duty of the seller of **calibrator** 2 to deliver, together with the **calibrator,** the higher levels of the **metrological traceability chain** with associated **measurement uncertainty**.

In many practical cases, the **metrological traceability chain** is longer than in the example of Figure 11.3.3–1.

11.3.6 Quantities derived from isotope amount-of-substance ratio(s)

11.3.6.1 Isotope abundance $f(^i\mathrm{E})$

In isotope measurements, much use is made of the **kind-of-quantity** ‘isotope abundance’ $f(^i\mathrm{E})$ which is the number fraction of atoms of one isotope $^i\mathrm{E}$ in the total number of atoms of the element E. Hence, the sum of abundances $\Sigma f(^i\mathrm{E})$ is, by definition, always equal to 1 exactly, i.e.

$$\Sigma f(^i\mathrm{E}) \equiv 1 \qquad \text{(Equation 11.3.6.1-1)}$$

and

$$f(^i\mathrm{E}) = f(^i\mathrm{E}) \,/\, \Sigma\, f(^i\mathrm{E}) \qquad \text{(Equation 11.3.6.1-2)}$$

$$f(^i\mathrm{E}) \;=\; [f(^i\mathrm{E}) \;/\, f(^j\mathrm{E})] \,/\, [\Sigma\, f(^i\mathrm{E}) \;/\, f(^j\mathrm{E})] \qquad \text{(Equation 11.3.6.1-3)}$$

$$= [N(^i\mathrm{E})/\, N(^j\mathrm{E})] \,/\, [\Sigma\, N(^i\mathrm{E}) \;/\, N(^j\mathrm{E})] \qquad \text{(Equation 11.3.6.1-4)}$$

$$= R_{i/j}(^i\mathrm{E}) \,/\, \Sigma\, R_{i/j}(^i\mathrm{E}) \qquad \text{(Equation 11.3.6.1-5)}$$

An isotope amount-of-substance ratio measuring device enables to measure ratios $R_{i/j}$ of an isotope abundance relative to a conveniently chosen abundance of another isotope ($^j\mathrm{E}$), thus enabling to calculate any isotope abundance $f(^i\mathrm{E})$.

Measurement uncertainty $u_c[f(^i\mathrm{E})]$ is obtained by propagating the **measurement uncertainties** of $R_{i,j}$.

11.3.6.2 Atomic mass M(E) or relative atomic mass (atomic weight) A_r(E) of an element

M(E) is calculated from $f(^i\mathrm{E})$ by

$$M(\mathrm{E}) = \Sigma\, f(^i\mathrm{E}) \cdot M(^i\mathrm{E}) \qquad \text{(Equation 11.3.6.2-1)}$$

where $f(^i\mathrm{E})$ is the abundance of isotope ^{i}E concerned, and $M(^i\mathrm{E})$ is the atomic mass of that isotope.

Substitution of $f(^i\mathrm{E})$ in Equation 11.3.6.2-1 according to Equation 11.3.6.1-5 leads to

$$M(\mathrm{E}) = \Sigma\, R_{i/j}(^i\mathrm{E}) \cdot M(^i\mathrm{E}) \;/\; \Sigma\, R_{i/j}(^i\mathrm{E}) \qquad \text{(Equation 11.3.6.2-2)}$$

Evaluation of **combined measurement uncertainty** $u_c[M(\mathrm{E})]$ is performed by propagating the **combined measurement uncertainty** $u_c(R_{\mathrm{i/j}})$ to $u_c[M(\mathrm{E})]$.

Note: “atomic weights” A_r(E) of the elements are ratios of the molar mass values of that element to 1/12th of the molar mass value of ^{12}C, the latter being set by convention to 12 g/mol exactly.

11.4 Mass fraction of glyphosate in an agricultural chemical

Since its discovery, nuclear magnetic resonance spectroscopy (NMR) has been used as a qualitative technique for the identification and elucidation of structures of an enormous variety of inorganic, organic and biological materials..Quantitative NMR (QNMR) has been reported as the basis of a **primary measurement method** for **measurement** of mass fractions of organic compounds such as agricultural chemicals [45]. The compound of the **calibrator** need not be the same as the analyte, provided it contains the nucleus of interest. For example, the analysis of the agricultural weedicide, *N*-phosphonomethyl glycine (‘glyphosate’): $HOOCCH_2NH_2CH_2PO(OH)_2$ uses a **CRM** of dimethylsulfone ($CH_3SO_2CH_3$) as a ^{1}H **calibrator** and a **CRM** of sodium phosphate (Na_3PO_4) as a ^{31}P **calibrator**.

11.4.1 Measurement method

The purity of a compound is determined by the following steps.

1 Weigh a mass of sample into an NMR tube by difference (about 5 mg glyphosate).

2 Weigh a mass of the **calibrator** into the NMR tube by difference to give approximately the same amount-of-substance of the target isotope as of the analyte.

3 Add deuterated solvent to an appropriate level.

4 Introduce the NMR tube into the instrument. Allow to equilibrate at the set temperature of the probe and measure with parameters for full relaxation (and suppression of the nuclear Overhauser effect as required).

5 Record the free induction decay (FID) spectrum.

6 Process the FID with window function as required, phase the spectrum manually, and establish the baseline.

7 Integrate the peaks to obtain the ratio of the integrated peak for the sample to the integrated peak for the **calibrator** ($I_{\text{sample}}/I_{\text{cal}}$).

11.4.2 Quantity equation

The **quantity equation** for the mass fraction of a sample based on the observation of the NMR signal for ^{1}H is

$$w_{\text{sample}} = \frac{I_{\text{sample}}}{I_{\text{cal}}} \times \frac{m_{\text{cal}}}{m_{\text{sample}}} \times \frac{N_{\text{cal}}}{N_{\text{sample}}} \times \frac{M_{\text{sample}}}{M_{\text{cal}}} \times w_{\text{cal}} \qquad \text{Equation (11.4.2 – 1)}$$

where “sample” and “cal” refer to the sample being measured and **calibrator** respectively; I is an indication of the NMR spectrometer for a given chemical shift (an integrated peak), m is the mass, N is the number of protons in one molecule, M is the molar mass, and w is the mass fraction. The mass fraction of the **primary calibrator** can be measured at an NMI by a combination of techniques, including gas chromatography, NMR, thermogravimetry, differential scanning calorimetry, Karl Fisher analysis for water, and elemental analysis. In this case the mass fraction can be calculated as one minus the sum of all impurities and reported with a GUM **measurement uncertainty**. For QNMR **measurements** in which the isotope of interest is a proton, the mass fraction of a **working measurement standard** of sodium acetate can be measured by QNMR calibrated by the dimethylsulfone **CRM**. The **metrological traceability chain** is shown in figure 11.4.2 – 1.

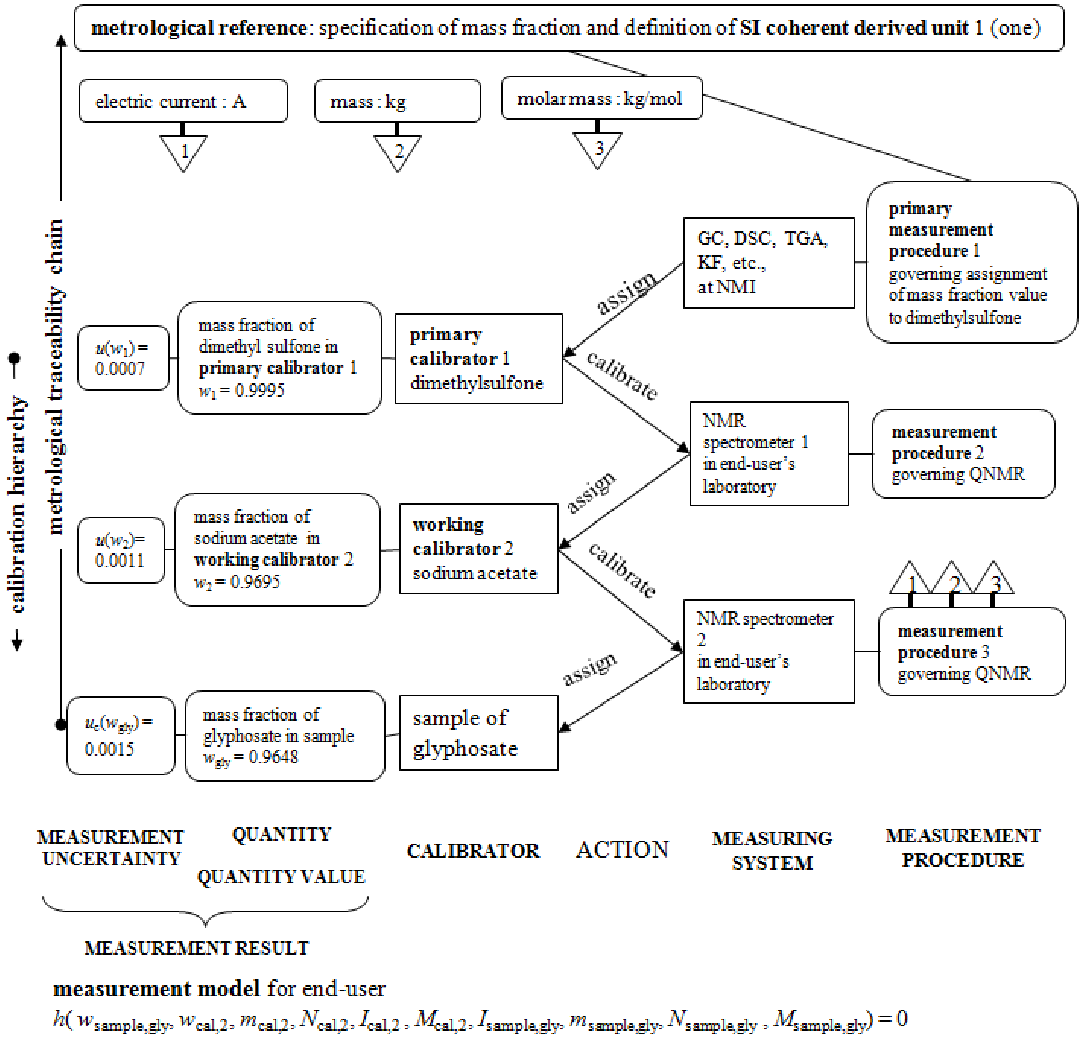


Figure 11.4.2 – 1. **Metrological traceability chain** of the **measurement result** of the mass fraction, *w*, of a sample of the agricultural chemical glyphosate. *I* = indication of the NMR

spectrometer, *m* = mass, *M* = molar mass, *n* = number of protons contributing to the NMR signal. GC = gas chromatography, DSC = differential scanning calorimetry, TGA = thermogravimetric analysis, KF = Karl Fisher.

11.5 Amount-of-substance concentration of creatininium in blood plasma

The amount-of-substance concentration of creatininium in blood plasma is an important inverse indicator of renal function. (“Creatininium” is the IFCC-IUPAC term for the sum of the species ‘Creatinine’ and ‘Creatininium ion’.)

A current commercial **measurement procedure** uses a four-stage enzymatic reaction scheme [46, 47]. The reactions involved are

$$\text{creatininium} + H_2O \xrightarrow{\text{creatininase (EC 3.5.2.10)}} \text{creatine}$$

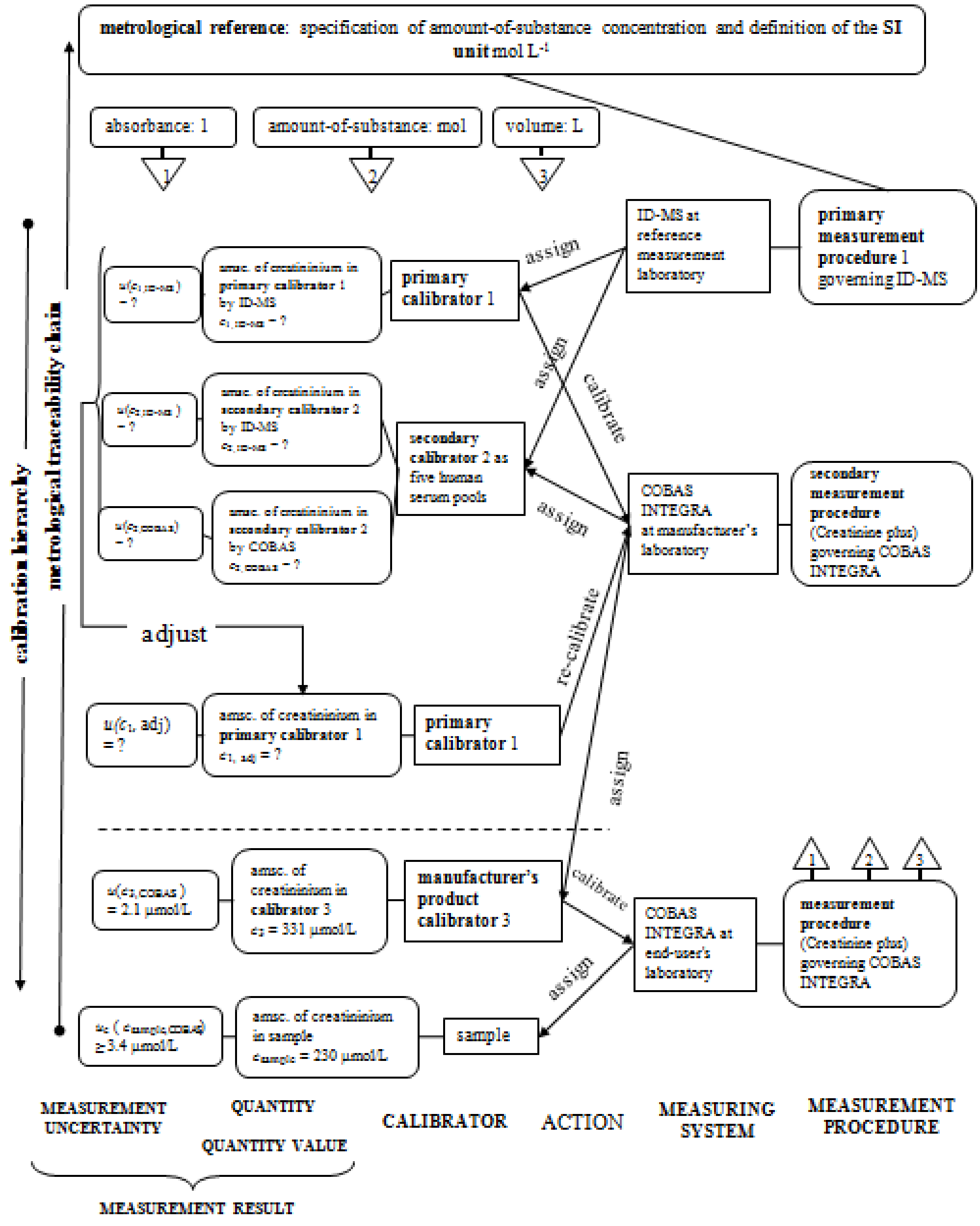
$$\text{creatine} + H_2O \xrightarrow{\text{creatinase (EC 3.5.3.3)}} \text{sarcosine} + \text{carbamide}$$

$$\text{sarcosine} + O_2 + H_2O \xrightarrow{\text{sarcosine oxidase (EC 1.5.3.1)}} \text{glycine} + HCHO + H_2O_2$$

$$H_2O_2 + \text{4-aminophenazone} + \text{2,4,6-triiodo-3-hydroxybenzoic acid} \xrightarrow{\text{peroxidase (EC 1.11.1.7)}} \text{quinone imine chromogen} + H_2O + HI$$

where the colour intensity change of the chromogen is directly proportional to the creatininium concentration and is recorded at an endpoint by absorbance at 552 nm corrected for blank at 659 nm [48].

The **measurement** may be performed on a Roche COBAS INTEGRA 800 and the **metrological traceability** to an **SI unit** is documented [49, 50]. The **calibration hierarchy** shown in Figure 11.5 – 1 should reflect this information.



measurement model for end-user: $h(c_{\text{sample}}, c_{\text{cal 3}}, I_{\text{cal 3}}, I_{\text{sample}}) = 0$

Absorbance, amount-of-substance and volume have their respective **measurement models** 1, 2, and 3

amsc. = amount-of-substance concentration

Figure 11.5 – 1. **Metrological traceability** of a **measurement result** for amount-of-substance concentration of creatininium in human blood plasma using a commercial **measuring system**

amsc. = amount-of-substance concentration.

Only data below the broken line are available to the end-user.

11.5.1 Primary measurement

A **primary measurement procedure** involving an isotope dilution-mass spectrometer (ID-MS) in a reference measurement laboratory is applied to a **primary calibrator**, called “masterlot calibrator“, and to five serum pools; both **primary calibrator** and serum pools are produced according to the manufacturer's standardized protocols. The six **quantity values** can be assumed to be near correct.

11.5.2 Secondary measurement

The **primary calibrator** is used to calibrate the manufacturer's **measuring system** operating according to his standing **secondary measurement procedure**. Both equipment, ie COBAS INTEGRA 800 with reagents, and **secondary measurement procedure** are essentially identical with those employed by the end-user, except that only the manufacturer has access to the stored **primary calibrator** whereas the end-user uses the **manufacturer's product calibrator**; this, however, is produced in the same way as the **primary calibrator**.

The manufacturer's standing **secondary measurement procedure** and COBAS INTEGRA calibrated with the **primary calibrator** are used to assign a second set of **quantity value** and **measurement uncertainty** to each of the five serum pools.

11.5.3 Adjustment of quantity value of primary calibrator

For the five serum pools, the ID-MS **quantity values** on the abscissa and manufacturer's COBAS **quantity values** on the ordinate allow the calculation of a regression line ($y = bx + a$). Then the ID-MS **quantity value** of the **primary calibrator** via this regression line corresponds to an ordinate **quantity value** that may be different from that on the abscissa. In that case, the **primary calibrator**’s **quantity value**, is adjusted so that the regression line within a reasonable interval around the adjusted **quantity value** goes through 0.0. The **measurement uncertainty** of the adjustment depends on the relative magnitudes of the constants a and b and must be a part of the **combined standard measurement uncertainty** of the **primary calibrator**’s adjusted **quantity value**.

The rationale of this type of adjustment is that it should reduce the effect of the lack of any analytical specificity of the manufacturer's standing **secondary measurement procedure** and **measuring system** as well as any lack of **commutability** of the **primary calibrator**. The relative magnitude of the adjustment is not available to the end-user.

Another perhaps more transparent approach would be to apply a correcting algorithm on the actual **indications** of the manufacturer's **measuring system**, involving both constants *a* and *b*, thus keeping the ID-MS-assigned primary **quantity value**.

11.5.4 Tertiary measurement

Using the **primary calibrator** with adjusted **quantity value** and **combined standard measurement uncertainty** to recalibrate the manufacturer's COBAS **measuring system** operated according to his **secondary measurement procedure**, the **manufacturer's product calibrator** obtains its assigned **quantity value** and **combined standard measurement uncertainty**, and is delivered to the customer, the end-user.

11.5.5 End-user's measurement

With the **manufacturer's product calibrator** with associated calibration factors for the end-user's **measuring system** operated according to his **measurement procedure**, routine human samples can now be measured to give directly a **measurement result**. The **quantity value** is assumed to be adequately correct for the given purpose because the **measurement system** and **measuring procedure** used by both manufacturer and end-user are essentially the same.

The **uncertainty budget** for the end-user's **quantity value** first of all relies completely on the adequacy of the **measurement uncertainty** assigned to the **quantity value** of the **manufacturer's product calibrator**. The **uncertainty budget** of this **calibrator** is only available to regulatory authorities, but should include sources of variation such as

- definition of **quantity**,

- **measurement uncertainty** of adjusted **quantity value** for **primary calibrator** 1 provided by reference measurement laboratory,
- inhomogeneity and instability of **primary calibrator**,
- inhomogeneity and instability of serum pools,
- **measurement uncertainty** of manufacturer's **measuring system**, twice,
- adjustment procedure,
- lot-to-lot differences for manufacturer's **product calibrator** (unless assigned individually), and
- inhomogeneity and instability of the **product calibrator**.

The end-user further has the following pre-examinational and examinational sources to consider and select according to the purpose:

- inter-individual variation,
- intra-individual variation,
- sampling,
- transport and storage of sample,
- separation and sub-sampling, and
- **intermediate precision conditions** (which subsumes some other sources).

The pre-examinational sources may well give the major contributions in this example.

The manufacturer lists the following information for his **product calibrator** with a **quantity value** of 331 μmol/L:

u = 2.12 μmol/L [50]

CV within run 0.7 % [48] (repeatability)

CV between run 0.9 % [48] (reproducibility)

With an end-user's **quantity value** of, say, 230 µmol/L, which is about twice the upper limit of a central 0.95-interfractile biological reference interval in healthy adults, this **quantity value** would give the following minimum **combined standard measurement uncertainty**, based solely on the assigned **combined standard measurement uncertainty** of the **manufacturer's product calibrator** and the **standard measurement uncertainty** under **intermediate precision conditions of measurement**:

$$\sqrt{2.12^2 + (0.007 \times 230)^2 + (0.009 \times 230)^2} \quad \mu\text{mol/L}$$

$$= \sqrt{4.49 + 2.59 + 4.28} \quad \mu\text{mol/L} = 3.37\ \mu\text{mol/L}$$

or CV(intermediate) = 3.37 µmol/L × 100/ (230 µmol/L) = 1.5 %

The values were obtained in the manufacturer's laboratory and the end-user should expect somewhat higher values for **measurement uncertainty** and increasing with lower **measured quantity value**.

11.5.6 Metrological traceability

A routine **measurement result** for amount-of-substance concentration of creatininium in the plasma of a given person at a stated time is metrologically traceable to the **SI unit** µmol/l. As the **calibration hierarchy** includes an empirical “holistic” adjustment element, it is necessary to specify the **measurement procedure** and **manufacturer's product calibrator**.

It should be added that various types of adjustment procedure such as the above are not infrequent in commercial measuring systems. It would be helpful to the end-user in evaluating their appropriateness if the data were available on request.

11.6 Mass fraction of protein in grain

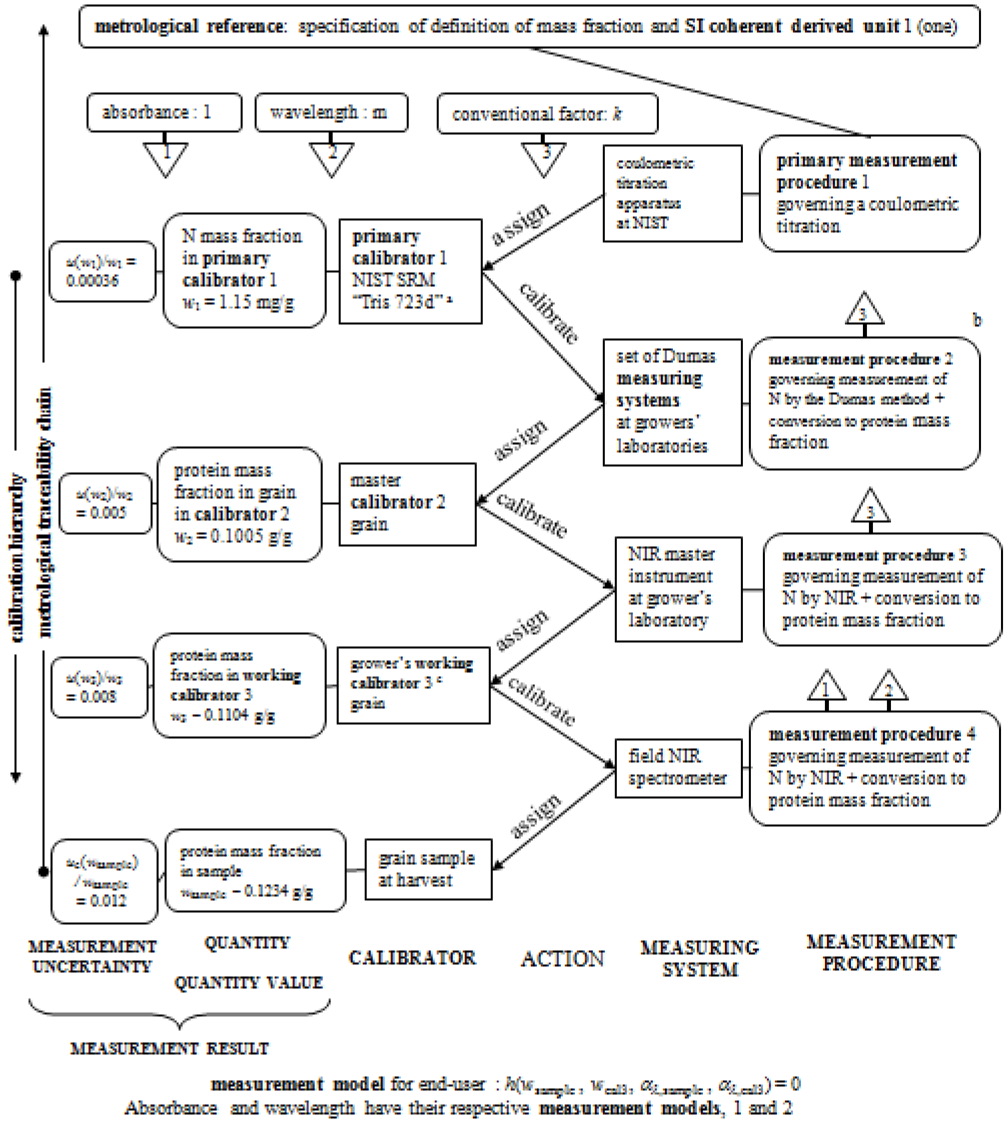
The price of a harvested grain, such as wheat, depends on its protein content. The nitrogen mass fraction is measured in the field by near infra-red (NIR) spectrometry and multiplication by a conventional factor gives a **measurement result** for the **measurand** "mass fraction of protein in the sample of grain". The use of near infra-red spectrometry requires multivariate **calibration** (i.e. the whole spectrum is used to calibrate the mass fraction of nitrogen) with a whole-grain **calibrator**. **Metrological comparability** between **measurement results** from growers in a particular region is important, and in Australia the industry has commenced work with the NMI to produce grain **calibrators** that have metrologically traceable **quantity values** to the **SI unit** one for the **kind-of-quantity** mass fraction. The **primary calibrator** selected is a NIST SRM 723d (Tris = 2-amino-2-hydroxymethyl-1,3-propanediol) that the NMI, under the powers of the National Measurement Act, has recognized as a legal **primary calibrator**. The **quantity value** of this SRM (where SRM is the NIST initialism for **CRM**) has been established by a **primary measurement procedure** giving **metrological traceability** to the **SI unit**.

11.6.1 Description of the calibration hierarchy

Measurement results are metrologically traceable to the nitrogen mass fraction of a NIST standard reference material (Tris). The mass fraction of titratable acid (purity) of the material has been established by coulometric titration, and the material is claimed to be metrologically traceable to the **SI coherent derived unit** one for mass fraction. This **CRM** is used to calibrate **measuring systems** for analysis of nitrogen by the Dumas method, which involves combustion of the sample followed by gas chromatographic analysis of the nitrogen oxides that are produced. The protein content of a master calibrator grain (usually taken from the previous year's harvest) is established in an interlaboratory materials-certification campaign that is supervised by the NMI, using the calibrated Dumas systems. The result from each laboratory, and hence the value assigned by the NMI, is metrologically traceable through the

Tris **CRM**. Note that a measured nitrogen mass fraction is converted to a protein mass fraction by multiplication by a conventional factor, *k*, that has no **measurement uncertainty**. The master grain is then distributed to all growers who use it to calibrate a near infra-red instrument (NIR) in each of their laboratories, so called master instruments. These master instruments measure the protein mass fraction of **working calibrator** grain samples that are then used in the field to calibrate NIR instruments that measure the harvested grain.

A schematic of the **metrological traceability chain** is shown in Figure 11.6.1 – 1.



a Tris = 2-amino-2-hydroxymethyl-1,3-propanediol b **Measuring systems** are calibrated and then certify grain samples in an **interlaboratory comparison**

c The master instruments each measure grain samples to act as grower's **working calibrator** for field **measurements**

Figure 11.6.1 – 1: **Metrological traceability chain** of protein **measurements** in harvested grain. **Measurement uncertainties** are given as relative **standard measurement uncertainties**.

12 Recommendations

12.1 Recommendations on measurement in chemistry

Planning and performing a **measurement**[1] should proceed as follows:

1 define the **measurand (**by system, component, and **kind-of-quantity** with any specifications);

2 decide the **metrological reference** for the final **measurement result**;

3 select the **target measurement uncertainty**;

4 choose and validate a **measurement procedure**;

5 establish the **calibration hierarchy** to enable the creation of a **metrological traceability chain** for the expected **measurement result**;

6 make a model **uncertainty budget;**

7 evaluate an approximate estimate of the expected **measurement uncertainty** of the **measurement result**, based on the established **calibration hierarchy;**

8 check whether the **target measurement uncertainty** will be met;

9 acquire the relevant **measuring system** and **calibrator(s);**

---

[1] Bold face indicates concepts and terms defined in this report, or in VIM3.

10 carry out the **measurement** according to the chosen and validated **measurement procedure**;

11 evaluate, then calculate the actual **measurement uncertainty**; and

12 report the **measurement result** with **measured quantity values** and **measurement uncertainty;** and

13 specify the **metrological traceability**.

12.2 Recommendations for the implementation of metrology in chemistry

1 Include basic features of **metrology** in chemistry in curricula of analytical chemistry.

2 Use concepts and associated terminology given in the International Vocabulary of Metrology (VIM).

3 Evaluate **measurement uncertainty** based on the Guide to the Expression of Uncertainty in Measurement (GUM) as applied, for example, in the EURACHEM/CITAC guide.

4 State the metrological reference of any (chemical) **measurement result**.

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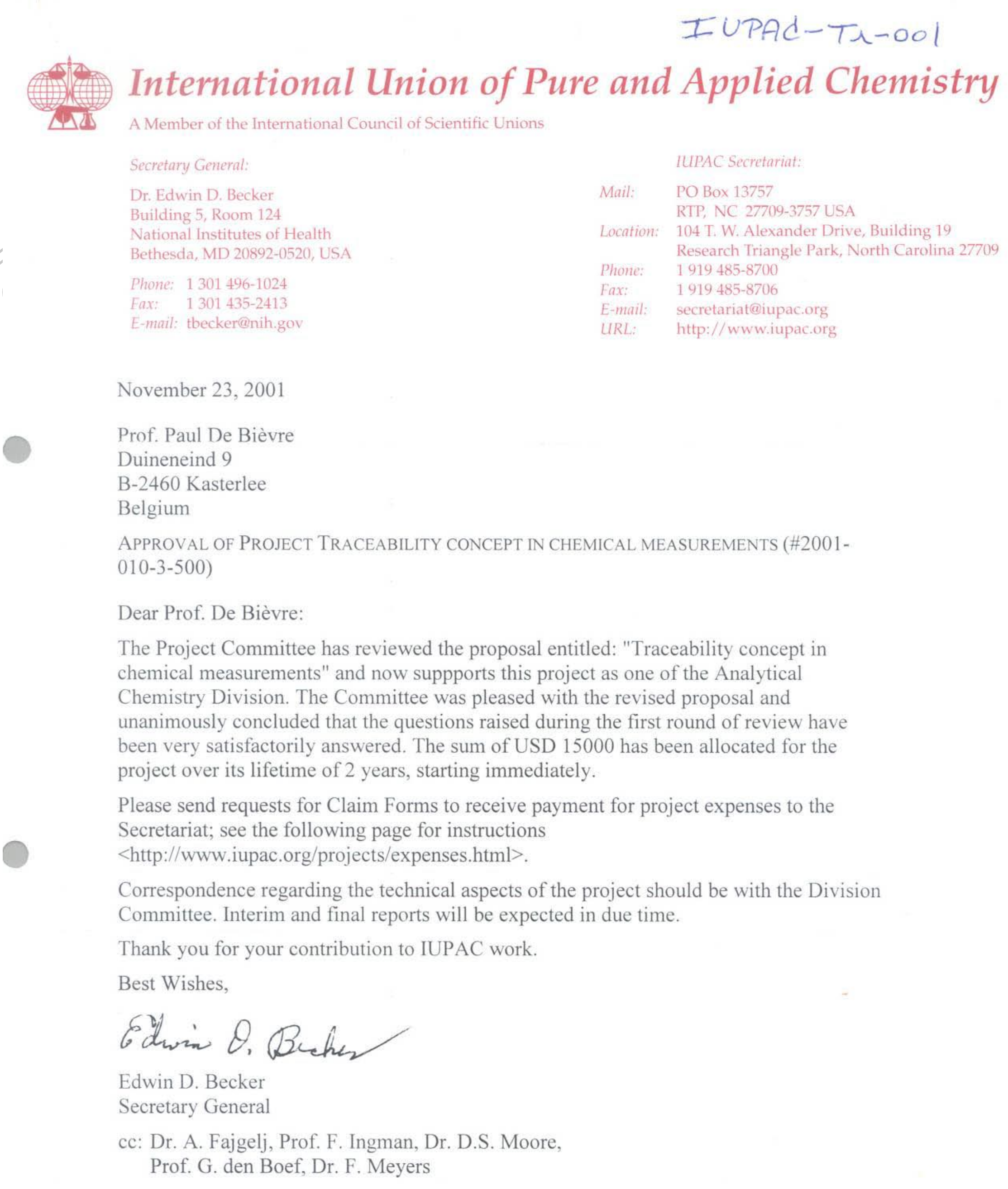
Official IUPAC Notification of Project Approval



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Secretary General:
Dr. Edwin D. Becker
Building 5, Room 124
National Institutes of Health
Bethesda, MD 20892-0520, USA
Phone: 1 301 496-1024
Fax: 1 301 435-2413
E-mail: tbecker@nih.gov

IUPAC Secretariat:
Mail: PO Box 13757
RTP, NC 27709-3757 USA
Location: 104 T. W. Alexander Drive, Building 19
Research Triangle Park, North Carolina 27709
Phone: 1 919 485-8700
Fax: 1 919 485-8706
E-mail: secretariat@iupac.org
URL: http://www.iupac.org

November 23, 2001

Prof. Paul De Bièvre
Duineneind 9
B-2460 Kasterlee
Belgium

APPROVAL OF PROJECT TRACEABILITY CONCEPT IN CHEMICAL MEASUREMENTS (#2001-010-3-500)

Dear Prof. De Bièvre:

The Project Committee has reviewed the proposal entitled: "Traceability concept in chemical measurements" and now suppports this project as one of the Analytical Chemistry Division. The Committee was pleased with the revised proposal and unanimously concluded that the questions raised during the first round of review have been very satisfactorily answered. The sum of USD 15000 has been allocated for the project over its lifetime of 2 years, starting immediately.

Please send requests for Claim Forms to receive payment for project expenses to the Secretariat; see the following page for instructions <http://www.iupac.org/projects/expenses.html>.

Correspondence regarding the technical aspects of the project should be with the Division Committee. Interim and final reports will be expected in due time.

Thank you for your contribution to IUPAC work.

Best Wishes,

Edwin D. Becker

Edwin D. Becker
Secretary General

cc: Dr. A. Fajgelj, Prof. F. Ingman, Dr. D.S. Moore,
Prof. G. den Boef, Dr. F. Meyers

Annexe I Terms of Reference

1 to elucidate the concept ‘metrological traceability’ of a measurement result and list its characteristics, and to describe the relations between metrological traceability and other concepts such as calibration, measurement uncertainty and comparability;

2 to formulate requirements for establishing metrological traceability;

3 to give specific examples of metrological traceability of chemical measurement results.

Annexe II Project Members

Professor P De Bièvre (Task Group Chair)

Former Adviser on 'Metrology in Chemistry' to the Director, IRMM Geel, Belgium
Past-President National Committee on Chemistry of the Royal Academies of Belgium
Past-President EURACHEM
Member IUPAC Commission on Isotope Abundances and Atomic Weights (II.1)
Founder IUPAC Former-Commission II.4 on Isotope-specific Measurements as References
Member IUPAC Interdivisional Working Party on Harmonization of Quality Assurance
Founder of the IMEP programmes REIMEP, IMEP, and NUSIMEP
Member CIPM-CCQM
Former Member ISO/REMCO and Chair SG 1 (International Coordination)
Former Liaison Officer ISO/REMCO to CCQM
Member ISO TAG 4 on Metrology
IUPAC Representative on the Joint Committee for Guides in Metrology, JCGM and JCGM-WG 2 (VIM)
Liaison Officer ISO/REMCO-JCGM (revision of the VIM)

Dr R Dybkaer
Director Department of Standardization in Laboratory Medicine, REGION H, Frederiksberg Hospital, Copenhagen, Denmark
Past-President, International Federation of Clinical Chemistry and Laboratory Medicine (IFCC)
Past-President European Confederation of Laboratory Medicine (ECLM) now Laboratory Medicine in Europe (LME)
Past-Chairman Danish Society of Clinical Chemistry, now Danish Society of Clinical Biochemistry
Member IUPAC (VII) Subcommittee and IFCC Committee (SD 8.2.6) on Nomenclature, Properties and Units
Member IUPAC Interdivisional Working Party on Harmonization of Quality Assurance
Member CIPM-CCQM (representing IFCC)
Member CIPM-CCU (representing IFCC)
Member Joint Committee for Guides in Metrology JCGM WG 1 (GUM) and WG 2 (VIM) (representing IFCC)
Member ISO TAG 4 on Metrology (representing Danish Standards)
Convener ISO/TC 212/WG 2 and CEN/TC 140/WG 4 on Reference Systems (representing Danish Standards)

Dr A Fajgelj
Quality Systems Manager, Agency's Laboratories Seibersdorf and Vienna, IAEA
Vice President IUPAC Analytical Chemistry Division Committee (V)
Chairman IUPAC Interdivisional Working Party on Harmonization of Quality Assurance (V)
IAEA and IUPAC representative to CIPM-CCQM
IAEA and IUPAC representative to ISO/REMCO
Convenor ISO REMCO Steering Group on International Cooperation
Member Co-operation on International Traceability in Analytical Chemistry (CITAC)

Professor D B Hibbert
Professor of Analytical Chemistry, University of New South Wales, Sydney, Australia
Chair, Programme Advisory Committee on pure reference material production, National Measurement Institute, Australia.

Former Commissioner National Standards Commission, Australia
Visiting Professor, National Measurement Institute, Australia
Former Chair Analytical Division Royal Australian Chemical Institute
Member Advisory Committee on Accreditation of Reference Material Providers, National Association of Testing Authorities (NATA), Australia
Member Joint Committee for Guides in Metrology JCGM WG 1 (GUM) (representing IUPAC)
Member, Advisory Committee on Chemical Testing, National Association of Testing Authorities (NATA), Australia
Chair Committee CH023 Standards Australia
Member Committee CH001 Standards Australia
Secretary IUPAC Analytical Chemistry Division, Committee (V)
Member IUPAC Interdivisional Working Party on Harmonization of Quality Assurance (V)

Annexe III Schedule of meetings

Preliminary meeting

University of New South Wales, Sydney, Australia, on 2001-06-25/26/27

Meetings

Institute for Reference Materials and Measurements, Geel, Belgium, on 2001-12-17/18/19

IAEA, Vienna, Austria, on 2002-07-01/02/03

Frederiksberg Hospital, Copenhagen, Denmark, on 2002-12-09/10/11/12

Kasterlee, Belgium 2003-01-20/21/22

IUPAC General Assembly, Ottawa, Canada, 2003-08-11/12/13/14

Kasterlee, Belgium, on 2004-01-19/20/21

IAEA Vienna, Austria, on 2004-02-18/19/20

Kasterlee, Belgium, on 2005-07-13/14

IUPAC General Assembly, Beijing, 2005-08-15/16/17/18/19

Kasterlee, Belgium, on 2005-11-24/25/26

UNIDO Vienna, Austria, on 2005-11-12/13/14/15/16

Kasterlee, Belgium, on 2006-02-27/28, -03-01, 09-09/10, 2007-03-14/15/16, -08-02/03

Torino, Italy, on 2007-08-02-10 (presentation to IUPAC bodies)

Kasterlee, Belgium, on 2007-08-22/23/25, 2007-12-01/03, 2007-12-05/06

Annexe IV Initialisms, acronyms, and abbreviations

AAS	atomic absorption spectrometry
BIPM	Bureau International des Poids et Mesures International Bureau of Weights and Measures, www.bipm.org
CCQM	Comité Consultatif pour la Quantité de Matière: Métrologie en Chimie Consultative Committee for Amount of Substance: Metrology in Chemistry (under CIPM)
CCU	Comité Consultatif des Unités Consultative Committee for Units (under CIPM)
CGPM	Conférence Générale des Poids et Mesures General Conference of Weights and Measures
CIPM	Comité International des Poids et Mesures International Committee for Weights and Measures
CITAC	Cooperation on International Traceability in Analytical Chemistry
CMC	calibration and measurement capability (published on the website of the BIPM)
CODATA	Committee on Data for Science and Technology (under ICSU)
CRL	Community Reference Laboratory (in the EU)
CRM	certified reference material
CV	coefficient of variation
DSC	differential scanning calorimetry
DIN	Deutsches Institut fuer Normung
EA	European co-operation for Accreditation
EAL	European co-operation for Accreditation of Laboratories (now called EA)
EC	European Commission
EQA	external quality assurance
EQALM	European Committee for External Quality Assurance Programmes in Laboratory Medicine
EQAS	external quality assurance scheme
EN	European Norm

EU	European Union
FID	free induction decay
GC	gas chromatography
GLP	Good Laboratory Practice
GUM	Guide to the expression of uncertainty in measurement [2] Guide pour l'expression de l'incertitude de mesure
IAEA	International Atomic Energy Agency
ICP OES	inductively coupled plasma optical emission spectrometry
ICSU	International Council of Scientific Unions
ICTNS	Interdivisional Committee on Terminology, Nomenclature and Symbols (under IUPAC)
ID-MS	isotope dilution-mass spectrometry
IEC	International Electrotechnical Commission
IFCC	International Federation of Clinical Chemistry and Laboratory Medicine
ILAC	International Laboratory Accreditation Cooperation
ILC	interlaboratory comparison
IMEP	International Measurement Evaluation Programme at IRMM
IRMM	Institute for Reference Materials and Measurements of the Joint Research Centre of the European Commission
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
IUPAP	International Union of Pure and Applied Physics
JCGM	Joint Committee for Guides in Metrology
KCRV	Key comparison reference value
KF	Karl Fischer (measurement of mass fraction of water in material)
MiC	Metrology in Chemistry
METAS	Bundesanstalt fuer Metrologie und Akkreditierung Schweiz
MRA	Mutual Recognition Arrangement (under CIPM)
MLA	Multilateral Recognition Arrangement (under ILAC)

NARL	National Analytical Reference Laboratory (NMI, Australia)
NATA	National Association of Testing Authorities (Australia)
NIR	near infra-red
NIST	National Institute for Standards and Technology (USA)
NMI	National Metrology Institute, National Measurement Institute
NMR	nuclear magnetic resonance
NUSIMEP	Nuclear Signatures International Measurement Evaluation Programme at IRMM
OIML	Organisation Internationale de Métrologie Légale International Organization of Legal Metrology
PAC	Pure and Applied Chemistry (journal of IUPAC)
PCR	polymerase chain reaction
PRMP	primary reference measurement procedure
PMS	primary measurement standard
PTB	Physikalisch-Technische Bundesanstalt (Germany)
PTS	proficiency testing scheme
QNMR	quantitative nuclear magnetic resonance
QUAM	Quantifying uncertainty in analytical measurement [28]
REIMEP	Regular European Interlaboratory Measurement Evaluation Programme at IRMM (for nuclear measurements)
REMCO	Council Committee on Reference Materials (under ISO)
RM	reference material
RMP	reference measurement procedure
SI	Le Système International d´Unités The International System of Units
TGA	thermo-gravimetric analysis
TMU	**target measurement uncertainty**
unc	**measurement uncertainty**
UNIDO	United Nations Industrial Development Organization
UTC	Coordinated Universal Time

VIM2	BIPM, IEC, IFCC, ISO, IUPAC, IUPAP, OIML. *International vocabulary of basic and general terms in metrology, VIM2*, 1993, International Organization for Standardization, Geneva. [14]
VIM3	JCGM. *International vocabulary of metrology – Basic and general concepts and associated terms (VIM3)*, JCGM 200:2007, (in the name of BIPM, IEC, IFCC, ILAC, ISO, IUPAC, IUPAP, OIML), International Organization for Standardization, Geneva, www.iso.com. [17]
WHO	World Health Organization

Annexe V Bibliography

Annexe V.1 Research Papers

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Annexe VI Alphabetical index of terms

	VIM3 [*]	Concept
kind-of-quantity	1.2	2.1
manufacturer’s product calibrator		3.1-6
manufacturer’s working calibrator		3.1-5
measurand	2.3	2.1-4
measured quantity value	2.10	2.1-6
measurement	2.1	2.1-1
measurement capability		8.4-1
measurement function	2.49	2.1-8
measurement method	2.5	2.1-11
measurement model	2.48	2.1-7
measurement principle	2.4	2.1-10
measurement procedure	2.6	2.1-12
measurement procedure validation		5-3
measurement result	2.9	2.1-3
measurement standard	5.1	2.5-1

	VIM3 [*]	Concept
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measuring system	3.2	2.1-13
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metrological compatibility of measurement results	2.47	5-6
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metrological traceability	2.41	1.1-2
metrological traceability chain	2.42	2.3-2
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primary calibrator		3.1-2
primary reference measurement procedure	2.8	3.2-2
primary measurement standard	5.4	2.5-2
quantity	1.1	2.1-2

	VIM3 [*]	Concept
quantity equation	1.22	2.1
quantity value	1.19	2.1-5
recovered quantity ratio		2.10-4
reference material	5.13	3.1-1
reference measurement procedure	2.7	3.2-1
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secondary reference measurement procedure		3.2-3
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validation	2.45	5-2
validation of a measurement result		5-4
verification	2.44	5-1
working measurement standard	5.7	2.5-5

[*] Absence of a number indicates a definition from another source or proposed within this document.